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53rd Child Neurology Society Annual Meeting

Presented at

Marriott Marquis San Diego Marina

San Diego, California

November 11 – 14, 2024

CME Joint Sponsorship Provided by Minnesota Medical Association and the Child Neurology Society

AMERICAN NEUROLOGICAL ASSOCIATION
INNOVATORS IN DISCOVERY, EDUCATION, AND CARE

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Annals of Neurology

AN OFFICIAL JOURNAL OF THE AMERICAN NEUROLOGICAL ASSOCIATION AND THE CHILD NEUROLOGICAL SOCIETY

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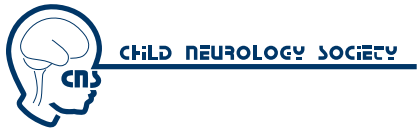
November 11-14, 2024



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Sonia Partap 2020-2022
Sucheta Joshi 2021-2023
Janet Soul 2021-2023
Diana Cejas 2022-
Alison Christy 2022-

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2025
October 8-11
Charlotte, North Carolina

2024
November 11-14
San Diego, California

2023
October 4-7
Vancouver, BC Canada

2022
October 12-15
Cincinnati, Ohio

2021
Boston, Massachusetts

2020
San Diego, California
The Joint 16th ICNA Congress
& 49th Annual CNS Meeting
Together • Apart Virtual

2019
Charlotte, North Carolina

2018
Chicago, Illinois

2017
Kansas City, Missouri

2016
Vancouver, British Columbia, Canada

2015
Washington, DC

2014
Columbus, Ohio

2013
Austin, Texas

2012
Huntington Beach, California

2011
Savannah, Georgia

2010
Providence, Rhode Island

2009
Louisville, Kentucky

2008
Santa Clara, California

2007
Quebec City, PQ, Canada

2006
Pittsburgh, Pennsylvania

2005
Los Angeles, California

2004
Ottawa, Ontario, Canada

2003
Miami Beach, Florida

2002
Washington, DC

2001
Victoria, British Columbia, Canada

2000
St. Louis, Missouri

1999
Nashville, Tennessee

1998
Montreal, Quebec, Canada

1997
Phoenix, Arizona

1996
Minneapolis, Minnesota

1995
Baltimore, Maryland

1994
San Francisco, California

1993
Orlando, Florida

1992
New Orleans, Louisiana

1991
Portland, Oregon

1990
Atlanta, Georgia

1989
San Antonio, Texas

1988
Halifax, Nova Scotia, Canada

1987
San Diego, California

1986
Boston, Massachusetts

1985
Memphis, Tennessee

1984
Phoenix, Arizona

1983
Williamsburg, Virginia

1982
Salt Lake City, Utah

1981
Minneapolis, Minnesota

1980
Savannah, Georgia

1979
Hanover, New Hampshire

1978
Keystone, Colorado

1977
Charlottesville, Virginia

1976
Monterey, California

1975
Hamilton, Ontario, Canada

1974
Madison, Wisconsin

1973
Nashville, Tennessee

1972
Ann Arbor, Michigan

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2024
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St. Louis, MO

2023
Phillip L. Pearl
Boston, MA

2022
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Chicago, IL

2021
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Rochester, NY

2020
Kenneth J. Mack
Rochester, MN

2019
James F. Bale, Jr.
Salt Lake City, UT

2018
Bernard L. Maria
Morristown, NJ

2017
Nina F. Schor
Rochester, NY

2016
Harvey Singer
Baltimore

2015
E. Steve Roach
Columbus, OH

2014
Michael Shevell
Montreal

2013
John Bodensteiner
Rochester, MN

2012
Ann Tilton
New Orleans, LA

2011
Deborah Hirtz
Bethesda, MD

2010
Sakkubai Naidu
Baltimore, MD

2009
Peter Camfield
Halifax, NS, Canada

2008
Stephen Ashwal
Loma Linda, CA

2007
Robert S. Rust
Charlottesville, VA

2006
Michael Painter
Pittsburgh, PA

2005
Alan Percy
Birmingham, AL

2004
John Freeman
Baltimore, MD

2003
Michael E. Cohen
Buffalo, NY

2002
Peter H. Berman
Philadelphia, PA

2001
Charles Barlow
Boston, MA

2000
Arthur Prensky
St. Louis, MO

1999
Marvin Fishman
Houston TX

1998
N. Paul Rosman
Boston, MA

1997
Gerald Fenichel
Nashville, TN

1996
William Bell
Iowa City, IA

1995
Salvatore DiMauro
New York, NY

1994
Hugo Moser
Baltimore, MD

1993
Bengt D. Hagberg
Goteborg, Sweden

1992
Darryl C. De Vivo
New York, NY

1991
Karin B. Nelson
Bethesda, MD

1990
Joseph J. Volpw
Boston, MA

1989
Manuel Gomez
Rochester, NY

1988
Bruce Berg
San Francisco, CA

1987
Isabelle Rapin
Bronx, NY

1986
Jean Aicardi
Paris, France

1985
RaymondD.Adams
Boston, MA

1984
Peter Huttenlocher
Chicago, IL

1983
Betty Q. Banker
Cleveland, OH

1982
Patrick F. Bray
Salt Lake City, UT

1981
Kenneth F.Swaiman
Minneapolis, MN

1980
John H. Menkes
Beverly Hills, CA

1979
Paul I. Yakovlev
Boston, MA

1978
Philip R. Dodge
St. Louis, MO

1977
David B. Clark
Lexington, KY

1976
Sidney Carter
New York, NY

1975
Randolph K. Byers
Boston, MA

1974
Douglas Buchanan
Chicago, IL

Bernard Sachs Award Recipients

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Elizabeth Engle
Boston, MA

2023
Amy R. Brooks-Kayal
Sacramento, CA

2022
Steven Paul Miller
Vancouver, BC, Canada

2021
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2020
Joseph Gleeson
San Diego, CA

2019
Scott Pomeroy
Boston, MA

2018
William B. Dobyns
Seattle, WA

2017
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Bronx, NY

2016
Harvey Sarnat
Calgary, AB, Canada

2015
Harry T. Chugani
Detroit, MI

2014
Gabrielle deVeber
Toronto, ON, Canada

2013
Tallie Z. Baram
Irvine, CA

2012
Roger Packer
Washington, DC

2011
Laura Ment
New Haven, CT

2010
Thomas Jessell
New York, NY

2009
Gregory Holmes
Lebanon, NH

2008
Michael Johnston
Baltimore, MD

2007
Frederick Andermann
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2003
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Huda Zoghbi
Houston, TX

2000
Joseph Volpe
Boston, MA

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1998
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Rochester, NY

1997
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Baltimore, MD

1996
Verne S. Caviness
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1995
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Boston, MA

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1993
C. Thomas Caskey
Houston, TX

1992
Louis M. Kunkel
Boston, MA

1991
Marcus E. Raichle
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1990
Roscoe O. Brady
Bethesda, MD

1989
Salvatore DiMauro
New York, NY

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London

1987
Hugo Moser
Baltimore, MD

1986
Louis Sokoloff
Bethesda, MD

1985
Patricia Goldman-Rakic
New Haven, CT

1984
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1983
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Dallas, TX

1982
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1978
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1977
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2023
Siddharth Srivastava
Boston, MA

2022
Bhooma Aravamuthan
St. Louis, MO

2021
Monica Lemmon
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2020
Hsiao-Tuan Chao
Houston, TX

2019
Louis Dang
Ann Arbor, MI

2018
Christopher Elitt
Boston, MA

2017
Audrey C. Brumback
Austin, TX

2016
Diana Bharucha-Goebel
Bethesda, MD

2015
Jimmy Holder, Jr.
Houston, TX

2014
Christopher Smyser
St. Louis, MO

2013
Peter Tsai
Boston, MA

2012
Yoon Jae-Cho
Stanford, CA

2011
James Dowling
Ann Arbor, MI

2010
Stephen Maricich
Cleveland, OH

2009
Jeffrey Neul
Houston, TX

2008
Laura Jansen
Seattle, WA

2007
Mirjana Maletic-Savatic
Stony Brook, NY

2006
Elliott Sherr
San Francisco, CA

2005
Mustafa Sahin
Boston, MA

2004
Terri Inder
Melbourne, Australia

2003
Bradley Schlaggar
St. Louis, MO

2002
Nigel Bamford
New York, NY

2001
Daniel J. Bonthius
Iowa City, IA

2000
Stephen Back
Portland, OR

1999
Amy Brooks-Kayal
Philadelphia, PA

1998
Joseph Gleeson
Boston, MA

1997
William A. Weiss
San Francisco, CA

1996
Michael Rivkin
Boston, MA

1995
Adre J. du Plessis
Boston, MA

1994
Mia MacCollin
Boston, MA

1993
Jeffrey J. Neil
St. Louis, MO

1992
Kelvin A. Yamada
St. Louis, MO

1991
Kenneth J. Mack
Madison, WI

1990
Evan Y. Snyder
Boston, MA

Harris Gelbard
Rochester, NY

1989
Scott L. Pomeroy
St. Louis, MO

1988
Huda Zoghbi
Houston, TX

1987
Vinodh Narayanan
Pittsburgh, PA

1986
Faye S. Silverstein
Ann Arbor, MI

1985
Richard J. Konkol
Milwaukee, WI

1983
Michael Pranzatelli
Washington, DC

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Donna M. Ferriero
San Francisco, CA

Roy D. Elterman
Rancho Palos Verdes, CA

2023
Robert S. Greenwood
Chapel Hill, NC

James John Riviello, Jr.
Houston, TX

Radha Giridharan
Brooklyn, NY

2022
Jeff Buchhalter
Calgary, AB, Canada

Roger Larson
St. Paul, MN

Michael Noetzel
St. Louis, MO

2021
Robert Baumann
Lexington, KY

Sidney Gospe, Jr
Seattle, WA

2019
Carol Camfield
Halifax, NS, Canada

W. Edwin Dodson
St. Louis, MO

2018
Gerald Erenberg
Cleveland, OH

William Logan
Toronto, ON, Canada

Alfred Spiro
Bronx, NY

2017
Abe Chutorian
New York, NY

W. Donald Shields
Los Angeles, CA

2016
Kalpathy Krishnamoorthy
Boston, MA

Doris Trauner
La Jolla, CA

2015
Pat Crumrine
Pittsburgh, PA

Suresh Kotagal
Rochester, MN

2014
G. Robert De Long
Durham, NC

2013
Arthur Rose
Brooklyn, NY

A. David Rothner
Cleveland, OH

2012
Bhuwan Garg
Indianapolis, IN

M. Richard Koenigsberger
Demarest, NJ

2011
Warren Grover
Philadelphia, PA

2010
Russell Snyder
Albuquerque, NM

2009
Mary Anne Guggenheim
Helena, MT

G Dean Timmons
Akron, OH

2008
Cesare Lombroso
Boston, MA

Niels Lowe
Tenafly, NJ

2007
William Kennedy
Watertown, ME

Gordon Watters
Montreal, QC, Canada

2006
Raymond Chun
Madison, WI

Barry Russman
Portland, OR

2005
Robert Eiben
Cleveland, OH

Arnold Gold
New York, NY

2004
Jean Holowach Thurston
St. Louis, MO

Arnold P. Gold Foundation Humanism in Medicine Award Recipients

2024
Dave F. Clarke
Austin, TX

2023
Yasmin Khakoo
New York, NY

2022
Jorge Vidaurre
Columbus, OH

2021
Mary Zupanc
Irvine, CA

2019
H. Terry Hutchison
Fresno, CA

2018
Audrey Foster-Barber
San Francisco, CA

2017
David Coulter
Boston, MA

2016
Oscar Papazian
Miami, FL

2015
Robert Zeller
Houston, TX

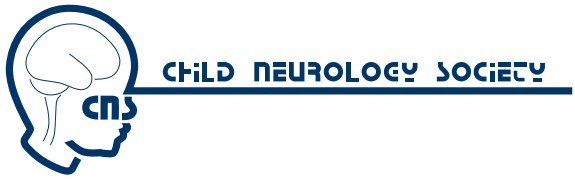
2014
Kenton Holden
Mt. Pleasant, SC

2013
Douglas Postels
East Lansing, MI

2012
Marvin Fishman
Houston, TX

2011
Shaul Harel
Tel Aviv, Israel

2010
Ruth Ness
New York, NY



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2023
William Davis Gaillard
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2022
Michael Shevell
Montreal, QC, Canada

2021
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Chicago, IL

Bernard D'Souza International Fellowship Award Recipients

2024
Bolivar Quito-Betancourt
Cuenca, Ecuador

Thembi Katangwe-Chirwa
South Africa

2023
Prem Chand
Karachi, Sindh, Pakistan

Priyanka Madaan
Faridabad, Haryana, India

2022
Robert K. Sebunya
Kampala, Uganda

Paulina C. Tejada
Santiago, Chile

2021
Chaw Su Hlaing
Myanmar, Asia

Alireza Tavasoli
Iran

2019
Nicolás Garófalo Gómez
Havana, Cuba

Jitendra Kumar Sahu
Chandigarh, India

2018
Suvasini Sharma
New Delhi, India

2017
Charles Hammond
Kumasi, Ghana

Aye Mya Min Aye
Yangon, Myanmar

2016
Arushi Gahlot Saini
Chandigarh, India

Tipu Sultan
Lahore, Pakistan

2015
Edward Kija
Tanzania

2014
Jithangi Wanigasinghe
Dehiwela, Sri Lanka

2013
Samson Gwer
Nairobi, Kenya

2012
Inga Talvik
Tartu, Estonia

2011
Kyaw Linn
Maynmar

2010
Parayil S. Bindu
Bangalor, India

2009
Uduak Mayen Offiong
Abuja, Nigeria

2008
Ikeolu Lagunju
Ibadan, Nigeria

2007
David E. Kombo
Dars Es Salaam, Tanzania

2006
Gia Melikoshvili
Tbilisi, Georgia

2005
Lusine Kirakosyan
Yerevan, Armenia

2004
Natalia A. Yermolenko
Voronezh, Russia

2003
David Chkhartishvili
Tbilisi, Georgia

2002
Vedrana Milic Rasic
Belgrade, Serbia

2001
Dimitrios Zafeiriou
Thessalonikki, Greece

2000
Brahim Tabarki-Melaiki
Brussels, Belgium

1999
Magda L. Nunes
Porto Alegre, Brazil

1998
Ana Keleme
Novi Sad, Yugoslavia

1997
Aleksandra Djukic
Belgrade, Yugoslavia

1996
Shan Wei Song
Beijing, China

1995
Nina Barisic
Zagreb, Croatia

1994
Lai Choo Ong
Kuala Lampur, Malaysia

1993
Anu Soot
Tartu, Estonia

1992
Qin Jiong
Beijing, China

1991
Sergi A. Antoniuk
Curitiba, Brazil

1990
Najoua Miladi
Tunis, Tunisia

1989
Meral Ozmen
Istanbul, Turkey

Taeun Chang Outstanding Junior Member Award

2024
Ashley M. Bach
Children's Hospital of Philadelphia

Eman Hamed
Jersey Shore University Medical Center

Austin Layton
University of California – San Diego

Seva Khambadkone
Doernbecher Children's Hospital

2023
Claudia Gambrah-Lyles
Children's Hospital of Philadelphia

Mary Rolfes
University of California

Alexandra Santana Almansa
Boston Children's Hospital

Alexander J. Sandweiss
Texas Children's Hospital

2022
Mekka Garcia
NYU Langone Health

Laura Gilbert
Washington University in St. Louis

Riley Kessler
Children's Hospital of Philadelphia

Ezgi Saylam
Nationwide Children's Hospital

2021
Rhandi Christensen
University of Toronto

Darius Ebrahimi-Fakhari
Boston Children's Hospital

Laura Gilbert
Washington University in St. Louis

Hannah Wellman
University of Colorado

2020
Natalie K. Katz
Children's Mercy Hospital

Travis Larsh
Children's Hospital Cleveland Clinic

Kshama Ojha
University of Louisville

Sonal Sharma
Children's Mercy Hospital & Clinics

2019
Lauren Chamberlain
Duke University Medical Center

Darius Ebrahimi-Fakhari
Boston Children's Hospital

Aram Kim
Children's Hospital of Pittsburgh

Youssef A. Kousa
Children's Hospital National Medical Center

2018
Adrienne Bruce
Cincinnati Children's Hospital Medical Center

Sara Fridinger
Children's Hospital of Philadelphia

Melissa Hutchinson
Children's Hospital of Philadelphia

Jeffrey A. Strelzik
Children's National Health System

Elizabeth Troy
University of Colorado

2017
Ka Ye Clara Chan
Loma Linda University Children's Hospital

Hsaio-Tuan Chao
Baylor College of Medicine

Rachel Goldstein Hirschberg
Boston Children's Hospital

Carla Watson
Children's Hospital of Michigan

2016
Sonika Agarwal
Baylor College of Medicine

Darius Ebrahimi-Fakhari
Boston Children's Hospital

Juliane Gust
Seattle Children's Hospital

Manisha Malik
Emory University

2015
Robert Blake
Cincinnati Children's Hospital Medical Center

Dana Marafie
Texas Children's Hospital

Davut Pehlivan
Texas Children's Hospital

Siddharth Srivastava
Kennedy Krieger Institute

2014
Jonathan Kurz
Children's National Medical Center

Neggy Rismanchi
University of California San Diego

Siddharth Srivastava
Kennedy Krieger Institute

Kavita Thakkar
Pittsburgh Children's Hospital

Taeun Chang Outstanding Junior Member Award | continued

2013
Anuja Jindal
Pittsburgh Children's Hospital

Archana Patel
Boston Children's Hospital

Pilar Pichon
Loma Linda University

Mark Schomer
Boston Children's Hospital

Mitchell Williams
Children's Hospital of Michigan

2012
Partha Ghosh
Clevland Clinic Foundation

J.J. Gold
University of California San Diego

Gayatri Mainali
Cleveland Clinic Foundation

Christopher B. Oakley
Johns Hopkins Medical Institute

2011
Partha Ghosh
Cleveland Clinic Foundation

Andrea Pardo
Cincinnati Children's Hospital Medical Center

Thitiwan Simasathien
University of Alabama-Birmingham

Syndi Seinfeld
Virginia Commonwealth University

2010
Dawn Gano
University of British Columbia

Radhika Dhamija
Mayo Clinic

Patricia Musolino
Massachusetts General Hospital

Thitiwan Simasathien
University of Alabama-Birmingham

2009
Bennett Gertz
Children's National Medical Center

Ryan Lee
Kennedy Krieger Institute

John Mytinger
University of Virginia

Brandon Zielinski
University of California San Francisco

2008
Gregory Aaen
Loma Linda University

Robert Avery
Children's Hospital of Philadelphia

Joseph Scafidi
Children's National Medical Center

Karen Powers
Virginia Commonwealth University

2007
Keith Abe
Stanford University Medical Center

Tarannum Lateef
Children's National Medical Center

Joseph Scafidi
Children's National Medical Center

Marie-Pierre Thibeault-Eybalin
McGill University

2006
Nicholas Abend
Children's Hospital of Philadelphia

Lori Billinghurst
University of Alberta

Holly Dudley-Harrell
Children's Hospital of Cincinnati

Jena Khera
The Cleveland Clinic

2005
William Benko
Children's National Medical Center

Alexander Bassuk
Children's Memorial Hospital Chicago

Josh Bonkowsky
University of Utah Medical Center

Robert Safier
Children's Hospital of Pittsburgh

Renée Shellhaas
Children's Hospital of Philadelphia

2004
Ignacio Valencia
St. Christopher's Hospital

Brannon Morris
Mayo Clinic

Haim Bassan
Boston Children's Hospital

William Benko
Children's National Medical Center

2003
Taeun Chang
Children's National Medical Center

Yoshimi Sogawa
Schneider Children's Hospital

Ignacio Valencia
St. Christopher's Hospital

Adeline Vanderver
Children's National Medical Center

2002
Taeun Chang
Children's National Medical Center

Mirjana Maletic-Savatic
SUNY Stony Brook

Lauren Plawner
Stanford University Medical Center

Michael Seyffert
University of Washington Medical Center

Taeun Chang Outstanding Junior Member Award | continued

2001
Maria Acosta
Children's National Medical Center

Randa Jarrar
Mayo Clinic

Steven Miller
UC San Francisco

Jayne Ness
Children's Hospital of Alabama

2000
Sucheta Joshi
Stanford University Medical Center

Lauren Plawner
Stanford University Medical Center

Monique Ryan
Boston Children's Hospital

Mustafa Sahin
Boston Children's Hospital

1999
June Caruso
Rhode Island Children's Hospital

Debra Holder
Texas Children's Hospital

Carolyn Menache
Boston Children's Hospital

1998
June Caruso
Rhode Island Children's Hospital

Andrea Gropman
Children's National Medical Center

Alyssa Reddy
Children's Hospital of Alabama

Janet Soul
Boston Children's Hospital

1997
Gyula Acsadi
Children's Hospital of Detroit

Ann Bergin
Johns Hopkins University

Edwin Demeritte
Children's Hospital of Detroit

Sanford Shu
Loma Linda University

1996
Gyula Acsadi
Children's Hospital of Detroit

Joseph Gleeson
Boston Children's Hospital

Andrea Gropman
Children's National Medical Center

Mary Sutton
Boston Children's Hospital

CHILD NEUROLOGY SOCIETY
CNS

Taeun Chang Outstanding Junior Member Post-Graduate Award Recipients

2024
Stephen Chrzanowski
University of Massachusetts Chan Medical School

Saba Jafarpour
Children's Hospital of Los Angeles

2023
Mliena Andzelm
Boston Children's Hospital

Jennifer Harmon
Atrium Health Wake Forest Baptist Medical Center

2022
Travis Larsh
Cincinnati Children's Hospital Medical Center

Avantika Singh
Boston Children's Hospital

2021
Eric M. Chin
Kennedy Krieger Institute,

Thiviya Selvanathan
The Hospital for Sick Children

2019
Giulia Beneditti
Seattle Children's Hospital

2018
Bhooma Aravamuthan
Boston Children's Hospital

Elana Pinchefsky
The Hospital for Sick Children

M. Richard Koenigsberger Memorial Scholarship Recipients

Awarded in memory of M. Richard Koenigsberger, MD to the CNS Junior Member submitting the best abstract in genetics, neonatal neurology, HIV or metabolic disorders.

2024
Whitney Fitts
Children's Hospital of Philadelphia

2023
Hui Li
University of Wisconsin Hospitals and Clinics

2022
Stephen Chrzanowski
Boston Children's Hospital

2021
Jennifer Keene
Washington University in St Louis

2020
Katelyn Bricker
North Carolina Memorial Hospital

2019
David Ritter
Cincinnati Children's Hospital Medical Center

2018
Tayyba Anwar
Children's National Medical Center

2017
Davut Pehlivan
Baylor College of Medicine

2016
Ann McCarthy
Children's Hospital Philadelphia

2015
Vincent Carson
Pittsburg Children's Hospital

2014
Joshua Bear
University of California San Francisco

2013
Louis Dang
Children's Hospital of Michigan

American Academy of Pediatrics Section on Neurology Travel Grant Recipients

2024
Miles Fisher
Vanderbilt Child Neurology

2023
Miranda Creasey
Virginia Commonwealth University

2022
Alexis Karlin
Children's Hospital of Philadelphia

2019
E. Justine Record
Children's Hospital National Medical Center

2018
Kerri Neville
Michigan Medicine

2017
Audie Espinoza
University of Utah

2016
Sharoon Qaiser
University of Kentucky

2015
Jennifer Jaskiewicz
Walter Reed National Military Medical Center

Training Director Award Recipients

2024
Nancy Bass
Milwaukee, WI

2023
Rana R. Said
Dallas, TX

2022
Timothy Edward Lotze
Houston, TX

2021
Miya Asato
Pittsburgh, PA

2019
Karen Ballaban-Gil
Bronx, NY

2018
Bruce K. Shapiro
Baltimore, MD

2017
Sidney M. Gospe Jr.
Seattle, WA

2016
David K. Urion
Boston, MA

2015
Robert Rust
Charlottesville, VA

2014
Steve Leber
Ann Arbor, MI

2013
Harvey Singer
Baltimore, MD

Bhuwan Garg High School Student Neuroscience Research Prize Recipients

2024
Allison Duh
Burlingame, CA

2023
Rania Sophia Lateef
Manassas, VA

2022
Aliya Fisher
New York, NY

2021
Meagan Ryan
Ossining, NY

2020
Pratik Vangal
Portland, OR

2019
Shan Lateef
Manassas, VA

2018
Amy Shteyman
Great Neck, NY

2017
Lauren Singer
Scarsdale, NY

2016
Ryan Infante
Armonk, NY

2015
Amrita Mohanty
Woodbury, MN

2014
Laura Mariah Herman
Ft. Lauderdale, FL

2013
Anna Thomas
San Jose, CA

2012
Vincent Shieh
Bronx, NY

2011
Spencer Chan
Forest Hills, NY

2010
Pragya Kakani
Jericho, NY

2009
Inar Zhang
Mercer Island, WA

2008
Lauren Lisann
Dix Hills, NY

2007
David Shiovitz
Briarcliff Manor, NY

2006
Shoshana Tell
Coral Springs, FL

2005
Max Christie
Briarcliff Manor, NY

2004
Debashish Zircar
Bronx, NY

2003
Henry Marr
Alhambra, CA

2002
Corinna Zygourakis
Houston, TX

2001
Melanie Napier
Laurelton, NY

2000
Rishikesh Dalal
Lenexa, KS

1999
Nihar Gupta
New York, NY

1998
Karla Malloy
Richmond, VA

ACNN
ASSOCIATION OF CHILD NEUROLOGY NURSES

Claire Chee Award for Excellence in Child Neurology Nursing Award Recipients

2024
Keri Ramsey
Phoenix, AZ

2023
Colleen Gagnon
Boston, MA

2022
Tristen Dinkel
Aurora, CO

2021
Toni Kavanagh
Pelham, New York

2020
Jennifer McCrave
Boston, MA

2019
Courtney Wellman
Kansas City, MO

2018
Cheryl Cahill
Boston, MA

2017
Jennifer Boyd
Toronto, ON, Canada

2016
Kathryn O'Hara
Richmond, VA

2015
Nancy Elling
Washington, DC

2014
Jo Ellen Lee
Columbus, OH

2013
Cheryl Fischer
New York, NY

2012
Jane Lane
Birmingham, AL

2011
Yolanda Harris
Birmingham, AL

2010
Julie Sprague-McRae
Fremont, CA

2009
Christine O'Dell
Bronx, NY

2008
Irene M. Elliott
Toronto, ON

2007
Elizabeth Tate
Springfield, IL

2006
Amy Vierhile
Rochester, NY

2004
Jane Meyer
Cottage Grove, WI

2003
Elizabeth F. Hobdell
Chester Brook, PA

2002
Rhonda Roell Werner
New Berlin, WI

2001
Claire Chee
Philadelphia, PA

2000
Jan Mims
Minneapolis, MN

Nurse Practitioner Award for Excellence in Child Neurology Nursing Award Recipients

2024
Deanna Duggan
Waco, TX

2023
Rasha Srouji
Boston, MA

2022
Nancy A. Auer
Columbus, OH

2021
Patricia McGoldrick
Pelham, NY

2020
Dianne Kulasa-Luke
Akron, OH

2019
Erin Fecske
Kansas City, MO

2018
Scott B. Turner
Birmingham, AL

2017
Rebecca Schultz
Houston, TX

2016
Sue Yudovin
Los Angeles, CA

2015
Regina Laine
Boston, MA

53rd Child Neurology Society Annual Meeting

Schedule at a Glance - Wiley 2024

Monday, November 11

Start	End	Meeting/Session/Event
7:30 AM	5:00 PM	The 9th Annual John M. "Jack" Pellock Resident Seminar on Epilepsy
8:00 AM	11:00 AM	Symposium I: CNF Symposium: Caring for Children with Medical Complexity
8:00 AM	2:00 PM	Program Coordinators of Child Neurology (PCCN)
11:30 AM	2:00 PM	Kenneth F. Swaiman CNS Legacy Luncheon
1:45 PM	5:45 PM	Child Neurology/NDD Educator Symposium: Child Neurology/ NDD Educator Updates and Hot Topics in Child Neurology/ NDD MedEd (formerly PECN)
2:00 PM	7:00 PM	Exhibits and Poster Review
3:00 PM	4:00 PM	Workshop #1: FDA 101: The Lifecycle of Drug Development in Pediatric Neurology
4:15 PM	5:15 PM	Workshop #2: How YOU Can Find NIH Funding Opportunities (On Your Phone)!
5:15 PM	6:00 PM	SIGs
6:00 PM	7:30 PM	Welcome Reception
8:00 PM	10:00 PM	Movement Disorders Video Rounds
8:00 PM	10:00 PM	Industry-Sponsored Event - Satellite Symposium: Test Your Expertise in Rett Syndrome: A Live Medical Simulation on Diagnosis and Management

Tuesday, November 12

Start	End	Meeting/Session/Event
8:00 AM	10:15 AM	Symposium II: Presidential Symposium: Childhood Neuromuscular Disorders: A New Landscape and a Vision for the Future
8:00 AM	4:15 PM	Association of Child Neurology Nurses (ACNN)
8:00 AM	4:00 PM	Program Coordinators of Child Neurology (PCCN)
10:30 AM	11:00 AM	Martha Bridge Denckla Award Lecture: Shafali Jeste, MD
11:15 AM	12:15 PM	Workshop #3: Diagnostic Challenge: Mimickers of Neuroinflammatory Diseases
11:15 AM	12:15 PM	Workshop #4: Clinical Trial Readiness for Rare Neurological Diseases
11:15 AM	12:15 PM	Workshop #5: Reviewing Manuscripts: What, When, Why, and How
11:15 AM	12:15 PM	SIGs
11:30 AM	7:00 PM	Exhibits and Poster Review
12:00 PM	1:00 PM	Industry-Sponsored Event - Product Theater: Advancements in Rett Syndrome (RTT) Care
12:15 PM	1:45 PM	Dedicated Exhibit Time
12:30 PM	1:45 PM	Guided Abstract Tour #1
12:00 PM	2:00 PM	Industry-Sponsored Event - Satellite Symposium: Patient, Provider, and Caregiver Connection: Pediatric Myasthenia Gravis - Current Treatment and Emerging Concepts
2:00 PM	3:15 PM	Seminar 1: Genetic Testing: Essential Skills for Daily Practice
2:00 PM	3:15 PM	Seminar 2: The Clinician-Educator Path for Child Neurologists
2:00 PM	3:15 PM	Seminar 3: Clinical Registry Implementation: The How-To and the Value
3:30 PM	4:45 PM	Seminar 4: Caring for a Person with Cerebral Palsy from Infancy to Adulthood
3:30 PM	4:45 PM	Seminar: 5: Harnessing Technology for Career Growth and Development

3:30 PM	4:45 PM	Seminar 6: Bridging Academia and Industry to Advance Precision Medicine
5:00 PM	6:30 PM	Wine and Cheese Reception
5:00 PM	7:00 PM	Industry-Sponsored Event - Satellite Symposium: Spotlight on Infantile Spasms: Diagnosis, Treatment, and Beyond
5:30 PM	7:00 PM	Guided Abstract Tour #2

Wednesday, November 13

Start	End	Meeting/Session/Event
8:00 AM	4:00 PM	Program Coordinators of Child Neurology (PCCN)
8:00 AM	3:15 PM	Association of Child Neurology Nurses (ACNN)
8:00 AM	8:15 AM	CNS/CNF, ACNN and PERF® Awards
8:15 AM	8:45 AM	Philip R. Dodge Young Investigator Award Fiona M. Baumer, MD, MS
8:45 AM	9:30 AM	Bernard Sachs Award Lecture: Elizabeth Engle, MD
10:00 AM	11:15 AM	Seminar 7: The Effect of Global Socio-Cultural Factors on Child Neurology Care
10:00 AM	11:15 AM	Seminar 8: Addressing Gender Disparities in Academic Child Neurology
10:00 AM	11:15 AM	Seminar 9: Cerebellar Contributions to Neurodevelopment
11:30 AM	12:30 PM	Industry-Sponsored Event - Product Theater: Finding More Answers with Genetic Testing: Maximizing the Diagnostic Yield of Exome Sequencing
11:30 AM	1:30 PM	Industry-Sponsored Event - Satellite Symposium: Enabling Pediatric Neurogenetics: Answers to 5 Common Questions
12:30 PM	1:45 PM	Seminar 10: Restoring Function: Management of Functional Neurologic Disorders
12:30 PM	1:45 PM	Seminar 11: View from The Top: Hiring, Salary, and Promotion in Academia
12:30 PM	1:45 PM	Seminar 12: Untangling the Impact of Social Stress on Early-life Brain Injury
2:15 PM	4:00 PM	Platform Sessions 1, 2, and 3
4:30 PM	5:20 PM	Junior Member/Early Career Forum and Panel Discussions
5:00 PM	6:00 PM	Industry-Sponsored Event - Product Theater: Introducing Duvyzat™ (Givinostat)
5:00 PM	7:00 PM	Industry-Sponsored Event - Satellite Symposium: The Evolving Landscape of Dravet and Lennox-Gastaut Syndromes: A Focus on Early Diagnosis, Rational Polytherapy, and Non-seizure Symptoms
6:00 PM	7:00 PM	SIGs
7:00 PM	9:00 PM	Closing Gala

Thursday, November 14

Start	End	Meeting/Session/Event
8:00 AM	8:45 AM	Hower Award Lecture: Renée A. Shellhaas, MD, MS
8:00 AM	11:00 AM	Association of Child Neurology Nurses (ACNN)
9:00 AM	12:00 PM	Symposium III: Year in Review
12:15 PM	4:15 PM	Biomedical Writing Workshop
12:15 PM	4:15 PM	CNS Clinical Research Workshop: Data Quality and Analysis

PLATFORM PRESENTATIONS

PLATFORM SESSION 1: Wednesday, November 13 (2:15 PM – 4:00 PM)

PL1-1. Safety and Clinical Effects of STK-001, an Antisense Oligonucleotide (ASO), in Children and Adolescents with Dravet Syndrome: Phase 1/2a End-of-Study and Open-label Extension (OLE) Data

Sullivan J (San Francisco, CA), Cross H, Laux L, Perry S, Desurkar A, Schreiber J, Roberts C, Knupp K, Wheless J, Wirrell E, Wang F, Parkerson K, Ticho B

OBJECTIVE: DS is a severe and progressive genetic epilepsy that is typically caused by spontaneous, heterozygous loss-of-function SCN1A gene mutations, which encode the Nav1.1 protein. STK-001 is an investigational ASO that exploits modulation of pre-mRNA to upregulate functional brain Nav1.1 expression by leveraging the wild-type copy of SCN1A to restore physiological protein levels.
METHODS: Phase 1/2a studies, MONARCH (US) and ADMIRAL (UK), with the SWALLOWTAIL (US) and LONGWING (UK), assessed safety, tolerability, plasma pharmacokinetics, CSF exposure, and clinical effect of intrathecally (IT) administered STK-001 in patients with DS aged 2-18y. Patients have disease onset <12 months old with recurrent seizures and confirmed SCN1A variant. Adverse Events were monitored continuously.
RESULTS: 81 patients received ≥1 dose of STK-001 (10-70mg/dose). Patients were highly refractory to standard treatments with ongoing convulsive seizures despite 85% taking ≥3 ASMs and 54% taking ≥4 ASMs. Patients treated with ≥1 initial dose of 70mg demonstrated substantial and sustained reductions in convulsive seizure frequency. Patients receiving ongoing OLE treatment (30 or 45mg/4 months) demonstrated durable reductions in convulsive seizure frequency and clinically meaningful improvements in multiple measures of cognition and behavior through month 12. Single and multiple doses of up to 70 mg STK-001 was generally well-tolerated across these studies.
CONCLUSIONS: STK-001 has the potential to be the first disease-modifying therapy to address the genetic cause of Dravet syndrome.
KEYWORDS: Epilepsy, Neurodevelopmental Disorders

Pl1-2. Delineating the Molecular and Clinical Spectrum of Epilepsy-Dyskinesia Syndromes (The Epilepsy-Dyskinesia Spectrum Study)

Quiroz V (Boston, MA), Kunta A, Srouji R, Tam A, Battaglia N, Yang K, Uraba W B, Mohammad S, Pons R, Ortigoza-Escobar J D, Soliani L, Pinto A, Zea-Vera A, da Silva P, Desai S, Pringsheim T, Iype M, Lim W K, Necpál J N, Stamelou M, Zamani M, Jones H, Perez-Sanchez J, Crosiers D, Unal E, Castilioni C, Ebrahimi-Fakhari D

OBJECTIVE: To understand the spectrum and association of epilepsy-dyskinesia syndromes on a clinical and molecular level.
METHODS: A cross-sectional multicenter study administered through the Movement Disorders Society Pediatric Movement Disorders Special Interest Group. A multistep consensus review defined 102 genes associated with childhood-onset movement disorders and epilepsy. A standardized survey was used to collect clinical, molecular and neuroimaging data.
RESULTS: A total of 204 cases from 18 countries were included. Median age at last follow-up was 10.2± 7.8 (SD) years. The most prevalent genes were GNAO1 (14.7%), MECP2 (6.8%), PRRT2 (6.3%), and ATP1A3, CACNA1A, FOXG1, and SLC2A1 (4.9% each). Most patients were diagnosed in early childhood (1-3 years, 35.9%). Epilepsy was present in 66.1%, with peak onset in infancy (34.8%). The most common movement disorders were dystonia (40.6%), ataxia (14.2%), and chorea (12.7%). 55.3% of cases presented with more than one phenomenology, with dystonia/chorea (26.5%) being the most common combination. 42.3% presented with a Global Motor Function Classification Score of IV or V, indicating significant motor impairment. Global developmental delay or intellectual disability was observed in 86.2%. Neuroimaging abnormalities were observed in 39.7%, with cerebral atrophy observed on brain MRI or head CT being most common (16.7%).
CONCLUSIONS: Our findings confirm the phenotypic pleiotropy and clinical heterogeneity of epilepsy-dyskinesia spectrum disorders, reflecting the crucial role of many genes in brain development. This has implications for counseling, treatment and research aimed at creating clinical trial readiness.
KEYWORDS: Movement Disorders, Epilepsy, Neurogenetics

PL1-3. Defining the Spectrum of Extrapyramidal Movement Disorders in Childhood-Onset Hereditary Spastic Paraplegia: A Cross-Sectional Analysis of Over 500 Cases

Yang K (Boston, MA), Quiroz V, Tam A, Battaglia N, Schierbaum L, Srouji R, Alecu J, Ebrahimi-Fakhari D

OBJECTIVE: Extrapyramidal movement disorders have been reported in certain forms of hereditary spastic paraplegia (HSP); however, the prevalence, characteristics and natural history remain incompletely understood. The aims of this study are: 1) To define the spectrum of movement disorders in a well-characterized cohort of children and young adults with genetically-confirmed HSP, and 2) To identify gene variants associated with these symptoms.
METHODS: A detailed cross-sectional analysis of 541 patients enrolled in the Registry and Natural History Study for Early Onset Hereditary Spastic Paraplegia (NCT04712812), including a systematic review of clinical, imaging and molecular data, as well as a review of longitudinally acquired videos.

RESULTS: This study identified 41 unique genes associated with HSP. The most frequently observed variants were in AP4B1 (SPG47), AP4M1 (SPG50), SPAST (SPG4), AP4S1 (SPG52) and ZFYVE26 (SPG15). 169 patients (31%) exhibited at least one extrapyramidal movement disorder. Of these, 59 (35%) had two or more movement disorders, the most prevalent being ataxia (12%) and dystonia (11%). Other less common manifestations included postural instability (7%) and brady/hypokinesia (6%). Specifically, ataxia was most frequently reported in patients with HSP-ZFYVE26 (SPG15), while dystonia was most common in children with HSP-SPAST (SPG4) due to de novo variants.

CONCLUSIONS: Movement disorders beyond spasticity are common in childhood-onset HSP. Our findings advance the understanding of the phenotypic spectrum, genotype-phenotype correlations, and natural history of HSP, thereby improving counseling regarding disease progression, providing anticipatory guidance, and informing decisions related to targeted therapeutics. Finally, our extensive video archive serves as an invaluable resource for further research and education.

KEYWORDS: Movement Disorders, Neurogenetics, Neurodevelopmental Disorders

PL1-4. Predictors of Drug-Resistant Epilepsy after Perinatal Stroke

Fisher M R (Nashville, TN), Bolte K, Reddy S, Rodehgier M, Jordan L C

OBJECTIVE: To identify predictors of drug-resistant epilepsy (DRE) in children with a history of perinatal arterial ischemic stroke (PAIS).

METHODS: This single-center retrospective observational study of PAIS and epilepsy utilized ICD-9/10 codes, institutional stroke and epilepsy surgery databases, medical record and neuroimaging review from 2014–2023. DRE was defined as epilepsy not responsive after adequate trials of >2 anti-seizure medications. The pediatric stroke outcome measure (PSOM) was retrospectively scored.

RESULTS: Of 73 children with PAIS, 60% were male, 46 (63%) had epilepsy. DRE was present in 20 (27%), median age at last visit was 10.0 (8.0–17.3) years. In children with DRE, 75% had presumed PAIS while 25% had strokes symptomatic as neonates. Children with DRE had higher (worse) median PSOM=2.5 (IQR 1.0-4.0) across groups: non-DRE median PSOM=2.0, without epilepsy median PSOM=1.0, p<.004, paired comparisons for poorer neurological outcome were not significant (p=0.793).

Hippocampal volume reduction was the strongest predictor of DRE, odds ratio 5.13, 95% CI 1.39-18.94, p=.014 in a multivariable model that included sex, neonatal seizures, and total PSOM. Of 20 with DRE, 13 (65%) underwent surgical intervention for epilepsy. Surgical response was excellent: seizure-free or >90% seizure reduction in 8 (62%): 3 focal resections, 4 functional hemispherectomies, and 1 posterior quadrant disconnection. The remaining 5 children had ≤50% seizure reduction after vagus nerve stimulator placement (4) and focal resection (1).

CONCLUSIONS: Hippocampal volume reduction was the strongest predictor of DRE after PAIS. Epilepsy and DRE were more common in older children. Favorable seizure outcomes were achieved with hemispherectomy or focal resection.

KEYWORDS: Stroke, Neonatal Neurology, Epilepsy

PL1-5. Identifying Predictors and Mechanisms of Response to Comprehensive Behavioral Intervention for Tics: Methods of the TReC Study

Wang S (Minneapolis, MN), Greene D, Zreik S, Reiner G, Friedman J, Baim A, Mungai T, Khang I, Hodapp S, Mueller B, Nelson S, Conelea C

OBJECTIVE: Chronic tics affect 1-3% of youth in the US and are a disabling symptom associated with multiple childhood-onset neuropsychiatric disorders. Comprehensive Behavioral Intervention for Tics (CBIT) is the first-line, gold-standard, manualized treatment focusing on tic management. Despite its demonstrated efficacy, approximately 50% of youth do not fully benefit from CBIT. We present an NIH-funded clinical trial investigating the mechanistic aspects of pediatric CBIT to identify bio-behavioral predictors of treatment response and key elements of effective CBIT delivery.

METHODS: Multimodal measurements will identify predictors of response, therapeutic processes that activate change, and correlates of response. Study hypotheses predict that CBIT relies upon, engages, and strengthens functional connectivity (as measured with resting-state fMRI) within and between brain networks that support top-down control over motor functions.

RESULTS: Youth ages 10-17 years with chronic tics (N = 100) will undergo 8 outpatient, weekly CBIT sessions and pre-, post-, and 3-month follow up assessments. Assessments will include: 1) neural measures of fMRI and EEG, 2) direct-observation behavioral measurement of tics, and 3) psychosocial measures, including assessments of clinical symptoms and patient-centered outcome measures informed by our Patient Advisory Board. CBIT process will be assessed via a novel video-based behavioral coding of CBIT sessions.

CONCLUSIONS: Results will have a downstream clinical impact by informing individualized treatment planning and efforts to streamline and improve CBIT quality. Results will have an upstream impact by identifying novel neural targets for intervention and strategies for improving CBIT outcomes via refinement procedures.

KEYWORDS: Movement Disorders, Experimental Therapeutics

PL1-6. Low Incidence of Seizures in Neonates following Cardiac Surgery with Cardiopulmonary Bypass

Valencia E (Boston, MA), Kielian A, Smith-Parrish M, Staffa S, Kaza A, Nathan M, Nasr V G, Sansevere A

OBJECTIVE: Neonates with congenital heart disease (CHD) are at high risk for seizures following cardiopulmonary bypass (CPB), prompting the American Neurophysiology Society to recommend continuous electroencephalogram

(cEEG). Our institution implemented cEEG as routine post-operative monitoring in all neonates who undergo CPB. We aimed to identify the incidence of post-CPB seizures in neonates.

METHODS: We evaluated all neonates post-CPB at Boston Children's from November 2019-December 2022. cEEG data was collected prospectively and perioperative characteristics retrospectively.

RESULTS: 302 neonates were included. Median age, gestational age, and weight were 4.7 (3.6,7.8) days, 38.9 (37.3,39.3) weeks, and 3.2 (2.7,3.5) kg. 235 (77.3%) were prenatally diagnosed. The most common surgeries were aortic arch repair, Norwood and arterial switch operation. Median CPB, cross clamp, circulatory arrest (CA) and regional perfusion times were 174 (140,218), 107 (78,140;N=97.4%), 4 (2,9;N=43.4%) and 62 (49,80;N=46.4%) minutes. 47 (15.5%) had a genetic disorder/syndrome. Mortality was 4% (N=12). 91% (N=275) underwent cEEG for a median of 40 (33,50) hours. 5 (N=1.82%) had seizures without clinical correlate at a median of 28.5 hours post-CICU arrival. Median CPB and CA times in neonates with seizures were 205 (190,232) and 2 (1.5,2.5;N=2) minutes. 4 had preoperative neuroimaging, one significant for right frontoparietal injury. All had postoperative imaging positive for neurologic injury.

CONCLUSIONS: To our knowledge, this is the largest study to date and lowest reported incidence of post-CPB seizures in neonates. A future multi-center study could assess institutional differences in anesthetic, surgical, and critical care management that increase and decrease the risk of post-CPB seizures in this vulnerable population.

KEYWORDS: Neurocritical Care, Neonatal Neurology

PL1-7. Delta power during sleep is associated with MRI-visible perivascular space volume in adolescents and young adults

Khambadkone S G (Portland, OR), Yamamoto E A, Koike S, Iliff J J, Lim M M, Elliott J E, Barisano G, Morales A M, Muller-Oehring E M, Baker F C, Nagel B, Piantino J

OBJECTIVE: Enlarged, MRI-visible perivascular spaces (MV-PVS) are putative markers of impaired glymphatic function, and are increasingly recognized in the general pediatric population. The significance of MV-PVS in the developing brain remains unknown. In adults, slow-wave sleep has been shown to mediate glymphatic function, and poor sleep quality is associated with larger MV-PVS volume. The aim of this study was to determine the relationship between MV-PVS volume and polysomnographic (PSG) and electroencephalographic (EEG) measures of sleep in a healthy pediatric population.

METHODS: Data were analyzed from 111 participants (age range:12-21 years of age, mean: 15.3±2.2 years, 47 female) enrolled in a sleep arm of the National Consortium on Alcohol and Neurodevelopment in Adolescence, a multisite, cohort-sequential, longitudinal study. Participants underwent PSG studies and brain MRI scans at study entry. MV-PVS volume/white matter (WM; mm3/cm3) was quantified using an automated detection algorithm. Associations between MV-PVS volume and PSG and EEG measures (log transformed) were analyzed by linear regression including age, sex, BMI, and study site as covariates.

RESULTS: Males had significantly greater mean MV-PVS volume/WM than females (7.57±1.22 vs 6.72±1.22, p<0.001). MV-PVS volume/WM was negatively associated with delta EEG power in Stage N2 sleep (β=-0.50, SE=0.23, p=0.035), but not in Stage N3 sleep. There were no associations observed between MV-PVS volume/WM and PSG measures of wake after sleep onset, sleep efficiency, or time spent in N2 or N3 sleep.

CONCLUSIONS: Lower delta power in N2 sleep was associated with larger MV-PVS volume, highlighting potential physiologic relevance of MV-PVS in healthy adolescents and young adults.

KEYWORDS: Sleep, Neuroimaging

PLATFORM SESSION 2: Wednesday, November 13 (2:15 PM – 4:00 PM)

PL2-1. Early vs. Term Equivalent MRI in Very Preterm Infants: Which is More Predictive of Neurodevelopmental Outcomes at 36 Months?

Selvanathan T (Vancouver, BC, Canada), Oloomi S, Guo T, Ufkes S, Chau V, Branson H M, Synnes A, Ly L G, Kelly E N, de Vries L S, Grunau R, Miller S

OBJECTIVE: As white matter injury (WMI) is more robustly detected on early MRI brain scans, we assessed whether WMI severity and location identified on early-life versus term-equivalent age (TEA) brain MRI is more predictive of 36-month motor and cognitive outcomes in children born preterm.

METHODS: 393 neonates born preterm were recruited at three tertiary NICU centres. Infants completed brain MRIs in early-life (median 32.57, IQR 2.85 weeks post-menstrual age [PMA]) and TEA (median 40.71, IQR 3.57 weeks PMA). Moderate-severe WMI (volume >40 mm3) and location (anterior or posterior) were scored. 307 children completed Bayley-III Scales at 36 months. Multivariable logistic regressions, controlling for birth gestational age, study site, culture positive infection, retinopathy of prematurity requiring treatment, and grade III or IV intraventricular hemorrhage were used to assess the odds of adverse motor and cognitive outcomes for moderate-severe WMI and anterior location at each scan.

RESULTS: In multivariable logistic regression models accounting for other established predictors of neurodevelopment, adverse cognitive outcomes were associated with early-life moderate-severe (OR=3.82, 95% CI=1.43-10.21, p=0.007) and anterior location of WMI (adjusted OR=5.62, 95% CI=1.89-16.69, p=0.002) in multivariable logistic regression models. These associations were not observed at TEA.

Adverse motor outcomes at 36 months were associated with early-life anterior location (OR=3.22, 95% CI=1.28-8.07, p=0.01) but not with moderate-severe WMI on early-life scan and not at TEA.

CONCLUSIONS: WMI on early-life scans is more strongly associated with neurodevelopmental outcomes than WMI detected at TEA. These findings can inform optimal timing of brain MRI to detect WMI in preterm neonates.

KEYWORDS: Neonatal Neurology, Neuroimaging, Neurodevelopmental Disorders

PL2-2. Keratan Sulfate: Chemical Template for Neuroblast Migratory Pathways and Axonal Fascicles in Human Fetal Forebrain

Sarnat H B (Calgary, AB, Canada), Yu W

OBJECTIVE: Timing of keratan sulfate (KS) during morphogenesis in normally developing human fetal forebrain structures was studied. KS is a proteoglycan secreted in fetal brain by astrocytes and radial glia into extracellular parenchyma as granulofilamentous deposits. It envelops neurons except dendritic spines, repels glutamatergic and facilitates GABAergic axons even before they contain neurotransmitter. The same genes are expressed in both neuroblast migration and axonal growth.

METHODS: Twenty normal human fetal brains from 9-41 weeks gestational age were studied at autopsy. KS was examined by immunoreactivity in formalin-fixed paraffin sections, plus other markers including synaptophysin, S-100β protein, vimentin and nestin.

RESULTS: Radial and tangential neuroblast migratory pathways from subventricular zone to cortical plate were marked by KS deposits as early as 9wk GA, shortly after neuroblast migration initiated. During later gestation this reactivity gradually diminished and disappeared by term. Long axonal fascicles of the internal capsule and short fascicles of intrinsic bundles of globus pallidus and corpus striatum also appeared as early as 9-12wk, as fascicular sleeves before axons even entered. Intense KS occurs in astrocytic cytoplasm and extracellular parenchyma at 9wk in globus pallidus, 15wk thalamus, 18wk corpus striatum, 22wk cortical plate, and hippocampus postnatally. Corpus callosum and anterior commissure do not exhibit KS at any age. Optic chiasm shows reactivity at the periphery but not around intrinsic subfasciculi. Cross-immunoreactivity with aggrecan may confuse molecular distinctions.

CONCLUSIONS: KS forms a putative chemical template for many long and short axonal fascicles before axons enter and neuroblast migratory pathways at initiation.

KEYWORDS: Fetal Neurology, Neurometabolic, Epilepsy

PL2-3. Racial, ethnic, and socioeconomic associations with developmental outcomes in neonatal HIE: a 10-year retrospective cohort study.

Fitts W (Philadelphia, PA), Sandoval Karamian A G, Massey S L, Fung F W, Abend N S, Fitzgerald M P

OBJECTIVE: Neonatal hypoxic ischemic encephalopathy (HIE) is a significant contributor to perinatal morbidity and mortality. There is limited research on the impact of racial, ethnic, and socioeconomic disparities on HIE outcomes. We examined how these factors influenced long-term developmental outcomes in children diagnosed with neonatal HIE.

METHODS: This was a single-center retrospective study of infants at a level IV NICU with an admission diagnosis of HIE who underwent therapeutic hypothermia. A chart review was performed to extract demographic and clinical data. Socioeconomic factors included Social Vulnerability Index (SVI) and insurance type. Racial and ethnic minority status (REM) was obtained based upon self-reported demographic data obtained on admission. Motor and language delay were determined by physician assessment or standardized measure at the most recent follow-up visit. Logistic regressions were performed to evaluate the association between REM and socioeconomic factors and developmental delay while controlling for other clinical and demographic factors.

RESULTS: We assessed 211 infants, and 56% (n=117) were REM. At follow-up, 23% (n=49) of infants had motor delay and 28% (n=59) had a language delay. In multivariate analysis, REM, SVI, and insurance status were not significantly associated with motor delays. In multivariate analysis, REM status was significantly associated with language delays until insurance status was added to the model.

CONCLUSIONS: REM status is associated with higher risk of language delays when controlling for clinical factors. This was no longer significant when controlling for insurance type. This may suggest that REM disparities in neonatal HIE are related to socioeconomic factors such as access to care.

KEYWORDS: Neonatal Neurology, Cerebral Palsy

PL2-4. De Novo Variants in Immune Regulatory Genes in Down Syndrome Regression Disorder

Jafarpour S (Los Angeles, CA), Banerjee A K, Santoro J D

OBJECTIVE: Down Syndrome Regression Disorder (DSRD) is a rare and poorly understood disorder of the central nervous system, characterized by acute or subacute neuropsychiatric symptoms in previously healthy individuals with Down syndrome (DS). Many patients exhibit immunotherapy-responsiveness, indicative of immune dysregulation as a potential underlying etiology. The aim of this study was to investigate genes of immune regulation in persons with DSRD.

METHODS: This study included individuals with DSRD aged 10-30 years with trio exome sequencing performed during the diagnostic work up. Descriptive statistics and univariate analysis (Chi-square and Fisher's exact test) were used to describe and compare the characteristics of individuals with and without variants.

RESULTS: Forty-one individuals with DSRD had trio exome sequencing results. Eight (20%) had heterozygous de novo variants of immune regulatory genes, with 4 variants being pathogenic or likely pathogenic (UNC13D, XIAP, RNASEH2A, and DNASE1L3). All genes harboring pathogenic variants were associated with interferon type-1 inflammatory response. Individuals harboring variants were more likely to have a preceding trigger (p=0.03, 95%CI: 1.21-97.06), rapid clinical decline in less than one month

(p=0.01, 95%CI: 1.67-52.06), and MRI abnormalities (p<0.001, 95%CI: 4.89-527.71).
CONCLUSIONS: A distinct subset of individuals with DSRD exhibited pathogenic variants in immune regulation genes associated with interferon mediated inflammatory response, coinciding with previously established links between these genes and interferonopathies such as Aicardi-Goutieres syndrome. Our observations suggest that these variants might potentially contribute to the development of DSRD in individuals with DS.
KEYWORDS: Neurogenetics, Neuroimmunology

PL2-5. Insight into MECP2 Duplication Syndrome: Unraveling Disease Severity and Expression Variability using Multiomics and Deep Phenotyping

Pehlivan D (Houston, TX), Bengtsson J. D., Bajikar S S, Grochowski C M, Lun M Y, Harris H K, Suter B, Aras S, Ramocki M B, Abdelmoity A T, Lindstrandt A, Sedlazeck F J, Lupski J R, Zoghbi H Y, Carvalho C M

OBJECTIVE: X-linked intellectual developmental disorder Lubs-type (MRXSL) results from increased copy number of MECP2. It is an ultrarare, X-linked neurodevelopmental disorder with diverse clinical manifestations. Additionally, each individual's duplication size and genomic rearrangement structures are unique. We hypothesized that these genomic rearrangement structures contribute to interindividual clinical variability and disease severity.
METHODS: We performed extensive genomic studies including custom-designed aCGH, optical genome mapping and short-read/long-read genome sequencing (SR-GS/LR-GS), and correlated with transcriptomic and deep phenotyping analyses including Human Phenotype Ontology (HPO) semantic similarity scores on 137 MRXSL individuals.
RESULTS: The sizes of duplications varied from 64 kb to 16 Mb, exhibiting the following structural distribution: 48% tandem duplications, 22% terminal, 20% Duplication-Triplication-Duplication (DUP-TRP/INV-DUP) structure, and 10% represented other complex genomic arrangements (CGRs). Analysis of RNAseq data from lymphoblastoid cell lines highlighted statistically significant differences in the MECP2 transcript between MECP2 triplications and all other types of duplications, while no significant differences were observed among other genomic structures. Genotype-phenotype analyses revealed a progressive deterioration in phenotypic characteristics, including overall survival, developmental levels, microcephaly, epilepsy, and genitourinary/eye abnormalities, with the following order of severity: tandem duplications, other CGRs, terminal duplications/translocations, and MECP2 triplications. HPO analysis uncovered distinct patterns associated with different genomic structures.
CONCLUSIONS: MRXSL phenotype isn't solely influenced by MECP2 copy number alterations, rather we show the structure of genomic rearrangements also plays a crucial role in clinical manifestations and phenotypic severity. Utilizing a comprehensive analytical approach enriches our comprehension of the impact of genomic disorders, thereby informing more effective therapeutic design strategies.
KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

PL2-6. The unexpected and novel mitochondrial phenotype of the ex vivo patient-derived cellular model for SYNGAP1 encephalopathy

Greco M (Roanoke, VA), Uittenbogaard M, Chiaramello A E, Gropman A L

OBJECTIVE: A hallmark of brain metabolism is dynamic coupling between energy demand and supply involving regulation of mitochondrial bioenergetics during brain development. The brain is highly dependent on mitochondrial homeostasis for ATP production. SYNGAP1 is caused by sporadic pathogenic nuclear variants in the SYNGAP1, known to play a role in brain development, encoding a brain-specific synaptic Ras GTP-ase activating protein localized in dendritic spines of cortical pyramidal neurons. Patients exhibit intellectual disability, epileptic encephalopathy, and autism spectrum disorder. The main question addressed in this study is whether the SynGAP1 syndrome could be in part due to a dysregulated mitochondrial energy metabolism.
METHODS: We performed skin biopsy, Seahorse, comprehensive genetic analysis of the mitochondrial and nuclear genomes by long-range PCR, massively parallel sequencing (MitoNGS), and whole exome sequencing (WES). WES analysis revealed the pathogenic heterozygous nuclear variant c.1783del (p.L595Cfs*55) in the SYNGAP1 gene causing a frameshift located in exon 11.
RESULTS: With Seahorse technology, we found a profound deficit in spare energy capacity, required for cells to sustain a high energy demand. Fibroblasts displayed defective mitochondrial metabolic plasticity preventing use of glycolysis to curtail energy deficit.
CONCLUSIONS: Our study provides the first evidence of dysregulated mitochondrial energy metabolism associated with SYNGAP1 in an ex vivo patient-derived cellular model. The patient was started on MCT oil, medium chain fats which bypass complex 1 of the electron transport chain. After initiation, he exhibited cessation of seizures, and gain of cognitive and motor skills. This research has implications for precision therapy beyond seizure management with traditional antiseizure medication.
KEYWORDS: Neurometabolic, Neurogenetics, Epilepsy

PL2-7. Association of cerebrospinal fluid-restricted oligoclonal bands with relapsing disease in pediatric myelin oligodendrocyte glycoprotein antibody disease

Bach A M (Philadelphia, PA), Chang G, Grasso E A, Hopkins S, Narula S, Waldman A, Banwell B

OBJECTIVE: To assess the association of cerebrospinal fluid (CSF)-restricted oligoclonal bands (OCBs) with relapsing versus monophasic disease in children with myelin oligodendrocyte glycoprotein antibody disease (MOGAD).
METHODS: A retrospective single-center cohort study of children diagnosed using the 2023 international consensus criteria for MOGAD from 2014-2023 was performed. For

inclusion, all patients must have had at least one OCB evaluation. Clinical characteristics, laboratory data, and disease type (monophasic versus relapsing) were collected by chart review. Patients were considered OCB-positive if ≥2 CSF-restricted OCBs were detected on one or more CSF-serum evaluations at any time. Descriptive statistics summarized clinical characteristics. Fisher's Exact test evaluated the association of CSF-restricted OCB presence with relapsing disease.
RESULTS: We evaluated 74 children with median age 9.5 (IQR:5-13) years. Forty-four (59%) were female. Median follow-up duration from disease onset was 23.5 (IQR:10-53) months. Twelve (16%) were OCB-positive, with a median of 2 (IQR:2-5) bands. Among OCB-positive children, the most common clinical phenotype at time of OCB evaluation was optic neuritis (6/12). Relapsing MOGAD was observed in 27 (36%). Presence of CSF-restricted OCBs was associated with relapsing disease ($\chi 2=5.63$;$p=0.02$). Specifically, 67% (8/12) with OCBs had relapsing disease, 33% (4/12) with OCBs had a monophasic disease course, 31% (19/62) without OCBs had relapsing disease and 69% (43/62) without OCBs had a monophasic outcome. Duration of observation did not differ by group. Children were not treated with chronic immunosuppressive medication unless they had a relapse.
CONCLUSIONS: The presence of CSF-restricted OCBs in children with MOGAD was associated with a higher likelihood of relapsing disease.
KEYWORDS: Neuroimmunology, Pediatric Demyelinating Disease, Early Stage Investigator

PLATFORM SESSION 3: Wednesday, November 13 (2:15 PM – 4:00 PM)

PL3-1. Updated Clinical Activity and Safety From a Phase 1/2 Open-label Trial of GTX-102, an Investigational Antisense Oligonucleotide for the Treatment of Patients With Angelman Syndrome

Goodspeed K (Novato, CA), Brandabur M, Cimms T, Aquino P, Chen A, Tan W-H, Myers K A, Berry-Kravis E, Servais L, Sell E, Olugemo K

OBJECTIVE: Describe clinical activity of GTX-102, an investigational intrathecally administered antisense oligonucleotide (ASO) designed to target the UBE3A antisense transcript in patients with Angelman syndrome (AS).
METHODS: AS, a rare neurodevelopmental disorder with no approved disease modifying treatment, is characterized by seizures, severe speech/cognitive impairment, and sleep disorders/motor dysfunction. GTX-102-001 is an ongoing phase 1/2 open-label study (ClinicalTrials.gov: NCT04259281) in patients with full maternal UBE3A gene deletion. GTX-102 was administered in 3 to 4 monthly loading doses followed by quarterly maintenance dosing. Outcome measures were compared with those from deletion-positive 4 to 17-year-old AS Natural History Study (NHS) historical controls.
RESULTS: 74 participants enrolled, with 34 in dose-expansion Cohorts A/B. In 22 Cohort A/B participants with available Study Day 170 (D170) Bayley-4 data, least-squares (LS) mean (SE) change from Baseline was 5.1 (1.3) for the Cognitive Growth Scale Value (GSV) and 3.7 (1.1) for the Receptive Communication GSV, exceeding values observed in the AS NHS at 1-year of follow-up. In 24 A/B participants with available D170 Angelman Severity Assessment (ASA) data, LS mean (SE) change from Baseline was -0.8 (0.2) for Sleep severity and -0.7 (0.2) for Behavior severity, nearing the response threshold (-1.0) at this early timepoint. There were no unexpected serious adverse events; two A/B participants experienced reversible radiculopathy, remain on study, and are expected to redose.
CONCLUSIONS: Treatment with GTX-102 resulted in rapid and progressive improvement versus NHS in Bayley-4 Cognitive/Receptive Communication, and in ASA Sleep/Behavior at D170. Additional cohorts, timepoints, and assessment domains will be presented.
KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Neuromuscular

PL3-2. The ABCs of Child Neurology: Creating Lifelong Learning through Article Based Curriculum

Troy E T (Aurora, CO), Bernard T, Lockspeiser T

OBJECTIVE: While it is important for senior child neurology residents to learn about emerging treatments, it is essential for residents to first establish a strong foundation of child neurology. To address this educational mission, we created The ABCs of Child Neurology, an online article-based curriculum informed by the principles of the Master Adaptive Learner framework. Development of this curriculum is supported by the American Board of Psychiatry and Neurology (ABPN) Faculty Innovation in Education Award.
METHODS: Curriculum development was guided by review of ABPN Child Neurology Core Competencies1. The Oversight Committee, composed of four local child neurologists, identified eight broad topics and selected five articles for each topic. The Item Writing Committee, composed of six neurologists, wrote five assessment items per article. Each item followed national recommendations for best practices in multiple-choice questions2 and was reviewed by an item writing expert. As study participants, 11 local senior child neurology residents will read 12 articles over the academic year, complete an assessment for each article, and achieve at least 80% accuracy to receive credit.
RESULTS: The pilot curriculum will be implemented at our institution in the 2024-2025 academic year. Feasibility and impact will be evaluated by a survey immediately following each article, aggregate performance on items, pre- and post-intervention knowledge assessments, and resident and attending interviews.
CONCLUSIONS: By leveraging this asynchronous online curriculum, the ABCs of Child Neurology is positioned for dissemination to child neurology residency programs around

the country, offering a key step toward equitable educational support through a national curriculum.
KEYWORDS: Education

PL3-3. Hemiparetic cerebral palsy MRI injury patterns and symptoms by gestational age at birth

Piché J-V (Montreal, QC, Canada), Husein N, Shevell M, Dunbar M

OBJECTIVE: Our study evaluates how the risk factors, MRI findings, and neonatal symptoms of hemiparetic cerebral palsy (HCP) differ by gestational age (GA) at birth, to identify characteristics that might enable early recognition.
METHODS: Three groups of patients with HCP were defined: very preterm infants (GA at delivery less than 32 weeks), moderate-to-late preterm infants (GA 32-36 weeks), and term infants (GA 37-43 weeks). Descriptive statistics and chi square tests were used to compare characteristics between groups. Logistic regression was used to evaluate the relationship between MRI diagnosis and GA, or the presence of seizures and/or encephalopathy and GA.
RESULTS: In 855 children with HCP, GA was known in 826. Seizures or encephalopathy occurred in 12.1% of newborns. MRI findings showed focal injury (57.5%), white matter injury (14.4%), and malformations (8.8%). Odds of focal injury increased with GA (OR 1.06, 95% CI 1.02-1.1). White matter injury odds decreased with GA (OR 0.88, 95% CI 0.83-0.93). Odds of early seizures/encephalopathy increased with GA (OR 1.3, 95% CI 1.2-1.5). Preterm births (32-36 weeks) had lower odds of seizures/encephalopathy compared to term (OR 0.24, 95% CI 0.10 – 0.57).
CONCLUSIONS: In 826 children with HCP, we found that GA influenced brain injury patterns. Terms births were more prone to focal injuries. Recognition of seizures or encephalopathy increased with each week of GA. Infants born before 32 weeks are often monitored for CP and those over 37 weeks are likely symptomatic. Our study highlights a vulnerability window for those born between 32 and 36 weeks.
KEYWORDS: Cerebral Palsy, Neuroimaging, Neurodevelopmental Disorders

PL3-4. Worldwide epidemiology of pediatric multiple sclerosis: Data from the Multiple Sclerosis International Federation Atlas of MS, Third Edition

Gombolay G Y (Atlanta, GA), Johnson L, Hebert M, King R, Banwell B, Chitnis T, Helme A

OBJECTIVE: Limited data is available on the global rates of pediatric onset multiple sclerosis (POMS), which we report here.
METHODS: We included pediatric prevalence data in 2020-2022 (Multiple Sclerosis International Federation Atlas of MS) and the prevalence of child neurologists (International Child Neurology Association). The Atlas of MS data was obtained via survey of coordinators from the countries who use different tracking methods including national registries versus crude estimates. Data was split into prevalence bands per 100,000. Countries were classified by the WHO Region and World Bank Income. Descriptive analyses were performed. An estimated worldwide prevalence rate was calculated by summing 2020-22 pediatric prevalence counts and dividing by approximate pediatric populations in 53 countries. We adjusted the prevalence rate to reduce outliers' impact and to reflect worldwide income distribution.
RESULTS: Pediatric data was available in 24% (53/219) countries (38 higher and 15 lower income) with 31,419 total POMS cases. In 2022, 67% (10/15) of lower income countries reported prevalence bands of "<1.0" compared to 34% (13/38) of higher income countries. Only 7% (1/15) of lower income countries reported prevalence bands '<=3.1' compared to 34% (13/38) of higher income countries. The rates of child neurologists positively correlated with the prevalence band. In 2020/22, the estimated global prevalence (crude) was 2.53/100,000 (95% confidence interval-CI: 2.51–2.56), with an adjusted prevalence rate of 1.48/100,000 (95%CI: 1.45–1.51).
CONCLUSIONS: Access to data from resource limited countries is challenging including surveillance for case ascertainment. Increased resources and standard methodologies will facilitate understanding of rare disease epidemiology.
KEYWORDS: Pediatric Demyelinating Disease, Global Neurology, Diversity, Equity, Inclusion

PL3-5. CANaspire Trial of Systemic AAV9-mediated Gene Therapy for Canavan Disease: Biomarker, Imaging and Clinical Findings from the Low-dose Cohort

Laforet G (Bolton, MA), Fay A, Nagy A, Harmatz P, Mallack E, Burton C, Langer K, Townsend E, Kiefer M, Leiro B, Williams R, Shaywitz A, Bley A, Eichler F

OBJECTIVE: Canavan disease (CD) is a leukodystrophy caused by ASPA mutations leading to elevated N-acetylaspartate (NAA) and profoundly impaired psychomotor development. CANaspire (NCT04998396) is an ongoing first-in-human open-label study evaluating the safety, pharmacodynamic, and clinical activity of BBP-812, a recombinant AAV9 hASPA vector for the treatment of CD.
METHODS: Participants receive one IV infusion of BBP-812 along with glucocorticoid immune prophylaxis. Safety is followed by standard laboratory and physical/neurological assessments. NAA is quantified in urine and CSF by GC-MS and in brain by MRS. Effects on white matter pathology and brain volumes are evaluated by MRI. Clinical measures include the CD Rating Score, pediatric motor/developmental scales, and parent-reported outcomes. CANinform natural history data (NCT04126005) are used as a comparator.
RESULTS: Eight participants received low-dose BBP-812. Most adverse events (AEs) have been mild or moderate and unrelated to BBP-812. Related AEs have generally been consistent with other systemic AAV9 gene therapy products. All participants demonstrated rapid, robust and durable NAA decreases in urine, CSF and brain over 1-3 years of follow-up. MRI has shown resolution of white matter swelling and evidence of new myelination in the brainstem and cerebellar peduncles. Participants have generally stabilized existing motor skills or gained new skills, in some cases beyond the typical function of CD patients.

CONCLUSIONS: Participants receiving low-dose BBP-812 showed early and sustained decreases in NAA along with clinical stabilization or improvement. Safety has been manageable with few AEs considered related to BBP-812. Additional data are needed to further elucidate the relationship between NAA reduction and clinical benefit.
KEYWORDS: Experimental Therapeutics, Pediatric Demyelinating Disease, Neurodevelopmental Disorders

PL3-6. Eladocagene exuparvovec gene therapy improves motor development in patients with aromatic L-amino acid decarboxylase deficiency
Warn L (South Plainfield, NJ), Chien Y-H, Lee N-C, Werner C, Krolick A, Wang A, Turna J, Wuh-Liang Hwu P, Penematsa V, Golden L, Tai C-H

OBJECTIVE: To assess the long-term efficacy and safety of eladocagene exuparvovec gene therapy in pediatric patients with aromatic l-amino acid decarboxylase deficiency (AADCd).
METHODS: Patients with AADCd (n=30) aged 19–102 months received eladocagene exuparvovec via bilateral intraputaminal infusion. Achievement of motor milestones was assessed using the Peabody Developmental Motor Scales, 2nd edition (PDMS-2) and the Alberta Infant Motor Scale (AIMS) as primary and exploratory endpoints, respectively. Motor milestones were assessed every 3 months for 1 year post-gene therapy and every 6–12 months thereafter. Safety was also assessed.
RESULTS: Patients were followed for up to 127 months. At baseline, no patients had head control. PDMS-2 assessments at year 1 showed patients developed the following skills: partial head control (n=26), full head control (n=15), sitting unassisted (n=7) and standing with support (n=2). By year 5, patients reached more advanced milestones including: full head control (n=24), sitting unassisted (n=21), walking with assistance (n=8), walking to toy (n=7) and walking up stairs with support (n=4). Improved motor development was also reflected in the least-squares mean (standard error) total AIMS score, with an increase of 30.8 (2.3) from baseline to year 5 ($p<0.001$). The only treatment-related treatment-emergent adverse event (TEAE) reported in >20% patients was dyskinesia (83.3%), and treatment-related TEAEs reported in ≥5 to <20% of patients were initial insomnia (13.3%), salivary hypersecretion (6.7%) and feeding disorder (6.7%).
CONCLUSIONS: Eladocagene exuparvovec had a durable, positive impact on motor development in patients with AADCd, with an acceptable safety profile.
KEYWORDS: Neurodevelopmental Disorders

PL3-7. Two-step newborn screening algorithm of single dried blood spot test identifies disproportionate number of female Duchenne muscular dystrophy carriers
Chrzanowski S M (Boston, MA), Falk E N, Coyne F, Cherkerzian S, Parad R B

OBJECTIVE: Duchenne muscular dystrophy (DMD), a progressive X-linked muscle wasting disorder, is not nationally recommended for newborn screening (NBS), despite its lethality, new treatments, and approved screening tests. Female carriers of DMD are most commonly diagnosed following identification of an affected son and can have cardiomyopathies and variable weakness. This study aims to demonstrate the utility of performing CK analysis and next generation sequencing (NGS) on a single dried bloodspot (DBS) sample, rather than requiring multiple lab draws.
METHODS: 15,094 newborns were enrolled, from whom CK was measured on existing NBS DBS samples. 420 newborns with CK values greater than the 97.5th percentile underwent NGS testing from pre-existing DBS samples.
RESULTS: 99.5% of samples were collected between 24 to 48 hours of life. 2.8% of infants (210 males and 210 females) were referred for NGS, of whom 6 females (CK range 1048–1980 ng/mL) were found to have pathogenic mutations and 4 males (CK range 1320–2495 ng/mL) were found to have non-pathogenic variants on the DMD gene. Other perinatal variables associated with elevated CK included oxytocin use, gestational age, and events that required assistive maneuvers and/or resuscitation.
CONCLUSIONS: This study demonstrates the feasibility of measuring CK and performing NGS on a single DBS NBS sample. Unexpectedly, a disproportionately elevated frequency of female carriers was identified. Further discussion of optimal cutoffs for secondary testing, how to manage female carriers, and what long-term outcomes may result from earlier disease detection remain warranted.
KEYWORDS: Neuromuscular, Neonatal Neurology, Diversity, Equity, Inclusion

GUIDED ABSTRACT TOURS

GUIDED ABSTRACT TOUR 1: Tuesday, November 12 (12:30 PM – 1:45 PM)

GAT1-1. Atidarsagene autotemcel (autologous hematopoietic stem cell gene therapy) preserves cognition, language, and speech and slows brain demyelination and atrophy in early-onset metachromatic leukodystrophy
Fumagalli F (Milan, Italy), Calbi V., De Mattia F, Zambon A, Gallo V, Baldoli C, Recupero S, Fratini E S, Ciotti F, Fraschini M, Locatelli S, Facchini M, Clerici A, Morena F, Martino S, Moro S L, Christopherson K, Gallop N D, Yarzi M Y, Nutkins P, Shenker A, Brooks J, Campbell L, Aiuti A

OBJECTIVE: Metachromatic leukodystrophy (MLD), a demyelinating neurometabolic disorder caused by arylsulfatase A (ARSA) deficiency, results in progressive neurological impairment and early death. Patients rapidly lose all motor and cognitive skills and communication, severely impacting their quality of life (QoL). Here we present

outcomes of arsa-cel on cognition, language, speech, and brain MRI in 37 patients with MLD [18 presymptomatic late-infantile (PSLI), 8 presymptomatic early-juvenile (PSEJ) and 11 early symptomatic early-juvenile (ESEJ) MLD], compared to a natural history (NHx) cohort of 43 untreated MLD patients.

METHODS: Atidarsagene autotemcel (arsa-cel) consists of autologous CD34+ cells transduced ex vivo with a lentiviral vector encoding the ARSA gene, infused intravenously after busulfan conditioning.

RESULTS: Median follow-up was 6.76 years (range 0.64-12.19). Most arsa-cel treated patients (30/37) maintain performance and language standard scores representing normal or mildly impaired cognitive and language skills at last follow-up. In contrast, all NHx patients develop severe cognitive and language impairment early in their disease course. Furthermore, arsa-cel reduced the risk of experiencing complete loss of speech in PSLI ($p<0.001$), PSEJ ($p=0.042$), and ESEJ ($p=0.032$) treated subgroups versus NHx patients, most of whom lost all speech. Brain MRI total scores in arsa-cel treated patients were markedly lower at 5 years post-treatment compared to age-matched NHx [PSLI ($n=8$), $p<0.001$; PSEJ ($n=3$), $p<0.001$; ESEJ ($n=3$), $p=0.025$] and stabilized over time, indicating prevention or slowing of brain demyelination and/or atrophy.

CONCLUSIONS: With up to 12 years follow-up, arsa-cel shows benefits to treated patients' QoL by preserving cognition, language abilities, and speech, supported by evidence from brain MRI.

KEYWORDS: Neurometabolic, Pediatric Demyelinating Disease

GAT1-2. Magnetic Resonance Imaging Derived Biomarkers after Gene Therapy in a controlled GM1 Gangliosidosis Cohort

Acosta M T (Bethesda, MD), Lewis C J, Vardar Z V, Kuhn A L, Johnston J M, D'Souza P D, Shazeeb M S, Tifft C J

OBJECTIVE: To determine relevant magnetic resonance imaging (MRI) derived biomarkers for gene therapy in a GM1 Gangliosidosis cohort and demonstrate efficacy of intravenous gene therapy.

METHODS: We compared Type II GM1 patients ($n=10$) treated with an AAV9GLB1 intravenous gene therapy vector with untreated Type II GM1 patients ($n=16$) from our natural history study and age-matched normal controls ($n=30$). Volumetric, diffusion tensor imaging (DTI), and differential tractography (DT) derived analysis was performed from MRI. Vineland-3 domains and cognitive global impression (CGI) scores served as clinical markers for correlations

RESULTS: DTI assessed metrics of fractional anisotropy, mean diffusivity, and radial diffusivity showed statistically significant correlations with the four Vineland-3 domains in both treated and untreated cohorts. Baseline gray matter and ventricle volume showed a statistically significant relationship with baseline cognitive global impression (CGI) scores. Longitudinal change in ventricle volume alongside DT-assessed net fiber tract number and net fiber tract volume showed statistically significant correlations with longitudinal CGI scores. Lastly, DT demonstrated statistically significant groupwide differences where treated patients showed significant fiber tract growths with moderate losses, untreated patients showed substantial fiber tract losses with minimal growths, and normal controls showed moderate fiber tract growth with negligible losses.

CONCLUSIONS: This is the first study demonstrating the utility of differential tractography in evaluating longitudinal changes from therapeutic application. We found significantly beneficial groupwide effects resulting from gene therapy treatment as assessed by DT. We also found DTI and volumetric MRI derived metrics could be important biomarkers for GM1 and other neurodegenerative diseases.

KEYWORDS: Neuroimaging, Neurogenetics, Experimental Therapeutics

GAT1-3. Essential Child Neurology Training: A Program Director Consensus

Rogers D (Albuquerque, NM), Thompson Stone R, Gottlieb-Smith R J

OBJECTIVE: Child neurology residency training currently spans 5 post-graduate years; however, multiple pathways allow for only 4 years of clinical training in pediatrics and neurology. With substantial ACGME revisions coming soon, we need to further define the essential components of training.

METHODS: All 78 child neurology program directors(PDs) were invited to submit a 4-year block diagram using an Excel template. The template allowed specification of duration, post-graduate year, and category of each rotation(pediatrics, adult neurology, child neurology, or adult/child neurology). Data was analyzed to determine the percent of PDs who recommended each rotation, average recommended duration, and any consensus on categorization. We used an inclusion threshold of 75% to determine required rotations, and then surveyed all PDs to determine level of agreement with the consensus requirements.

RESULTS: Sixty-four percent of PDs($n=50$) submitted a block diagram. The following met the consensus criteria(rotation:weeks): pediatric inpatient floors:12, pediatric intensive care:12, child development:4, healthy newborn:2, pediatric emergency:4, genetics:4, adult neurology inpatient:12, child neurology inpatient:32, child neurology outpatient:16, adult/child neurology subspecialties:16, child psychiatry:4, EEG:8, neuroradiology:4, electives:28. Fifty-three PDs(72%) responded to the follow up survey. Of the respondents, 87% agreed that completing these consensus requirements would provide adequate training. Thirty-six percent of those who agreed suggested modifications or expressed concerns about implementation.

CONCLUSIONS: By constraining that all pediatric and neurology clinical rotations must fit into 4 years, we came to a consensus among PDs regarding essential rotations for adequate training in child neurology. The largest difference compared to most 5-year programs is a substantial reduction in preliminary pediatrics rotations.

KEYWORDS: Education

GAT1-4. Utilizing Large-Language Models to Extract Patient Verbal and Ambulatory Status from Multi-Institutional and Multi-Specialty Clinical Notes

Kaster L P (St. Louis, MO), Oh I, Vickstrom C, Lanzotti V, Payne P, Gurnett C A, Gupta A

OBJECTIVE: The Brain Gene Registry, a collaborative effort of the IDDRC Network, aggregates data for participants with rare neurodevelopmental disorders, including electronic health records (EHRs) and standardized neurobehavioral assessments. Natural history studies of rare disease require documentation of verbal and ambulatory ability which may be uniquely documented within clinical narratives. Large-Language-Models (LLMs) such as GPT have emerged as effective information extraction methods. Hence, we examined GPT-3.5's ability to extract verbal and ambulatory status from multi-institutional and multi-specialty notes.

METHODS: For 107 BGR participants with gold-standard verbal and/or ambulatory status documented in neurobehavioral assessments, we semi-randomly selected up to 10 clinical notes per patient from relevant specialties, excluding notes written when the participant was <3 years old.

Using a HIPAA-compliant API , we prompted GPT-3.5 to determine from each note "does the individual use any words?" and "can the individual walk without aid?", and respond 'yes', 'no', or 'unknown' to each question. For each participant, if more notes had a "yes" response than a "no" response, then the participant-level prediction was "yes", otherwise it was "no". Results were evaluated against gold-standard labels using weighted F1-scores.

RESULTS: 72/89 and 75/87 participants had gold-standard labels of "yes" for verbal and ambulatory ability, respectively. 932 notes were included. Weighted F1-scores for verbal and ambulatory status were 0.87 and 0.80, respectively.

CONCLUSIONS: The F1-scores suggest that LLMs successfully extracted patient verbal and ambulatory status, and that LLMs are a generalizable option for clinical information extraction across institutions and note types. Next steps include extracting more granular levels of function.

KEYWORDS: Neurodevelopmental Disorders

GAT1-5. Connectivity During Language Processing Differs in Self-Limited Epilepsy with Centrotemporal Spikes and is Associated with Phonological Awareness

Qi W (Palo Alto, CA), Lee K, Nix K C, Menchaca M, Wu W, He Z, Baumer F M

OBJECTIVE: To investigate if brain connectivity during language processing in children with Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS) differs from typically developing children and whether connectivity is associated with language performance.

METHODS: Children with SeLECTS, and typically developing age and sex-matched controls (31 SeLECTS and 32 controls, 9.3+/-2 years, 37% female) completed a language task (verb generation) and a resting task while undergoing an electroencephalogram. Additionally, phonological awareness was analyzed with the Comprehensive Test of Phonological Processing-2. Connectivity between four regions – left frontal and left temporal regions (critical for language); bilateral motor regions (implicated in SeLECTS) – was measured using the weighted Phase Lag Index. We assessed connectivity differences between groups in either task and whether connectivity correlated with phonological awareness.

RESULTS: SeLECTS had higher left frontal to left temporal connectivity than controls during verb generation (group difference=0.07, CI 0.02-0.11, p=0.003) but not at rest. Right motor to left temporal connectivity was elevated in SeLECTS during verb generation (difference=0.04, CI 0.01-0.07, p=0.008) and rest (difference=0.03, CI 0.01-0.05, p=0.001). Higher left frontal to left temporal (-33.1, CI -60.3 to -5.9, p=0.017) and right motor to left temporal (-55.8, CI -81.5 to -30.1, p<0.0001) connectivity during verb generation was associated with poorer phonological awareness in SeLECTS but not controls. Resting connectivity was not associated with phonological awareness in either group.

CONCLUSIONS: Hyperconnectivity during language tasks may contribute to language difficulties in SeLECTS.

KEYWORDS: Neuroimaging, Epilepsy, Neurodevelopmental Disorders

GUIDED ABSTRACT TOUR 2: Tuesday, November 12 (5:30 PM – 7:00 PM)

GAT2-1. Tracking Uncertainty in Germline Genetic Testing for Epilepsy and Neurodevelopmental Disorders: Sources, Attributes, and Resolution of Variants of Uncertain Significance in Over 70,000 Individuals

Ting Y (San Francisco, CA), Chen E, Facio F M, Hatchell K E, Aguilar S, Ouyang K, Aradhya S, Johnson B

OBJECTIVE: Genetic testing for epilepsy and neurodevelopmental disorders (NDDs) has diagnostic, prognostic and therapeutic implications; however, variant(s) of uncertain significance (VUS) are not actionable. As such, VUS are a challenge to the entire medical community. Here, we report on the prevalence of VUS in patients referred for genetic testing for these conditions and the results of reclassification.

METHODS: Patients were referred for testing between September 2014-September 2022. Variants were classified using a validated framework based on guidelines from ACMG/AMP. The number of unique VUS (uVUS) and the number of times they were observed in individuals (oVUS) were counted. All-time uVUS were separated as being reclassified and non-reclassified, and the relative impact of evidence types was analyzed.

RESULTS: During this 8-year period, 70,740 unrelated individuals were tested on an epilepsy (up to 302 genes) and/or NDD multigene panel (up to 241 genes) with a mean of 2.0 oVUS per individual. A mean of 2.5 oVUS were observed in 56,751 (80.2%) individuals without a molecular diagnosis. In total, 12.1% (9,000/74,559) uVUS were reclassified, affecting 16,982 individuals (24.0%); 86.4% (7,773/9,000)

of reclassified uVUS were downgraded to B/LB, and 13.6% (1,227/9,000) were upgraded to LP/P. Clinical observations evidence was enriched 60.0-fold in upgraded uVUS and 41.2-fold in downgraded uVUS when compared with non-reclassified uVUS.

CONCLUSIONS: Clinical evidence, including robust patient clinical information and data from family member testing was the most impactful type of evidence in VUS reclassifications. This highlights the partnership between laboratories and clinicians to resolve VUS.

KEYWORDS: Epilepsy, Neurodevelopmental Disorders, Neurogenetics

GAT2-2. Vigabatrin versus ACTH as second-line therapy after very high-dose prednisolone failure for the treatment of epileptic spasms

Layton A (San Diego, CA), Sattar S, Gold J, Zimbric M, Bui J, Sahagian M, Kim-McManus O, Guido-Estrada N, Jindal A, Wiegand S, Rismanchi N, Dove K, Frederick A, Nespeca M, Rho J, Montenegro M

OBJECTIVE: Infantile epileptic spasms syndrome (IESS) is one of the most devastating types of childhood epilepsy. It is debatable what the second medication choice should be if very high dose of prednisolone fails. The objective of this study is to evaluate the efficacy of ACTH versus Vigabatrin as second-line therapy in patients with IESS after high-dose prednisolone failure.

METHODS: Retrospective analysis of patients treated at a tertiary children's hospital from 2011-2024. Inclusion criteria encompassed diagnosis of IESS according to the ILAE criteria, age of IESS onset between 1 and 24 months-old, previous failure of very high dose prednisolone (6-8mg/kg/day) as the first antiseizure medication for the treatment of IESS, and use of vigabatrin or ACTH as second ASM. Patients were excluded if etiology of IESS was tuberous sclerosis, GLUT1 deficiency or known metabolic disorders. Demographics utilized descriptive analyses with group differences utilizing student T-test.

RESULTS: Thirty-eight patients met the inclusion criteria (F=18, M=20). Seventeen patients took vigabatrin and 21 took ACTH. There was no significant difference regarding age of IESS onset (p=0.3738) or sex between both groups (0.3248). There was no difference between epileptic spams control [5/17 (29.4%) patients in vigabatrin group and 4/21 (19%) in the ACTH group (p=0.7029)] or frequency of drug resistant epilepsy later in life (p=1). Follow up ranged from 15 to 147 months (median 50 months).

CONCLUSIONS: There was no difference in efficacy of vigabatrin compared to ACTH as second-line therapy for the treatment of IESS after failure of very high dose prednisolone.

KEYWORDS: Epilepsy, Neurodevelopmental Disorders, Early Stage Investigator

GAT2-3. A Clinical Brain Computer Interface Program for Children with Severe Physical Disabilities

Kirton A (Calgary, AB, Canada), Rowley D, Kelly D, Jadavji Z, Zewdie E, Barnfather A, Wieler A, Romanow N, Floreani E, Robu I, Keough J, Irvine B, Minhas A, Kim V, Comaduran-Marquez D, Kinney-Lang E

OBJECTIVE: Establish a family-centered clinical brain-computer interface (BCI) program to enable children with severe motor impairments to realize increased participation in life.

METHODS: Children and their families were identified within a population-based, tertiary care children's hospital. Criteria included: 1) age 5-18 years, 2) severe physical disability (non-ambulatory, minimal hand use, nonverbal), and 3) estimated grade 1 cognitive capacity. After initial screening for BCI competency, participants attended regular sessions, attempting commercially available and customized non-invasive BCI systems to operate a suite of applications (e.g., gaming, device control, art, communication). Outcome measures included personalized goal achievement (COPM), family engagement and experience (MPOC-20, PRIME-P), and technology efficacy and usability.

RESULTS: In 5 years, we enrolled 27 participants (median 11 years, range 5-18, 56% male, 17 etiologies). BCI systems and training were well tolerated with no serious adverse events. All but one participant could perform BCI tasks. More than 830 hours of participation have occurred across >600 sessions. Mental imagery-based tasks were the most successful, while other paradigms (P300, SSVEP) had lower efficacy and tolerability. Popular applications included painting, cooking, environment control, internet access, and video games. Six children chose and accomplished power mobility goals. Successful translation of BCI systems into home environments was demonstrated with 11 families, totaling >460 sessions. Families reported major impact and their high engagement informed program development. The program has been implemented in the provincial healthcare system, with increasing referrals and waitlists.

CONCLUSIONS: Family-centered clinical BCI programs can allow children with severe disabilities to achieve novel, personal goals that they previously considered impossible.

KEYWORDS: Cerebral Palsy, Diversity, Equity, Inclusion, Experimental Therapeutics

GAT2-4. Metabolic alterations in association with Intraventricular Hemorrhage in very low birth weights preterm infants

Bassan H (Ramat Gan, Isreal), Reichman B, Zaslavsky-Paltiel I, Almashnu S, Coster D, Sagiv N, Morag I, Schupper A

OBJECTIVE: Intraventricular hemorrhage (IVH) is an acquired lesion of preterm infants. Despite advances in perinatal medicine and implementation of neonatal care bundles, IVH incidence reached a plateau, suggesting that inborn factors could play a role in its pathogenesis. Our study aims to further explore the etiology of IVH by detecting early metabolic alterations in association with IVH in preterm infants.

METHODS: We measured 21 metabolites by dried blood tandem mass spectrometry between day 1-4 of life in 7313 preterm infants (gestational age 24-32 weeks), born between 2009 to 2019. Data was matched to the Israel National VLBW Infant Database for group comparison between IVH versus infants with normal sonography. We used multivariate logistic regression analyses. A significant elevation or decrease of a metabolite level was defined as a concentration in the highest or lowest quartile respectively.

RESULTS: 6431 neonates had normal neonatal sonography, 882 had IVH grades 2-4, 149 of them had IVH grade 4. Higher levels of free carnitine (Odds ratio (OR) 0.53, confidence interval (CI): 0.42-0.67) significantly lowered the risk for IVH 2-4 (P<0.0001). Higher levels of proline (OR 1.74, CI:1.4-2.17) and methionine (OR 1.5, CI: 1.21-1.86) significantly increased the risk for IVH (p< 0.0002). These trends were more apparent in the IVH 4 group.
CONCLUSIONS: In extremely preterm infants, elevated and decreased levels of specific metabolites in blood collected on postnatal days 1-4, are associated with sonographic findings of IVH. The association of low carnitine levels with IVH opens a novel avenue for IVH prevention research.
KEYWORDS: Neonatal Neurology,

GAT2-5. Exome sequencing vs chromosomal microarray for copy number variant detection

McWalter K (Gaithersburg, MD), Sanyoura M, Sack L, Lindy A, Douglas G, Juusola J, Kruszka P

OBJECTIVE: Broad genetic testing such as exome sequencing (ES) can identify copy number variants (CNVs). Professional guidelines support ES as a first line test, and the diagnostic utility of ES is significantly greater than chromosomal microarray (CMA). Given that ~15% of patients with epilepsy have disease-associated CNVs, we queried a large genetic testing laboratory to assess concordance of CNV detection between CMA and ES.
METHODS: Under an IRB research protocol using deidentified data, we evaluated concordance of CNV detection between ES and CMA, as well as detection of the ClinGen recurrent dosage-dependent microdeletions and duplications approved list (April 2024), for a cohort (N=11,930) that had both ES and CMA between 2022-2023. Variants were classified using ACMG criteria. Clinical notes were assessed for phenotypic characterization.
RESULTS: An indication of "seizures" or "epilepsy" was present in 2,043/11,930 (17%) individuals. The concordance of positive CNV findings (likely pathogenic/pathogenic) increased from a prior cohort: 93.4% (296/317) in the prior cohort versus 95.2% (591/621) in the current cohort. 11,770/11,930 (98.7%) had equivalent results or additional CNV findings on ES compared to CMA. ES testing detected 34/39 ClinGen recurrent CNVs and has sufficient coverage for all 39.
CONCLUSIONS: These data suggest good ES detection of CNVs, including CNVs in challenging categories and common microdeletions/duplications. Given that all genetic tests have technical limitations, ES could be considered first in patients with seizures due to ES's ability to (1) identify CNVs at high concordance with CMA, and (2) identify many other variant types (SNVs, UPD, indels, MEIs).
KEYWORDS: Neurogenetics, Epilepsy, Neurodevelopmental Disorders

GAT2-6. Arginine Vasopressin Alter Glymphatic Fluid Transport Within Hippocampus

Hamed E E (Wall Township, NJ), Zhang M, Majumdar S, Mohammed H, Sutton B, Gillette M

OBJECTIVE: The glymphatic system is a network of perivascular spaces (PVS) surrounding the vasculature in the brain. Cerebrospinal fluid (CSF) passes from the subarachnoid space surrounding the brain into these PVS. Aquaporin-4 (AQP4) channels on glial cells surrounding the PVS move CSF into the brain parenchyma. Arginine Vasopressin (AVP) is a neuropeptide responsible for maintaining body fluid homeostasis. Little is known about whether AVP affects glymphatic flow, and consequently, clearance of metabolic waste. We hypothesize that AVP enhances glymphatic flow.
METHODS: We used intracisternal injection of Gadobenate Dimeglumine (MultiHance®) and 9.4T MRI to assess AVP effect on glymphatic fluid transport within the whole brain and hippocampus. MultiHance® was injected into the cisterna magna of BlueGill rats and its spread to the brain parenchyma was recorded for 2 h using a 3D T1-weighted FLASH dynamic contrast enhancement (DCE) imaging sequence.
RESULTS: The hippocampal dentate gyrus, CA1, CA2, and CA3 showed enhanced glymphatic flow using 9.4T DCE imaging following AVP intracisternal injection. The effect of endogenous AVP on the glymphatic flow was not blocked following the intracisternal injection of the V1a receptor antagonist.
CONCLUSIONS: In summary, we identified a novel use of the neuropeptide AVP that enhanced the glymphatic flow hippocampus. This offers novel insights into strategies to modulate the glymphatic system. AVP enhanced the localized distribution of the glymphatic fluid tracer in the hippocampus.
NSF STC CBET 0939511, Neuroscience Program Fellowship, Beckman Graduate Fellowship, Nadine Barrie Smith Memorial Award, Beckman Imaging Center Award.
KEYWORDS: Experimental Therapeutics, Neuroimmunology, Sleep

ABSTRACT POSTERS

BEHAVIORAL NEUROLOGY

1. Core Signs and Symptoms in Children with Autism Spectrum Disorder Improved after Starting Risperidone and Aripiprazole in Combination with Standard Supportive Therapies: A Large, Single-Center, Retrospective Case Series

Alsayouf H A (Amman, Jordan), Talo H T, Biddappa M B

OBJECTIVE: There are a number of medications prescribed to address comorbid challenging behaviors in children with autism spectrum disorder (ASD), including risperidone and aripiprazole. This retrospective case series reports the use of these drugs in children aged 2 to 13 years.

METHODS: A total of 82 children (mean age, 5 years; 79% male) with ASD treated between January 2020 and September 2021 were included in this retrospective case series. All patients had comorbid challenging behaviors that were resistant to standard supportive therapies alone and warranted pharmacological intervention. The Childhood Autism Rating Scale—2nd Edition Standard form (CARS2-ST) and the Clinical Global Impression (CGI)—Severity (CGI-S) and CGI—Improvement (CGI-I) scales were used to assess the severity of ASD at baseline and to monitor response to treatment with risperidone or aripiprazole

RESULTS: Besides the expected improvement in comorbid challenging behaviors, 79/82 patients (96%) attained a CGI-I score of 2 or 1 following treatment, and 35/82 patients (43%) achieved both a CGI-I score of 1 and minimal-to-no symptoms as per the CARS2-ST test, with complete resolution of their ASD signs and symptoms. The main side effects were asymptomatic elevated prolactin ($n = 12$) and excessive weight gain ($n = 2$).

CONCLUSIONS: ASD core symptoms and comorbid behaviors in young children improved following chronic treatment with antipsychotic medications, either with or without medications for attention deficit hyperactivity disorder, when combined with standard supportive therapies. Double-blind, placebo-controlled clinical trials are needed to verify these findings.

KEYWORDS: Behavioral Neurology, Neurodevelopmental Disorders, Early Stage Investigator

2. Impact of Multidisciplinary Neurodevelopmental clinics on parent satisfaction.

Golla S (Orange, CA), Amin H, Kim K, Pionk M, Megerian J

OBJECTIVE: To assess the impact of multidisciplinary clinics for management of co-occurring conditions with Neurodevelopmental Disabilities on patient/caregiver satisfaction.

METHODS: Our study population included patients seen in our Neurodevelopmental multi-disciplinary clinic. Parents/caregivers were given anonymous surveys at clinic visit. The survey had 2 primary components – parent/caregiver expectations for the clinic visit and performance of the multidisciplinary clinic compared to prior experience and 5 subcomponents – Work/School Absence, Managing Comorbidities, Fewer Clinic Visits, Quality and Coordination of Care. Parents/caregivers rated each of these five components using a Likert Scale (1 to 5 for expectations and 1 to 7 for clinic performance). Goal sample size is 100.

RESULTS: W e currently have data from 24 surveys. Coordination of care, quality of care and co-morbidities management were the most important expectations, with scores (mean $\pm$ sd) of 4.96 ± 0.20, 4.79 ± 0.51 and 4.67 ± 0.76, respectively. Fewer clinic visits and absence from work/school were less important from parent/caregiver perspective, with scores of 4.25 ± 1.07 and 3.79 ± 1.47, respectively. Our multidisciplinary model was rated highly with respect to coordination of care, quality of care and co-morbidity management, with scores of 6.83 ± 0.49 for each of them. Performance was rated lower with respect to fewer clinic visits and work/school absence with scores of 6.61 ± 0.78 and 6.48 ± 0.85, respectively.

CONCLUSIONS: In this study, parent satisfaction with care received at our clinic was high. Multidisciplinary clinics have the benefit of providing comprehensive, coordinated and higher quality care to patients with complex medical conditions.

KEYWORDS: Behavioral Neurology, Neurodevelopmental Disorders

3. Sleep and Family Meals are Protective Against Structural Brain Changes in Children with Childhood Adversity

Ravichandran S (Ladera Ranch, CA), Agarwal R, Kilpatrick L, Zhang X, Vora P, Bharadwaj V, Jackson N, Labus J, Jamie-Lara R, Romero A, Gupta A

OBJECTIVE: Structural neuroimaging studies have identified distinct reductions in emotional-processing regions in children with adverse childhood experiences (ACE) in association with altered eating behaviors and obesity. While healthy weight-related behaviors have generally shown to be protective against these changes, the neural mechanisms underlying these associations have yet to be investigated in children with ACE. This study aims to evaluate the interactions between ACE burden, brain morphometry, disordered eating, and healthy weight-related behaviors in children.

METHODS: Surveys and structural MRI scans from 8150 child participants in the Adolescent Brain Cognitive Development (ABCD) dataset were assessed. Structural equation modeling was used to determine the burden of ACEs on cortical thickness and gray matter volume of brain regions involved in emotional regulation, executive control, and reward processing. A moderator-mediation analysis was conducted to examine the effect of ACE and healthy weight-related behaviors. Statistical significance was corrected for multiple comparisons at $q<0.05$.

RESULTS: Higher ACE burden was associated with gray matter volume reductions in the amygdala ($C=-5.75$, $p=0.02$) and nucleus accumbens ($C=-2.56$, $p=0.03$). Sleep and family meals buffered the deleterious effect of ACE on the cortical thickness of the dorsolateral prefrontal cortex ($B=-5.2x10-4$, $p<0.001$) and amygdala ($B=-3.227$, $p<0.001$).

CONCLUSIONS: Cortical reductions in emotional-processing brain regions seen in children with ACE may be associated with overactivation of the HPA axis resulting in disordered eating behaviors and obesity. Increased family meals and adequate sleep may prime neuroplastic changes that attenuate the effect of ACEs on the pediatric brain, suggesting the therapeutic value of incorporating healthy weight-related behaviors into clinical interventions.

KEYWORDS: Behavioral Neurology, Neuroimaging, Neurometabolic

4. Towards Improved Recognition and Diagnosis of Autism Among Females - A Novel Approach Using Machine Learning

Tangirala A (Seattle, WA), Lateef T

OBJECTIVE: Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by social and verbal

impairments, impacting 1 in 36 children. ASD diagnosis is based on behavioral observations, caregiver interviews, and clinical questionnaires. Autism in females is more likely to be missed compared to males as their behavioral symptoms present in ways that may not fit current diagnostic criteria. This study aimed to evaluate the gender bias in current autism diagnostic tests and identify behaviors that can predict autism more accurately in females.

METHODS: Exploratory data and Machine Learning (ML) analysis was performed on a public dataset (ABIDE) of 1112 individuals—948 males, 164 females, 539 autistic, and 573 non-autistic with test scores for the standard diagnostic instruments– Autism Diagnostic Observation Schedule (ADOS), Autism Diagnostic Interview-Revised (ADI-R), Social Communication Questionnaire (SCQ), and Social Responsiveness Scale (SRS).

RESULTS: The SCQ, SRS Total, and SRS Communication scores revealed statistical gender differences. ML analysis further validated the gender bias—autism classification accuracy with current behaviors was 95% for males versus 85% for females. A minimal set of 12 most predictive behaviors for females was identified from the original 23 (48% reduction) and tested on six ML classifiers. Random Forest had the highest accuracy(91%) in classifying female autism with this reduced behavior set versus original set (85%).

CONCLUSIONS: These results support potential modifications to autism diagnostic criteria for females to enable faster and more accurate diagnosis–reducing overreliance on ADOS and emphasizing questionnaire and interview-based tools (SCQ, SRS and ADI-R). Automated screening tools for these can facilitate streamlined, gender-equitable autism diagnoses.

KEYWORDS: Behavioral Neurology, Diversity, Equity, Inclusion

5. Alterations in TMS-stimulated motor evoked potentials in children with ADHD correspond to impairments in discrete functional domains

Ehrman J M (Cincinnati, OH), Huddleston D, Horn P S, Migneault K, Crocetti D, Sperry A, Gonzaga A, DeRonda A, Mostofsky S, Gilbert D

OBJECTIVE: Anticipation of and preparation for cognitive and motor tasks up-modulates motor cortex (M1) physiology. We have previously shown that, compared with typically developing (TD) controls, children with attention deficit/hyperactivity disorder (ADHD) have reduced task-related up-modulation (TRUM) in M1 during action selection/inhibition tasks. Here, we sought to replicate this finding in a new cohort of children with ADHD and estimate associations with discrete behavioral, emotional, and motor function domains affected in ADHD.

METHODS: This was a case-control study of 79 right-handed 8–12-year-old children (39 ADHD: mean 10.2 years, 21 male; 40 TD: mean 9.7 years, 22 male). The primary outcome was TRUM, measured using Transcranial Magnetic Stimulation (TMS)-induced motor evoked potentials, precisely timed during an anticipated response inhibition task. ADHD severity, emotional regulation, and motor function were assessed using validated clinical scales.

RESULTS: In children with ADHD, TRUM was reduced during stop trials ($p=0.04$), and response inhibition (stop signal reaction time) was worse ($p=0.03$). For both groups, TRUM was largest in stop compared to go trials ($p<0.0001$). This TRUM trial-type effect differed based on categorical diagnosis (lower in ADHD, $p<0.001$), more severe ADHD symptom ratings ($p<0.00001$), more impaired motor performance ($p<0.00001$), worse response inhibition ($p<0.00001$), and, marginally, emotional dysregulation ($p=0.10$) and lability ($p=0.05$).

CONCLUSIONS: In line with prior work, these data support significantly decreased TRUM in children with ADHD. Furthermore, reduced TRUM corresponds to more severe behavioral/motor impairment measurable via standardized rating scales.

KEYWORDS: Behavioral Neurology

6. Neurological and Psychological Outcomes 2 Years After Multisystem Inflammatory Syndrome in Children

Rollins C K (Boston, MA), Worhach J, Rodriguez S, Licht P, Wypij D, Newburger J, Randolph A

OBJECTIVE: Neurological and psychological sequelae were previously reported one-year after hospitalization for multisystem inflammatory syndrome in children (MIS-C). It is unknown if these concerns persist. The objective of the present study was to determine the trajectory of neurological, psychological, and quality of life sequelae two years after MIS-C.

METHODS: We conducted a longitudinal matched cohort study of children hospitalized for MIS-C at 6-12 and 18-24 months after hospital discharge. Participants were children diagnosed with MIS-C between August 2020 and August 2021 and sibling/community controls. A central study site remotely administered outcome measures including surveys, a neuropsychological assessment, and a neurological examination. Group differences were assessed using generalized estimating equations, accounting for matching.

RESULTS: Fifty-nine MIS-C and 36 control participants enrolled. While at 1-year follow-up, individuals with MIS-C had worse scores in executive functioning, quality of life, internalizing symptoms (depression and somatization), and sleep disturbance, by 2 years, the MIS-C group was similar to controls on all measures except somatization (mean difference 5.2 [95% CI 1.3 to 9.1]).Within the MIS-C group, scores generally improved between 1- and 2-year follow-up. At 1-year follow-up, one-quarter of children with MIS-C had an abnormal neurological exam, but most normalized by 2 years.

CONCLUSIONS: In this cohort study of children with MIS-C and controls followed sequentially for up to two years, patients with MIS-C showed improved neurological and psychological outcomes over two years, performing similarly to their matched peers on most measures by 2-year follow-up. Clinical improvement after MIS-C may continue for at least two years after discharge.

KEYWORDS: Behavioral Neurology, Neurocritical Care, Neuroinfectious Disease

7. Influence of socioeconomic status and sleep disturbance on neurocognitive outcomes in children with sickle cell anemia

Hoke T (St. Louis, MO), Payne A, Lim M, Quartuccio H, Lewis J, Dedkov I, Shah N, Power L, Fields M, Guilliams K

OBJECTIVE: Sickle cell anemia (SCA) has a risk of neurocognitive impairment. While general population studies have found associations among sleep quality and socioeconomic status (SES) with cognition, few studies have examined the combined impact of these factors in children with SCA.

METHODS: Participants with and without SCA completed the Sleep Disturbance Scale for Children (SDSC) and neurocognitive testing as part of a larger study. Sleep quality was measured with the total sleep score on the SDSC. The Weschler Abbreviated Scale Intelligence, 2nd Edition (WASI-II) provided full-scale intelligence quotient scores (FSIQ-2). SES was estimated using the area deprivation index (ADI) national percentile ranking. Non-parametric statistics provided univariate comparisons. A mixed multivariable model examined the combined impact of sleep disturbance and SES on FSIQ-2.

RESULTS: Twenty children with SCA and 46 age- ($p=0.87$) and sex- ($p=0.54$) matched controls had data available. ADI was higher in children with SCA (84 [49.5, 93]) compared to controls (51 [39,85]; $p=0.04$), and sleep scores were slightly higher in SCA (42 [35, 48]) than controls (38 [34, 42]) but this did not reach significance ($p=0.05$). Controls had a higher FSIQ-2 (110.5 [97, 118] than children with SCA (94 [81, 108]; $p=0.02$). In multivariable analysis, SCA status ($p=0.045$), ADI ($p=0.005$) and the interaction between sleep score and ADI ($p=0.03$) were significantly associated with FSIQ-2.

CONCLUSIONS: Social determinants of health, as reflected by the ADI national percentile, and sleep quality may impact the neurocognitive outcomes of children with SCA.

KEYWORDS: Behavioral Neurology, Sleep, Lifespan Manifestations of Childhood Onset Conditions

8. Autism subscores are correlated with tuber functional connectivity to cerebellar and somatomotor areas in tuberous sclerosis complex

Herman W X (Boston, MA), Miller G, Drew W, Sahin M, Peters J, Warfield S, Kreuger D, Bebin E, Northrup H, Wu J, Cohen A

OBJECTIVE: To examine networks in the brain related to autism severity and severity of different autism characteristics.

METHODS: In this study, we utilize data from the TSC Autism Centers of Excellence Research Network (TACERN), involving 115 participants with Autism Diagnostic Observation Schedule (ADOS) data and structural neuroimaging data. Employing lesion network mapping, a method that pinpoints functional brain circuits linked to lesions such as cortical tubers, we examined the correlation between particular ADOS variables and networks connected to tubers. We utilized normative data from 1000 9-year-olds from the Adolescent Brain Cognitive Development Study for comparison.

RESULTS: We discovered that there was limited localization of functional connectivity networks linked to the overall autism severity score. However, when modeling the subscores for social affect (SA) and repetitive restrictive behaviors (RRB), we observed a correlation between SA scores and heightened functional connectivity to both bilateral deep cerebellar nuclei and bilateral somatomotor areas. Additionally, we observed that the variance related to RRB severity largely seemed orthogonal to SA.

CONCLUSIONS: We observed a strong correlation between social affect and the engagement of a distinct network linked to bilateral somatomotor and cerebellar areas. However, no correlation when considering total ADOS scores, possibly contributing to the varied outcomes seen in neuroimaging studies relying solely on overall autism severity. Our results highlight a particular brain network associated with social affect in TSC-related autism, potentially holding relevance for idiopathic/non-syndromic ASD cases too.

KEYWORDS: Behavioral Neurology

CEREBRAL PALSY

9. Differences in Motor Learning Between Children with Cerebral Palsy and Typically Developing Peers Using a Dynamic Balance Task

Varma A (Greenville, NC)

OBJECTIVE: Children with cerebral palsy (CP) receive various therapies to improve gross motor skills. This ongoing study compares motor learning between children with CP and typically developing (TD) children using balance training.

METHODS: The motor task involved standing on a horizontal stability platform. Participants trained on this platform for 5 days (15, 30 second trials/day) before undergoing an assessment of 5, 30 second trials. Performance and variability were captured as time the participant maintained the platform within 5° of the horizontal mark versus time the platform spent on either side of it. Mixed-model ANOVA was performed with time (pre-test vs. post-test) as the within-subject variable and group (CP vs. TD) as the between-subject variable.

RESULTS: 22 children participated in this study (TD n=6, $\bar{x}$ age=11; CP n=16, $\bar{x}$ age=12). Both groups' performance improved (6.7 seconds versus 11.9 seconds, respectively) and variability decreased (3.35 seconds versus 6 seconds, respectively). ANOVA showed significant effects for time on mean center time ($F(1,40) = 26.0$, $p < 0.001$), group on mean center time ($F(1,40) = 20.9$, $p < 0.001$), time on variability ($F(1,40) = 1$, $p < 0.001$) and group on variability ($F(1,40) = 1$, $p < 0.001$).

CONCLUSIONS: Both groups demonstrated improved motor performance following five days of balance training; however, children with CP showed less variability improvement than TD children. While TD children achieved almost maximum performance with training, children with CP may

need additional balance training or another modality of intervention to reach optimal therapeutic outcomes and improve gross motor skills.
KEYWORDS: Cerebral Palsy, Movement Disorders

10. Provider Perception of Administration and Management of Intrathecal Baclofen in the United States
Shenoy S (Baltimore, MD), Chakraborty S, Lenz C, Robinson S, Riordan H

OBJECTIVE: Intrathecal baclofen (ITB) has been used to alleviate spasticity of cerebral/spinal origin for over 25 years. Despite this, there remains a lack of evidence or standardized guidelines for ITB management, necessitating providers to rely on anecdotal evidence. We hypothesized that lack of evidence-based literature leads to wide variation in practice.
METHODS: We documented provider perspectives on ITB management, while highlighting areas of convergence and/or divergence. We designed and administered an online questionnaire to 250+ US-based members of the Pediatric ITB Network.
RESULTS: We received 31 responses from 20+ institutions, representing 15 states. While most respondents preferred cervical placement of catheter tip for dystonia, there were mixed opinions for spastic diplegia and quadriplegia. Regarding maximum dose of ITB, 58% (n=18) providers reported exceeding 1599 mcg/day, and 26% (n=8) reported exceeding 2000 mcg/day. There were varying views on the usefulness of common approaches for ITB withdrawal evaluation, but 84% (n=26) respondents reported using >2 methods, with x-ray series used most widely. 71% (n=22) reported that patients may receive inpatient or intensive outpatient therapy following pump placement. Lastly, when asked about usefulness of ITB to manage dystonia, most responses were indefinite.
CONCLUSIONS: Consistent with our hypothesis, we observed varying levels of inter-institutional practice variation, depending on the context. These may be attributed to regional practice biases, respondent training/skill level, or clinical and/or demographic characteristics of the population served, providing scope for future research. Understanding divergent practice patterns is a critical step towards identifying research priorities to frame evidence-informed guidelines for ITB pump management.
KEYWORDS: Cerebral Palsy

11. Lower extremity dystonia features during a seated task in people with spastic cerebral palsy
Rust A (St. Louis, MO), Chintalapati K, Gandham S, Blackburn J, Gelineau-Morel R, Kruer M, Mingbundersuk D, O'Malley J, Tochen L, Waugh J, Wu S, Feyma T, Aravamuthan B

OBJECTIVE: Dystonia is a painful and debilitating symptom of cerebral palsy (CP). Unfortunately, dystonia is often underdiagnosed in children with CP, especially when it coexists with spasticity. To help address high rates of dystonia underdiagnosis in CP, we determined the key features experts use to assess lower extremity dystonia in people with CP.
METHODS: In this prospective cohort study, 8 pediatric movement disorders specialists assessed lower extremity dystonia in 24 videos of children with CP doing a seated alternating hand open-close task. The experts discussed each video during a consensus-building session and then each independently rated dystonia severity using the 10-point Global Dystonia Severity Rating Scale. Conventional content analysis of these discussions revealed salient features ("codes") that experts used to describe lower extremity dystonia. The most frequent codes were compared across dystonia severity groups.
RESULTS: "Foot inversion," "leg extension," and "hip adduction" were cited significantly more when experts discussed videos with dystonia. "Toe extension" was seen more when experts discussed mild dystonia while "foot dorsiflexion" was seen more when experts discussed the absence of dystonia. "Impact on function or mobility" was only mentioned when dystonia was present. "Asymmetric movements" were described more commonly when experts discussed the presence of dystonia but an "asymmetric baseline position" was described when experts discussed the absence of dystonia.
CONCLUSIONS: Expert clinicians use distinct movement features to assess lower extremity dystonia in people with CP. Attention to specific movements, such as foot inversion, leg extension, and hip adduction can help guide clinical recognition of dystonia.
KEYWORDS: Cerebral Palsy, Movement Disorders

12. Motor profile of genetic neurodevelopmental disorders
Santana Almansa A (Boston, MA), Registry Consortium B, Srivastava S

OBJECTIVE: In monogenic causes of autism spectrum disorder (ASD) and intellectual disability (ID), motor abnormalities are frequently present, and some may be associated with cerebral palsy (CP). However, the motor profile of genetic neurodevelopmental disorders (NDDs) remains undercharacterized. We aimed to characterize the motor profile of individuals with genetic NDDs using data from a national registry.
METHODS: We assessed data from the Brain Gene Registry (BGR). Among those with pathogenic or likely pathogenic variants, we evaluated prevalence of tone abnormalities and Gross Motor Function Classification System (GMFCS) levels.
RESULTS: Tone information was available for 69 individuals, representing 44 genes. Prevalence of hypertonia was as follows: SPAST (3/4), DYRK1A (1/2), GRIN2B (1/2), KMT2A (1/2), DNMT3A (1/4), SLC6A1 (1/4), CACNA1A (1/6), FOXP1 (1/1), TUBB3 (1/1) and ZMYND11 (1/1). Prevalence of dystonia was as follows: SPAST (3/4), DYRK1A (1/2), CACNA1A (2/6), DNMT3A (1/4), BCL11B (1/1) and FOXP1 (1/1).
GMFCS levels were available for 48 individuals. 89% had a GMFCS level of 3 or higher. Disorders in which there was at least one individual with a GMFCS level of 3 or higher included ANKRD11, ARHGEF9, ARID1B, ASH1L, ASXL3, BCL11B, BDNF, CACNA1A, CAMTA1, CHAMP1, CHD4, DNMT3A, FBXW11, GDI1, GRIN2B,

HIVEP2, KANSL1, KMT2A, MYT1L, NFIX, PTCH1, SCN2A, SETD5, SLC6A1, SPAST, TRIP12, TUBB2B, TUBB3, TUBB4A, WAC, ZMYND11 and ZNF711.
CONCLUSIONS: There is a growing number of genetic NDDs associated with motor phenotypes. Future directions include formally assessing which participants meet criteria for CP, which would continue to expand the genetic landscape of CP.
KEYWORDS: Cerebral Palsy, Neurodevelopmental Disorders, Neurogenetics

13. Thalamocortical overconnectivity in adults with bilateral cerebral palsy, white matter injury, and neuropathic pain

Salib P (Baltimore, MD), Riordan H, Hoon A, Jantzie L, Robinson S, Chin E

OBJECTIVE: To test the hypothesis that neuropathic pain in adults with cerebral palsy (CP) is caused by somatosensory overconnectivity in addition to previously-reported thalamic volume loss.
METHODS: We enrolled 12 adult volunteers (6 with CP, 6 typically developed). Adults with CP had predominant bilateral white matter injury, were independently communicative, and could lie still for MRI. Participants self-reported neuropathic pain (PROMIS v2 T-scores) and underwent 3T MRI (high-resolution anatomic MPRAGE and 2-shell HARDI). We examined correlations between somatosensory tract functional anisotropy (FA; assessed within MRICloud-defined regions of interest) and neuropathic pain scores. We also performed probabilistic tractography (MRtrix3 iFOD2)--visualizing streamlines to semi-quantitatively validate continuity of somatosensory tracts from spinal cord through thalamus through the posterior limb of the internal capsule (PLIC) to somatosensory cortex in the postcentral gyrus. FA-pain score correlations (Spearman's ρ) within adults with CP were tested against H0 of no correlation.
RESULTS: Study groups were similar in age and sex distribution, but adults with CP had higher neuropathic pain scores ($p=0.04$). Neuropathic pain scores in adults with CP were positively correlated with PLIC FA ($\rho>0.9$; $p<0.01$). HARDI tractography seeded from PLIC projected inferiorly (through thalamus to spinal cord) and superiorly (to sensory and motor cortex) for all participants. PLIC-postcentral gyrus projections were particularly exuberant in the individual with CP reporting the most neuropathic pain (sensory>motor projections).
CONCLUSIONS: Overconnectivity may represent a maladaptive response to impaired circuit maturation. Thalamic injury with thalamo-cortical overconnectivity is a promising diagnostic biomarker for central neuropathic pain in adults with CP.
KEYWORDS: Cerebral Palsy, Neuroimaging

14. Use of the Prechtl General Movements Assessment (GMA) for Early Detection of Cerebral Palsy in Infants with Hypoxic Ischemic Encephalopathy (HIE) that Underwent Therapeutic Hypothermia

Kerner-Rossi M (New York, NY), Gomes W, Bain J, Kim F

OBJECTIVE: To determine the associations between HIE clinical severity, neonatal course, and brain MRI injury pattern, with GMA performance at three months and diagnosis of CP before one year of age in infants with HIE that underwent therapeutic hypothermia (TH).
METHODS: Retrospective cohort study of 15 late preterm and term infants with HIE admitted to a level IV NICU who underwent TH. Based on modified Sarnat criteria, 67% (10/15) were categorized as having moderate HIE, 27% (4/15) severe HIE, and 6.7% (1/15) mild HIE. All underwent cEEG analysis throughout TH and rewarming and had a brain MRI obtained, which was scored individually using a standardized system.
RESULTS: To date, 20% (3/15) of infants (2 with severe HIE and 1 with moderate HIE) were diagnosed with CP before one year of age. Absent fidgety movements at 12-16 weeks postmenstrual age were 100% sensitive and 100% specific for CP. Grey matter injury score on MRI was the most predictive measure for absent fidgety movements and CP diagnosis prior to 1 year of age (sensitivity and specificity 100%). Seizure activity had 100% sensitivity and 72% specificity for absent fidgety movements and CP diagnosis.
CONCLUSIONS: Absence of fidgety movements on the GMA is associated with severity of hypoxic ischemic injury on MRI and CP diagnosis before one year of age. Incorporation of the GMA as an early outcome in the follow-up of infants with HIE who underwent TH may aid in the early identification of CP and allow for earlier counseling and intervention.
KEYWORDS: Cerebral Palsy, Neonatal Neurology, Neurodevelopmental Disorders

DIVERSITY, EQUITY, INCLUSION

15. From Coast to Coast- Unmasking the disparities in Early Developmental Screening

Anand P (New York, NY), Bheemavarapu B

OBJECTIVE: Developmental disorders, marked by deficits in physical, language, learning, or behavioral areas, significantly impacts life quality and social interactions. The American Academy of Pediatrics (AAP) advocates for universal screening for early diagnosis and intervention, enhancing outcomes for affected children. Our aim is to examine the current developmental screening prevalence and surveillance across varied demographics, focusing on factors underlying disparities.
METHODS: We conducted a comprehensive review of the combined 2020-2021 National Survey of Children's Health, a nationally representative survey of US children aged 9 to 35 months whose parent or caregiver had received a developmental screening using a parent-completed screening tool available through the nschdata.org website.
RESULTS: During 2020-2021, 34.8% of US children underwent developmental screening using a parent-completed

tool. However, screening rates exhibited significant regional disparities, ranging from 18.9% in Nevada to 50.6% in Oregon. Subgroup analysis further revealed consistently lower screening prevalence rates among specific demographic groups: Hispanic children (29.5%), children residing with caregivers other than parents (21.4%), households with incomes falling within the 0-199% range of the Federal Poverty Level (28.8%), uninsured children (15.5%), and children with public insurance only (29.3%).

CONCLUSIONS: National guidelines advocate screening at 9, 18, and 24-30 months, for early detection of developmental issues and timely intervention. Although the U.S. Department of Health and Human Services aspires to achieve a national screening rate of 35.8%, the present figure remains slightly below at 34.8%. Initiatives aimed at promoting the widespread adoption of standardized screening tools during routine well-child visits could boost children benefiting from screenings.

KEYWORDS: Diversity, Equity, Inclusion, Neurodevelopmental Disorders, Behavioral Neurology

16. Student-Led Initiative to Bridge the Gap Between Resource Awareness and Utilization for Pediatric Patients with Spina Bifida

Rodriguez L R (Houston, TX), Tripathy M, Pampattiwar T S, Feik M, Neerukonda S, Au j

OBJECTIVE: Individuals with disabilities, an underserved population within our community, experience higher rates of unemployment, poverty, and chronic diseases. These disparities exist within pediatric populations, such as those with spina bifida, who are at greater risk of living with obesity. Project Support, Empower, and Engage with the Disability Community (Project S.E.E.D) was developed by medical students with support from the Albert Schweitzer Fellowship to improve health and social quality of life (QOL) and address these disparities.

METHODS: Through the project, families of patients with spina bifida are screened for resource needs and subsequently connected with resources. To understand the role this initiative has in improving awareness of non-medical resources and fostering support for patients, surveys were completed by families before and after encounters to assess knowledge of resources. Parents' perceptions of their child's overall health and QOL were gathered with questions created using PROMIS metrics. Responses were collected using a 5-point Likert scale and analyzed with STATA.

RESULTS: Mean survey scores for categories related to resource knowledge, utilization, and QOL were not significantly different between pre-survey (n=65) and post-survey (n=16) responses. Notably, health-related QOL (4.04) had significantly higher scores than other categories (<2.63) in the pre-survey.

CONCLUSIONS: Though this study did not reveal significant findings between timepoints, the high baseline health-related QOL may be suggestive of the importance of multidisciplinary clinics for children with chronic illness. Further long-term investigation of these findings in a larger cohort would be useful given the limitations of this study.

KEYWORDS: Diversity, Equity, Inclusion, Education

17. Disparities in Social Determinants of Health Associate with Pediatric MS Compared to MOGAD

Kornbluh A B (Washington, DC), Har C, Suslovic W, Hague C, Merrill C, Kahn I, Wells E, Sepeta L

OBJECTIVE: Factors related to race, ethnicity, socioeconomic status, and local societal infrastructures lead to disparate multiple sclerosis outcomes. Research on similar associations in other pediatric acquired demyelinating syndromes (ADS) is lacking. Our study aims to explore social determinants of health (SDOH) in pediatric ADS utilizing childhood opportunity index (COI), area deprivation index (ADI), and social vulnerability index (SVI).

METHODS: Single center retrospective review comparing SDOH variables between pediatric multiple sclerosis (POMS) and pediatric myelin oligodendrocyte glycoprotein antibody-associated (MOGAD) patients using one-way ANOVA and linear regression.

RESULTS: Among 135 patients (76 POMS, 59 MOGAD), there were significant differences in race/ethnicity composition and SDOH variables. POMS patients, primarily Black (44%, $p=0.005$), had lower COI scores at national, state, and metro levels ($p=0.006$, $p<0.001$, $p=0.003$ respectively) compared to predominantly White (54%, $p=0.005$) MOGAD patients. All COI national sub-domains were lower in POMS, including education ($p=0.001$), health/environment ($p=0.011$), and social economic ($p=0.018$). POMS patients also showed higher ADI state percentile ($p=0.002$), national percentile ($p=0.04$), and SVI scores ($p=0.008$), indicating greater socioeconomic deprivation and vulnerability.

CONCLUSIONS: In this urban pediatric academic center analysis, POMS patients were more predominantly Black compared to predominantly White MOGAD patients. Across all measures, POMS patients were more disadvantaged with more socioeconomic vulnerabilities than MOGAD patients. These findings provide insights into the SDOH underpinnings of neuroinflammatory diseases in pediatric populations. Future studies will assess the impact of SDOH on neuropsychological outcomes in pediatric ADS and explore driving factors that may contribute to the development of disparities among pediatric neuroinflammatory diseases.

KEYWORDS: Diversity, Equity, Inclusion, Pediatric Demyelinating Disease, Neuroimmunology

18. Simplifying the transition to adult neurology care, the step we cannot afford to miss: A quality improvement initiative

Chiujdea M (Thornton, NH), Mann N, Heins M, Laurino J, Shanske S, Rashid-Khan T, Laine R

OBJECTIVE: Transitioning patients from pediatric to adult healthcare is complex, particularly within Neurology. Many patients remain in pediatric care far beyond childhood, creating access issues for pediatric patients. We describe a quality improvement initiative aimed at simplifying transition to improve the ratio of pediatric to adult patients in one Pediatric Neurology department.

METHODS: A multi-disciplinary Transition Task Force was developed in May 2022. Using quality improvement methodology, we iteratively designed interventions, including two pilots to increase transition planning and documentation of counseling. We developed two guidelines - one for transition to adult care and one for triage of new adult patients. We also provided resources for both providers and patients. A dashboard was developed to monitor visit data over time and qualitative feedback is solicited on an ongoing basis to drive improvements.
RESULTS: Between October 2022 and March 2024, visits for patients aged ≥18 decreased from 15% to 13%. Application of the ICD-10 code Z-71.89: Encounter for pediatric-to-adult transition counseling increased. Transition planning increased significantly from 13% pre-intervention to 61% post-intervention (p>.00000), and 21% patients had documented transfer plans to establish them with an adult provider for their next neurology visit. In April 2024, a department-wide rollout was initiated and new SMART aims were developed.
CONCLUSIONS: Creating infrastructure that simplifies transition is necessary to engage pediatric neurology providers in transition efforts. Using a quality improvement approach may be useful. Consistent positive messaging about transition and clearly outlined goals from leadership are essential, as is ongoing feedback from frontline staff to address barriers with transition.
KEYWORDS: Diversity, Equity, Inclusion, Lifespan Manifestations of Childhood Onset Conditions

19. Balancing Acts Amidst Inequity: Salary, Adequacy of Compensation, and Work-Life Balance of Women Neurologists

Miller D (New Orleans, LA), Xiang X

OBJECTIVE: Salary is overlooked in surveys and proposed solutions that assess physician happiness and workplace satisfaction. The goal of this study was to ascertain the relationship between salary, perception of compensation fairness and work-life balance in women neurologists in the US.
METHODS: This was a multicenter, observational, cross-sectional, quality improvement study. Analysis was performed on results of The Women Neurologists Group Compensation Survey, a nationally representative sample of women neurologists (N=368). The survey contained 40 items assessing many aspects related to compensation.
RESULTS: Statistical analysis was performed using SPSS Version 26. Median years post training was 5-10. 79% of women were full time, and 21% were part time. Salary data (n=356) showed a mean annual income of $291,887 with standard deviation of $95,671. Median was $275,000. Salary was positively and significantly correlated with years post training (r=0.214, p<0.001) and feeling adequately compensated (r=0.348, p<0.001). Salary was not significantly correlated with acceptable work life balance (r=0.068, p=0.255). Feeling adequately compensated was positively and significantly correlated with acceptable work life balance (r=0.329, p<0.001). Knowledge of inequity negatively and significantly correlated with salary (r=-0.175, p=0.022) and feeling adequately compensated (r=-0.350, p<0.001).
CONCLUSIONS: We present evidence that feeling fairly compensated is significantly associated with acceptable work-life balance, whereas absolute salary value is not. Thus, physicians' perception of compensation fairness may be a more important determinant of well-being than the absolute value of compensation. Those with the lowest salaries and who felt least fairly compensated reported greater knowledge of inequity. Subgroup analysis for child neurologists is ongoing.
KEYWORDS: Diversity, Equity, Inclusion

20. Enhancing SDOH Screening and Resource Connectivity in Pediatric Neurology: A Quality Improvement Initiative

Guzman-Karlsson M C (Houston, TX), Edmondson E, Evans B, Chandrasekar A, Peek C, Lee P, Gay C, DiCarlo S

OBJECTIVE: To enhance social determinants of health (SDOH) screening and resource connectivity in pediatric neurology at a large academic medical center, aiming to achieve a 50% improvement in screening rates and successful resource referrals within one year.
METHODS: Within a quality improvement (QI) framework, we used a survey-based problem analysis of neurology clinicians to identify barriers to SDOH screening and counseling. Utilizing a multidisciplinary approach, we engaged medical assistants to administer Hunger Vital Signs-based questionnaires and track responses in our electronic medical record (EMR). We integrated FindHelp.org modules within the EMR to facilitate counseling, supported by smart phrases to optimize neurology resident workflow efficiency. Outcome measures included the percentages of SDOH screenings and successful referrals, while process measures focused on staff training and EMR tool usage. Balance measures assessed social work referrals frequency and their impact on staff workload to ensure intervention sustainability.
RESULTS: Our analysis revealed critical barriers to SDOH screening and counseling, including time constraints, lack of training, unclear protocols, and inadequate tools. Most neurology providers (81%) expressed interest in EMR-integrated tools, prioritizing user-friendly and resource-linked functionality. Since the initiative's start, routine SDOH screening rates increased by 60%, with 25% of patients screening positive for food insecurity.
CONCLUSIONS: This QI initiative provides a framework for enhancing SDOH screening and counseling in pediatric neurology, equipping neurologists with the necessary knowledge and skills for efficient and effective intervention delivery. Future research will explore the longitudinal impact of SDOH on access to neurologic care, healthcare utilization, disease management, and patient outcomes.
KEYWORDS: Diversity, Equity, Inclusion, Education, Practice Parameters

21. Neuroscience Equity and Unity (NEU): A Multidisciplinary Approach to Promoting Diversity, Equity, and Inclusion in Neurology

Guzman-Karlsson M C (Houston, TX), Salazar K, Das A, Nnyagu A, Hardwick V, Risen S, Lotze T, Maletic-Savatic M, Edmondson E

OBJECTIVE: To describe the development and implementation of a multidisciplinary initiative to promote diversity, equity, and inclusion (DEI) in neurology that addresses health disparities and minority underrepresentation and serves as a framework for other institutions.
METHODS: The initiative assembled a diverse team of stakeholders from various disciplines and institutions within a large academic medical center. The project made use of technology for collaboration, conducted needs assessments, and developed a strategic plan. Targeted recruitment strategies, mentorship programs, DEI education, community outreach, and social determinants of health screening were implemented, utilizing a continuous feedback loop for refinement.
RESULTS: Since 2022, the project has fostered a network of 232 professionals, including pediatric and adult neurologists, neuroscientists, allied health professionals, trainees, and faculty. The initiative organized 11 grand rounds, 8 workshops, and 3 multicultural events, covering unconscious bias, cultural competency, health disparities, inclusive practices, and community-based participatory research. A "Brain Fair" targeting 42 underrepresented youth resulted in 92% of participants expressing interest in neuroscience-related careers. Social determinants of health screening was established in a pediatric neurology resident clinic, with a 60% screening rate and 25% food insecurity rate identified.
CONCLUSIONS: This initiative demonstrates the effectiveness of a synergistic, multidisciplinary approach in promoting DEI within neurology. By simultaneously addressing health equity, education, and workforce diversity, the project amplifies the impact of each aspect. The project's data-driven, community-centered approach and continuous refinement serve as a model for driving meaningful change in neurology.
KEYWORDS: Diversity, Equity, Inclusion, Education

22. Demographics of child neurologists practicing in the U.S. and Canada.

Brumback A C (Austin, TX), Funk A T, Cohen B H, Zupanc M, Pearl P, Wilson R, Carrasco McCaul M, Hassan A, Kim R, Hernandez R, Salter A, Waugh J

OBJECTIVE: To understand the demographics of child neurologists practicing in the United States and Canada.
METHODS: We identified child neurologists and neurologists who primarily treat children who practice in the U.S. or Canada. Participation was voluntary and anonymous. All data was collected and stored in REDCap. The study had the approval of an academic medical center institutional review board (IRB). Here, we report analyses of the age, gender, race / ethnicity, country of origin and medical training, sexual orientation, number of dependents, disability status, and history of adversity among the child neurology workforce.
RESULTS: Of the 2632 invitations sent, 51.9% participants responded. Of those, 72.4% completed the questionnaire completely.
Respondents completed residency over a broad time range: 1961-1980 (3%), 1981-1990 (10%), 1991-2000 (14.2%), 2001-2010 (23.3%), 2011-2020 (44.3%), and 2020 and after (5.2%). Age of respondents ranged from early 30's to late 70's years old.
Most respondents (55%) identified as female, with the proportion of women increasing from 20% in the 1961-1980 cohort to 66% in the 2011-2020 cohort.
Respondents self-identified with a wide range of racialized groups: White (64.2%), Asian (13.3%), South Asian (7.2%), Hispanic (6.6%), Middle Eastern / Southwest Asia / North African (3.1%), Sub-Saharan African or African American / Black (2.8%), or Multiracial (1.1%).
24.1% of respondents reported at least one indicator of surviving childhood aversity.
CONCLUSIONS: These preliminary analyses show that the demographics of the child neurology workforce is diverse and evolving. During the presentation, we will explore each of these characteristics and their relationships.
KEYWORDS: Diversity, Equity, Inclusion

23. Work settings of child neurologists practicing in the U.S. and Canada

Waugh J L (Dallas, TX), Cohen B H, Zupanc M L, Hassan A, Funk A, Kim R, Hernandez R, Salter A, Brumback A

OBJECTIVE: To understand the practice settings of child neurologists in the United States and Canada.
METHODS: We administered an electronic survey to physicians within the U.S. and Canada we had identified as child neurologists or neurologists who treat children as part of their practice. Participation was voluntary. All data were de-identified and stored in REDCap. The study had the approval of an academic medical center institutional review board (IRB). Here, we report analyses of board certification, type and location of practice, years in practice, if academic or private, subspecialty or general, salary, % time in clinical care and other professional activities.
RESULTS: Most respondents (94.6%) were certified by the American Board of Psychiatry and Neurology with Special Qualifications in Child Neurology. Most (59.2%) reported completing a subspecialty fellowship after residency. The most commonly reported subspecialty was epilepsy (59.2% of those completing fellowships). Most respondents worked within a university-based practice either within a department of Neurology (31.4%) or Pediatrics (33.5%). Many (15.1%) reported working at a free-standing children's hospital not affiliated with a university. Private practitioners made up a small fraction of child neurologists: solo practice with only Child Neurologists (6.2%), multi-specialty groups (3.8%), or combined Child and Adult Neurology (3.6%). Rural and low-population areas have few child neurologists.
CONCLUSIONS: These preliminary analyses suggest that the majority of child neurologists practice in a university setting. During the presentation, we will explore the types and locations of Child Neurology care compared to U.S. census data to identify geographical gaps in care access.
KEYWORDS: Diversity, Equity, Inclusion

EDUCATION

24. Child Neurologists' Opinions on Transition from Pediatric to Adult Care

Reddy M (Newark, NJ), Hayes-Rosen C, Reichner H, Grew E

OBJECTIVE: Transition from pediatric to adult care prepares patients for independent health management and self-advocacy. Inadequacies in transition are associated with poor health outcomes. This study evaluated child neurologists' opinions surrounding transition of care.

METHODS: An anonymous survey sent to a maximum of ten child neurologists from each state inquired about transition of care in their practice and barriers to transition, and included an optional section for elaboration.

RESULTS: The survey received 31 responses. 19/31 respondents predominantly serve low-income populations. 9/31 predominately serve patients who identify as ethnic minorities. 25/31 practice at academic centers. Average length of practice was 22.8 years.

30/31 respondents reported discussing transition of care with patients. On average, patients were 17.5 years old when discussions took place. The majority (17/31) ranked decreased comfort of adult neurologists with treating pediatric-onset illnesses as the biggest barrier. Respondents elaborated that few adult neurologists are willing to see their patients due to insurance concerns, discomfort treating pediatric-onset conditions, medical complexity, and/or accessibility concerns.

22/31 respondents recommended solutions. 9/22 recommended collaboration with adult neurologists to establish care for/increase comfort in treating adult patients with pediatric-onset conditions. 6/22 recommended early transition of care discussions. 4/22 reported success with a "Transition Clinic." 5/22 reported inability to transition patients to adult neurologists.

CONCLUSIONS: This survey identified child neurologists' viewpoints on barriers to transition of care and recommendations for more accessible transition. These findings can be used to develop solutions to ease transition of care.

KEYWORDS: Education

25. Development of an Interactive Online Training Module for Providing and Discussing a New Diagnosis of Autism Spectrum Disorder

Miller C T (Nashville, TN), Foster T E, Minor T J, Hine J

OBJECTIVE: Parents of children newly diagnosed with autism spectrum disorder report challenges with navigating the diagnosis, making sense of their child's developmental differences, and connecting to services. Therefore, we created an open-access online training module to provide a framework for professionals discussing a new autism diagnosis while acknowledging cultural contexts, common concerns, and misperceptions.

METHODS: An open-access online training module was created via the Articulate Rise 360 platform with topics including discussing a new diagnosis, promoting hope, cultural contexts, next steps, and commonly asked questions. The module includes modeled scripts, audio/visual examples, interactive tools such as flashcards, matching activities, and case-based learning. A voluntary pre- and post- survey method was utilized to evaluate the module.

RESULTS: Participants included professionals with and without prior specialized training in autism including advanced practice providers, physicians, psychologists, medical trainees, and graduate students. Most participants indicated that the training had a positive impact on future practice, provided them with "more comfort," and they felt "more prepared" for discussing the diagnosis. Preliminary data show an increase in participants average confidence levels across multiple practice parameters including discussing concerns for autism diagnosis, identifying autism characteristics in children 3 and under, making a formal autism diagnosis in children 3 and under, communicating with families about an autism diagnosis, counseling families on next steps, and discussing comorbidities.

CONCLUSIONS: This training facilitated preliminary steps in improving and standardizing care for patients with autism. Next steps include further data collection and analysis, as well as creation of standardized patient encounters.

KEYWORDS: Education, Neurodevelopmental Disorders

26. Strengthening Pediatric Neurology Quality through a Capacity-Building Approach for Clinicians & Staff

Albor L (Atlanta, GA), Shapiro R, Wood E, Encalarde T

OBJECTIVE: To design and test a new quality improvement (QI) capacity-building model tailored to educate pediatric neurology clinicians and staff

METHODS: This work will take place in three phases: 1) Design a light-touch QI training and support model accessible to Neurology clinicians and staff at all levels, and aligned with the Institute for Healthcare Improvement (IHI) Model for Improvement 2) Pilot the proposed capacity-building model 3) Evaluate the model's effectiveness upon completion in October 2024.

RESULTS: The planned pilot contains three components which are being implemented between April and October of 2024: four lunch & learns on core improvement science topics which are accessible to all Neurology clinicians and staff, a small cohort-based "quality incubator" whereby eight selected participants will combine classroom didactics with application via small-scale improvement projects of their choice, and monthly office hours offering individual coaching in process improvement, data analysis and project management by quality team members. The current model relies exclusively on already-budgeted FTE to design, execute, and support quality capacity building work in Neurology, making this initiative cost-effective and practical.

CONCLUSIONS: The development and implementation of tailored, accessible education and training in quality improvement may hold promise in driving Neurology quality while limiting costs and time. This model may be applicable within other institutions to foster a culture of quality improvement in pediatric neurology.

KEYWORDS: Education

27. Inpatient Implementation of Portable Ocular Fundus Photography Among Neurology Residents

Silverman A (Palo Alto, CA), Schwartz N, Beres S, Moss H, Galetta K

OBJECTIVE: Prior work has demonstrated utility of non-mydriatic fundus photography in evaluating emergency department neurological complaints. However, potential benefits of a portable fundus camera for neurology housestaff have not been explored.

METHODS: This study was approved by the local IRB to lease the Optomed Aurora® handheld fundus camera for 30 days. Residents took fundus photos for pediatric and adult patients with one or more of the following inclusion criteria: (1) Headache (2) Visual disturbance (3) Neuroinflammatory disorder (4) User discretion. Photos were uploaded to charts and reviewed by a neuro-ophthalmology attending. Housestaff completed deidentified surveys before and after the trial period; surveys were compared using non-parametric statistics (SPSSv29, significance set at $p<0.05$).

RESULTS: Images from 21 patients (42 eyes) were compiled. Compared to pre-trial surveys (n=13), aggregate unmatched post-trial surveys (n=12) across training levels revealed increased confidence using the camera ($p=0.004$), identifying ($p=0.02$) and describing ($p=0.033$) the optic nerve, identifying the macula ($p=0.004$), and fundus interpretation ($p=0.017$). Feedback thematic analysis and chart review revealed many benefits from clinical (improved fundus visualization, triage/discharge, sharing with offsite staff), educational (group discussion, repeated exams, learning anatomic variations), and health systems perspectives (reduced neuroimaging and lumbar puncture reliance, fewer ophthalmology consults, patient satisfaction).

CONCLUSIONS: Inpatient portable fundus photography is feasible and effective for rapid fundus visualization, enhancing the ability to share, document, and trend exams among neurology housestaff. Further work will entail permanently securing camera access, formalized training, streamlined staffing and billing, and broadening usage to additional cases.

KEYWORDS: Education, Neuroimaging

28. Feasibility of a Novel Immersive Virtual Reality Tool for Teaching Visual Field Deficits

Silverman A (Palo Alto, CA), Nevins A, Bloom C

OBJECTIVE: Incorporating immersive virtual reality (VR) into medical education wields the potential to enhance learning, though no studies have examined the feasibility of immersive VR for introductory neuro-ophthalmology.

METHODS: Following local IRB approval, an unbiased third-party consented first-year physician associate students in their preclinical neuroscience course. The class (n=28) attended a traditional neuro-ophthalmology lecture and then was randomized into two groups: half engaged in a problem-based learning seminar on visual fields, while the other half donned immersive headsets. The headsets ran software co-created by the Cleveland Clinic and Zygote®, comprising a three-dimensional, interactive, and multi-step module on visual pathway lesions and corresponding field deficits. Learners completed deidentified surveys before and after the curriculum. Results were compared using non-parametric statistics; thematic analysis was performed on qualitative data.

RESULTS: Students in the VR group (n=14) performed similarly on pre- vs. post-module knowledge assessments (63.2 vs. 66.6%, $p=0.34$), comparable to the seminar group (60.7 vs. 70.3%, $p=0.14$). On Likert scale post-module questionnaires, all students in the VR group agreed or strongly agreed that they would recommend the course. Most VR students felt the session enhanced neurologic knowledge (71.4%) and established clinical connections (85.7%). Narrative feedback revealed that students enjoyed the hands-on and three-dimensional aspects. Constructive feedback pertained to software troubleshooting and the desire for fewer students per session.

CONCLUSIONS: Immersive VR illustrating visual field deficits and visual pathway anatomy was feasible and well-liked. Although pre- vs. post-module knowledge assessment scores were similar, students shared that they found the module engaging, unique, and informative.

KEYWORDS: Education

29. Commitment to Patient Education Leading to High Rates of Lifestyle Changes and Improved Outcomes in Headache Patients

Hall M T (Florence, KY), Qaiser S

OBJECTIVE: This study aims to determine if educating headache patients on their condition and the rationale behind recommended treatment plans, including lifestyle changes, leads to high adherence rates and improved headache frequency and disability.

METHODS: A single-center retrospective chart review at The University of Kentucky Children and Young Adult Headache Center. Data from 200 initial consultation patients from 8/18/2022 - 6/28/2023 was obtained through a questionnaire and secured in RedCAP. Of these, 97 were included, excluding those lacking follow-up or missing data. At least half the initial consult time was spent on education with lifestyle discussions including increasing leafy green vegetable intake, meeting hydration goals, and adequate sleep. Questionnaires from follow-ups through 1/18/2024 were analyzed. A significance level with $\alpha=0.05$ was used for a Kruskall Wallis test and post-hoc Dwass-Steel-Critchlow-Fligner test using Jamovi software.

RESULTS: 97 patients were each given the opportunity to make up to 3 lifestyle modifications (291 potential changes), wherein 80.4% of actual changes were implemented. The groups that made 2 or 3 changes had a significantly greater reduction in PedMIDAS scores at follow-up compared to the 0-1 change group ($p=0.009$ and $p=0.012$ respectively), with no difference between the 2 and 3 change groups. The same pattern was observed for headache frequency, with significantly larger decreases in the 2 and 3 change groups ($p=0.050$ and $p=0.026$ respectively) compared to the 0-1 change group, but no difference between the 2 and 3 change groups.

CONCLUSIONS: By prioritizing patient education, clinicians have the power to effectively promote lifestyle changes resulting in improved outcomes.

KEYWORDS: Education, Headache

30. Neurologists Demonstrate Differential Learning Needs in Rett Syndrome Based on Results from an Online CME-certified Survey

Finnegan T (Newtown Square, PA), Aboulsaoud P, Hanley K, Neul J

OBJECTIVE: Rett syndrome (RTT) is a severe and progressive neurodevelopmental disorder that is characterized by a variety of neurologic and behavioral features. There remains limited data on the quality of care delivered to patients with RTT. The goal of this study was to gain insight into the gaps in confidence, knowledge, and competence regarding the recognition and management of RTT among neurologists.

METHODS: A continuing medical education (CME)-certified clinical practice assessment consisting of 25 multiple-choice questions on knowledge, competence, and confidence was made available to an audience of US-based neurologists. Questions categories included: pathophysiology, diagnosis, management, clinical trial data associated with RTT. Data for were collected from June 22, 2022 through August 31, 2022.

RESULTS: A total of 45 neurologists completed the survey. Approximately 70% of neurologists indicated low confidence in diagnosing and managing RTT. Topics associated with the greatest knowledge (50%-65% choosing a correct answer) included awareness of diagnostic criteria, the relationship between disease staging and disease phenotype, making a probable diagnosis of RTT, and the phenotypic relationship with MECP2 mutations. Topics associated with the greatest educational need (≤20% choosing the correct answer) included pathophysiologic mechanisms and the identification of atypical RTT symptoms. Questions on prognostic factors, treatment selection, and agents in development were associated with intermediate (21%-50% choosing the correct answer) educational need.

CONCLUSIONS: This study demonstrated that there is a spectrum of awareness across questions topics on RTT. Future education on RTT should focus on pathophysiologic mechanisms, symptoms of atypical RTT, the development of personalized treatment plans, and investigational therapies.

KEYWORDS: Education, Neurodevelopmental Disorders, Neurogenetics

31. Expert Perspective in the Diagnosis and Management of Late-Onset Pompe Disease: A Survey of 29 Specialists

Kronn D (Valhalla, NY), Schoser B, Peña L DM, Fults M, Gianatasio C, Vuong S, Greenwald J, Moss B

OBJECTIVE: To document expert clinical experience and recommendations in late-onset Pompe disease (LOPD) diagnosis and management.

METHODS: An international cohort of 29 clinicians with expertise in LOPD were invited via email to complete a 39-item survey from October through December 2023. Data were aggregated and analyzed to be utilized within a CME activity. Respondents were compensated for their time.

RESULTS: Of the 29 respondents (55% US, 45% international), the majority were adult neurologists (65%) and medical geneticists (34%). Most respondents (55%) felt that they were somewhat often referred patients with LOPD who had been inappropriately managed. Almost one-half (46%) felt that patients are not easily classified into categories of "classic infantile," "non-classic infantile," and "LOPD." When counseling patients on enzyme-replacement therapy (ERT), experts were most likely to recommend avalglucosidase alfa (79%) and cipaglucosidase alfa + miglustat (62%) compared with alglucosidase alfa (31%). When presented with a case study examining an 11-year-old patient with asymptomatic LOPD but abnormal laboratory findings (elevated creatine kinase and urine hexose tetrasaccharide), experts were split with 50% stating they would initiate ERT. The largest group of experts (45%) stated ERT efficacy begins to wane after 3-4 years and that nearly one-half of patients (48%) require switching ERT during their disease course.

CONCLUSIONS: Survey results underscore ongoing challenges in LOPD diagnosis and management. With broad agreement on ERT efficacy and switching strategies, challenges remain in disease categorization and ERT timing for asymptomatic patients with abnormal lab findings. These findings highlight the need for ongoing education and clinician collaboration to enhance care.

KEYWORDS: Education

32. Using Co-Design To Develop an Education Guide on Inclusive Care for Patients with Autism Spectrum Disorder (ASD)

Ibarra L S (San Diego, CA), Jindal A

OBJECTIVE: Current evidence suggests patients with autism spectrum disorder (ASD) experience increased medical and social inequities, as compared to neurotypical patients. The highest-rated barriers reported relating to communication: not feeling understood (67%) and difficulty communicating with their doctor (53%). Through a co-design process, the aim is to create educational material for medical professionals on how to identify and understand the nuanced needs of patients with ASD and their caregivers.

METHODS: We conducted 30 semi-structured interviews and co-design activities with 9 physicians, 12 medical students, and 9 caregivers to explore the context and constraints in improving representation of ASD patient care in medical education and healthcare system management. Five rounds of consensus coding, with 85% consensus, were completed to synthesize design goals for prototyping.

RESULTS: We derived a codebook of 89 codes. The most prevalent codes included: focusing medical curriculum on communication adaptations (26%) and patient need for environmental adaptations of clinics (39%). The most prevalent code for caregivers and experienced providers when asked about educational content was to include an adult transition care curriculum (10 mentions).

CONCLUSIONS: There exist many essential resources for the ASD community, yet there is a lack of awareness of resources by adult care providers and few resources for transition-age patients. The sudden lack of resources for both patient and provider leave these patients most vulnerable to inadequate care. Based on our findings, we plan to develop a

prototype of a healthcare curriculum focused on patient-centered accommodations for transition-age patients.
KEYWORDS: Education, Diversity, Equity, Inclusion, Neurodevelopmental Disorders

33. "Child Neuro Chat": Development and Distribution of a Child Neurology Podcast for Patients and Parents

Moss S N (Salt Lake City, UT), Orton K, Tam R, Wilson C

OBJECTIVE: Podcasts continue to rise in popularity to distribute medical knowledge. We developed a discussion-based podcast between medical providers and staff for patients and parents to improve access to reliable information regarding common child neurology topics. Our aim is to measure the impact through podcast listenership and download trends.
METHODS: The podcast titled "Child Neuro Chat" was developed with topics ranging from the basics of child neurology, how to prepare for visits, and discussions on epilepsy, headaches, neuromuscular, neonatal neurology, and more. Most episodes were recorded in a sound studio and published through Buzzsprout. Episodes were free to download via all major podcast directories. Episode and download data were collected from October 2019 - April 2024.
RESULTS: Fourteen episodes were released with 7075 total downloads (544 downloads/episode) and an average of 35 minutes/episode. The most downloaded episode focused on vaccines (N = 1023). Listeners spanned 6 continents, with the majority (77%) occurring in the United States and about 10% locally. Most downloads occurred via mobile devices (85%), and from Apple Podcast (49%) with a rating of 4.8/5 stars.
CONCLUSIONS: We developed a unique child neurology podcast hosted by medical professionals with a target audience of patients and parents. Our reach and reviews suggest that professionally guided medical knowledge on child neurology topics can be disseminated locally and globally and resonates with listeners. Improving access and delivering reliable information can improve health outcomes and trust in the medical system. Future works include episodes on cultural humility in child neurology and understanding the podcast's impact.
KEYWORDS: Education, Diversity, Equity, Inclusion, Practice Parameters

34. Developing Consensus in Child Neurology Residency Training Requirements using a Delphi-Based Process

Gottlieb-Smith R (Ann Arbor, MI), Gilbert D L, Rogers D A

OBJECTIVE: Recent surveys demonstrate that child neurologists favor revising the current training requirements; however, no formal consensus exists regarding specific changes. We aimed to understand current areas of consensus and develop a consensus training pathway.
METHODS: We invited a representative sample of board certified child neurologists to participate. Panelists evaluated 25 statements regarding current American Board of Psychiatry and Neurology (ABPN)/Accreditation Council of Graduate Medical Education (ACGME) requirements, 21 statements about core rotation durations, and 69 questions about which subspecialty rotations should be mandatory. Statements that failed to reach predefined levels of consensus (≥75%) or strong consensus (≥90%) were re-queried in round 2; panelists had access to anonymized comments. In round 3, panelists evaluated updated statements regarding individual rotation durations. The final modifications were presented in round 4 as a complete proposal.
RESULTS: Twenty-seven panelists participated representing diverse U.S. geographic regions, private and academic practice, educational and institutional leadership, and subspecialties. Consensus was reached on the age scope of child neurology practice spanning fetal period through adolescence. There was no consensus regarding current time requirements, current name of board certification, or other current ACGME program requirements. By round 4, consensus emerged for a set of requirements with the following rotations-months: neonatal and pediatric intensive care-4, emergency-1.5, adolescent-0.5, inpatient pediatrics-3, outpatient pediatrics-3.5, inpatient child neurology-9.5, outpatient child neurology-6, inpatient adult neurology-3, outpatient adult neurology-2, genetics-2, EEG/neurophysiology-2, neuroimaging-1, child psychiatry-1, and electives-7.5.
CONCLUSIONS: This national consensus confirms the appropriateness of revision of ACGME and ABPN training and certification requirements in child neurology.
KEYWORDS: Education

35. Perspectives and Progress in Mental Health Education During Early Pediatrics Residency Training

Rosen A (Philadephia, PA), Fletcher K, Lockwood K

OBJECTIVE: Mental health education during pediatrics training is required for ACGME standards and foundational for Child Neurology training. We aimed to evaluate a new mental health curriculum for pediatric residents based on self-report. We wondered how perceived competency would change after individual curricular elements and over intern year.
METHODS: We surveyed interns (N=59) through REDCap at orientation (N=52, 88%), the end of intern year (N=11, 18.6%), before and after an asynchronous anxiety learning module (N=40, 67.7%) and a live mild agitation simulation (N=26, 49.1%).
RESULTS: Feelings of "moderate" or "very much" confidence in assessment improved for anxiety (19.2% vs 36.4%), ADHD (21.1% vs 45.5%), and agitation (0% vs 27.3%) over the year, whereas depression was stable (28.8% vs 27.3%). Confidence in agitation assessment shifted from mostly "slightly" (44.2%) to "somewhat" (36.4%) and those reporting "not at all" decreased from 26.9% to 9.1%. Pre and post survey data from the agitation simulation (N= 26, 49%) show immediate increases in comfort (mean likert scale value 1.96 to 3.04) and confidence (1.73 to 2.96) with managing mild agitation, which persisted at 3 (N=33, 62.3%) and 6 (N=15, 28.3%) months. While most (73.1%) incoming interns identified that they required direct supervision of patients with mental health concerns, at the end of intern year most (70%) identified that they could be trusted with distance supervision.

CONCLUSIONS: After completion of one year of a mental health curriculum, interns increased their confidence in assessment and management of common conditions and identified less direct supervision need.
KEYWORDS: Education, Behavioral Neurology, Neurodevelopmental Disorders

36. Headache Action Plan Implementation for school setting

Rosengrant, E (Atlanta, GA), Forte J

OBJECTIVE: Headaches are challenging to treat in the school setting and delayed treatment can lead to more missed days of school and refractory headaches. Misinformation and mismanagement of headache pain in school can to further mental health issues resulting in increased headaches. Here we propose a plan to increase education and timely treatment of migraines in the school setting.
METHODS: We reviewed multiple headache action plans from different hospitals, including from the American Headache Society. Inclusion criteria include: publicly available information published on the websites from hospital systems, headache programs, and the American Headache Society. Exclusion criteria: any headache plan that is not from a hospital system, headache program, or the American Headache Society.
RESULTS: We investigated plans from Cincinnati Children's Hospital, Boston Children's Hospital, Children's Hospital of Philadelphia, and The American Headache Society. The plans were all similar in treatment plans and recommendations. Some variations were noted in formatting and medications used. Some were more open ended, where others listed commonly used medications such as ibuprofen, naproxen, or sumatriptan. Based upon these plans, we created our own plan that was tailored to our specific population and commonly used medications in our practice.
CONCLUSIONS: We have now created a headache action plan and we have disseminated this to our practice providers to be used in an inpatient and outpatient setting. A statewide presentation was given to school nurses educating them on the Headache Action Plan was completed. Future studies will look at efficacy and utilization of the plan.
KEYWORDS: Education, Headache

37. Parent Communication and Sibling Knowledge of Neurogenetic Conditions

Turnwald A (Cincinnati, OH), Rosenberg A, Collins-Ruff K

OBJECTIVE: Neurogenetic conditions impact the entire family unit. Limited research investigates how parents communicate about neurogenetic diagnoses with their unaffected children (siblings). Understanding parent communication, including barriers, will allow for the creation of targeted resources and best practice strategies for healthcare providers in discussing siblings with the family.
METHODS: A mixed method survey for parents and siblings, aged 7-17 yrs., was developed based on literature review and discussion with rare disease parents. Families were recruited through family support organizations.
RESULTS: All parents (n=72) reported they discussed the neurogenetic diagnosis with the siblings (n=72). Parents most commonly discussed delayed milestones and differences in attention from parents. 14 parents (19%) reported a healthcare provider asked about siblings' knowledge of the diagnosis or impact on the sibling. 86% of parents felt it would be helpful for a healthcare professional to provide advice or resources for talking with siblings. Although all parents reported discussing the diagnosis, 58 siblings (81%) wanted to learn more about the diagnosis and 29 siblings (40%) had questions about the diagnosis. The most common themes from sibling questions included cause of diagnosis and progression of symptoms.
CONCLUSIONS: Parents want additional support to discuss neurogenetic diagnoses with siblings, and siblings have unanswered questions and a desire to learn more about the diagnoses. To address sibling needs, healthcare professionals with knowledge of the neurogenetic diagnoses, including genetic counselors, can ask about siblings needs and provide families with available resources.
KEYWORDS: Education, Neurogenetics

38. "Breaking Bad- News: preparing Child neurology residents for tough conversations with families"

Roman A (Lexington, KY), Qaiser S, Schaefer S, Thamann A

OBJECTIVE: Understand how palliative care training in child neurology can improve the experience of residents, especially those in PGY 3 and beyond, as they often face difficult situations with families.
Assess whether a palliative care bootcamp should be part of the child neurology training process.
Practice a standardized approach for handling difficult conversations with families.
Enhance skills for discussing end of life situations and prognosis with families facing challenging circumstances.
Use simulated scenarios to improve the skills of child neurology residents to navigate those circumstances.
METHODS: Pediatric palliative department will offer) a bootcamp to child neurology residents (PGY2-PGY5) to teach and practice how to proceed with goals of care discussion, as well as difficult conversations with families.
Residents will complete a pretest before the bootcamp, a post test after the bootcamp and a third test after one month of in service work (either stroke, general neurology or child neurology wards). This will help measure the impact in preparing residents for real life situations.
RESULTS: Results pending analysis of pre and post tests from PGY2 to PGY5 child neurology residents, will happen in August.
CONCLUSIONS: Pending analysis of results.
KEYWORDS: Education, Global Neurology, Ethics

39. Reflective Practice & Learning (RP&L) for Fellows

DiMario Jr. F J (Hartford, CT), Zalneraitis E

OBJECTIVE: RP&L is a hypothesis driven analytical method whereby clinical trainees and faculty analyze and manage complex professional problems through collaborative

team mentoring by faculty and peers. We examined how RP&L can accelerate improvement in fellow skills by learning how to:

• Identify important psycho-social and career challenges they will face as a professional
• Enhance self-awareness and comfort with their personal reactions in challenging situations
• Develop a clear thought process and plan of action to help resolve those challenges and manage personal stress induced by those challenging situations for fellows and participating faculty

METHODS: A combined group of varying subspecialty fellows in training assembled each 4-6 weeks September through June. A seminar method comprised of six components similar to classic problem based learning was exercised. Seminar sessions incorporated six key components:

1. Presentation of a challenging case with "framing" questions posed (fellow)
2. Reflection directed at systematic analysis of pertinent circumstances (faculty sharing)
3. Formulation of a working hypothesis (diagnosis)
4. Development of a strategic plan of action
5. Summary and evaluation of discussion
6. Faculty review

RESULTS: The initial 4 years of the program incorporated 32 sessions, 8-18 (total=24) fellow participants per session. Fellows rated the peer support component and improved competence for navigating stressful professional encounters as the most important outcomes. A didactic summary sheet was prepared after sessions and pertinent references were subsequently shared with fellows.

CONCLUSIONS: An RP&L seminar series can be an important supplement to enhance trainee wellbeing, peer support and foster professionalism.

KEYWORDS: Education

40. More than a Checkbox: Implementing a Narrative-Based Child Neurology Resident Assessment

Latimer C (Aurora, CO), Stone R, Troy E

OBJECTIVE: End-of-rotation evaluations in graduate medical education are best utilized as assessments for learning. We aimed to design a narrative-based assessment that shapes the clinical and professional development of our learners.

METHODS: The 26 Accreditation Council for Graduate Medical Education (ACGME) Child Neurology milestones were translated into 24 questions and then mapped to clinical environments, creating 15 unique assessment forms. Evaluators included physicians, advanced practice providers, peers, nurses, and EEG technologists. Forms included up to 3 sections: (1) evaluators selected two competencies – a strength and an area for improvement, (2) evaluators provided narratives on one to four clinical or professional competencies of their choosing and (3) evaluators rated resident overall performance as either below, meeting, or exceeding expectations. Prior to project launch, a faculty development session addressed best practices in narrative feedback.

RESULTS: For 9 senior child neurology residents and 22 evaluators, 53 assessments or 5.9 per resident were completed from January to March 2024. This compares to 28 assessments or 3.1 per resident in the prior 3 months. The most common competencies chosen as strengths were outpatient management and communication, and the most common identified for improvement were localization/clinical reasoning, interpersonal communication, and physician role in healthcare. There were 243 narratives, and all available competencies were commented on at least once.

CONCLUSIONS: The narrative-based, adaptable evaluation system led to an increase in overall assessments submitted, and the comments were spread across all the available competencies. The next step would be to evaluate the quality of those comments.

KEYWORDS: Education

EPILSEPY

41. Healthcare Resource Burden of Selected Nonseizure Symptoms Among Patients With Lennox-Gastaut Syndrome (LGS) in the US

Lu M (Lexington, MA), Noman A, Kumparatana P, Taylor K, Ma X, Ip Q, Wei Y, Rao S

OBJECTIVE: To quantify healthcare resource utilization (HCRU) burden associated with nonseizure symptoms of interest (NSS; communication issues, lack of alertness, and disruptive behaviors) among patients with LGS.

METHODS: Using Komodo's Healthcare Map™ (2016-2022) closed claims data, this retrospective analysis included patients with ≥2 diagnoses of LGS. HCRU was compared between patients with and without NSS using negative binomial models during a similar continuously enrolled 12-month period.

RESULTS: Patients with LGS included 1754 with and 2924 without NSS. Of patients with NSS, 834 reported communication issues, 302 reported lack of alertness, 294 reported disruptive behavior, and 324 reported some combination of NSS. Median age was 13 and 18 years for patients with and without NSS, respectively. Most patients (NSS/without NSS) were male (57.5%/53.8%) and Medicaid-insured (78.1%/73.5%). Compared with patients without NSS at baseline, patients with NSS had higher percentages of comorbidities (NSS/without NSS), including autism spectrum disorder (23.2/18.2), other developmental delays (87.7/77.7), and brain congenital malformations (22.6/6.8); rates of seizures (any: 95.5/93.0; status epilepticus: 45.0/38.6) and seizure-related injuries (21.8/16.3) were also higher. During the 12-month follow-up, mean numbers of patients who utilized all-cause medical resources were significantly higher among those with NSS versus those without (NSS/without NSS, all $P<0.01$): inpatient stays (1.2/0.4), emergency room visits (2.0/0.9), outpatient visits (87.6/48.3), home health and durable medical equipment (62.7/48.1), and rescue antiseizure medications (2.3/1.9). The combination of NSS increased HCRU.

CONCLUSIONS: This real-world analysis demonstrated that patients with LGS with NSS had more HCRU than those without, and that NSS may add to the burden of patients with LGS.
KEYWORDS: Epilepsy, Neurodevelopmental Disorders

42. Optimizing responsive neurostimulation device parameters: increasing stimulation current may not always be the answer

Philliben R (Salt Lake City, UT), Swartwood S, Espinoza A C

OBJECTIVE: Responsive neurostimulation (RNS) is a closed-loop device that detects and responds to abnormal brain activity in epilepsy. Despite demonstrated efficacy, RNS lacks FDA approval in pediatric patients, prompting off-label use. Initial device optimization typically involves adjusting stimulation to increase charge density incrementally until desired response is achieved. We present a case of increasing current associated with worsening seizures at low charge density, with subsequent improvement upon decreasing current.
METHODS: Descriptive case report.
RESULTS: An 11-year-old female with drug-resistant epilepsy in the setting of bilateral frontal focal cortical dysplasia underwent intracranial electroencephalogram which revealed left orbitofrontal ictal onset. She underwent laser ablation of the left frontal region with subsequent return of seizures post-operatively prompting RNS implantation April 2022 with left anterior frontal cortical strip and left posterior-lateral orbital frontal depth electrodes. In January 2023, current was increased from 2.0mA (1.0 μC/m2) to 3.0mA (1.5 μC/m2) with minimal detection parameter adjustment. The following week clinical seizures and RNS long episodes worsened dramatically. No antiseizure medication changes or triggers were identified. Seizures did not improve with near return to prior detection parameters April 11th but improved rapidly with current decrease back to 2.0mA April 19th with a sustained improvement in seizures for eight months.
CONCLUSIONS: Increasing RNS stimulation current, even at low charge density, can result in a dramatic and sustained worsening of seizure activity in some patients. This highlights the necessity for additional research, ongoing clinical review of RNS data, and establishment of RNS programming clinical guidelines to optimize therapeutic benefits while minimizing adverse effects.
KEYWORDS: Epilepsy, Experimental Therapeutics, Early Stage Investigator

43. Effect of concomitant antiseizure medications on the safety and efficacy of ganaxolone for the treatment of seizures associated with CDKL5 Deficiency Disorder (CDD): Findings from the Phase 3 MARIGOLD Study

Flatt J (Radnor, PA), Rajaraman R, Amin S, Aimetti A, Hulihan J, Perry M S

OBJECTIVE: In the Marigold Study (NCT03572933), major motor seizure frequency (MMSF) was reduced with ganaxolone treatment by a difference of 27.1% over placebo. Here we report the safety and efficacy of ganaxolone in patient subgroups who were taking the most frequently-used concomitant antiseizure medications (ASMs).
METHODS: N=101 patients with CDD aged 2-19 were enrolled in Marigold. Patients were permitted to take ≤4 concomitant ASMs during the study. The four most frequently-used ASMs were valproate (n=34), levetiracetam (n=26), clobazam (n=25), and vigabatrin (n=24). Efficacy was assessed by the placebo-adjusted percent reduction in MMSF during the 17-week treatment period versus baseline. Safety outcomes included treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs).
RESULTS: The greatest reductions in MMSF were observed in patients who were taking clobazam or valproate; a 53.4% (28.1–83.1) and 46.1% (13.4–78.2) Hodges-Lehmann difference (95% CI) was observed in these groups, respectively. The difference was 15.9% (-19.4–76.8) and 14.2% (-13.2–37.3) in patients who were taking vigabatrin and levetiracetam, respectively. TEAEs and SAEs were similar in ganaxolone-treated patients across all concomitant ASM subgroups. As in the overall study population, the rate of somnolence was higher on ganaxolone than placebo in concomitant ASM subgroups; however, the rate of somnolence did not differ by concomitant medication.
CONCLUSIONS: Reduction in MMSF was greater for patients who were taking concomitant clobazam or valproate. However, these results may be confounded by baseline differences in patient characteristics in concomitant ASM subgroups and varying placebo responses. Safety findings were comparable between ASM subgroups.
KEYWORDS: Epilepsy

44. Interictal Cardiac Changes in Children with Pharmaco-Resistant Epilepsy

Ibrahim A I (Ismailia, Egypt), Soliman W S, Mesbah B M, Salem A S

OBJECTIVE: To study the prevalence of left ventricular dysfunction and cardio-autonomic imbalance among children with drug-resistant epilepsy.
METHODS: A comparative cross-sectional study that included 40 children with drug-resistant epilepsy (cases group), and 40 healthy age- and sex-matched children (control group). left ventricular function was evaluated by M-mode, two-dimensional, pulse-wave Doppler, and tissue Doppler (TDI) echocardiography while cardiac autonomic function was assessed through heart rate variability measurement (using 24-hours Holter electrocardiographic study).
RESULTS: All time domain measures were found significantly lower in the patient group compared with control group, in the values of SDNN (P=0.003), SDANN (P=0.002) and RMSSD (P=0.006). As for frequency domain measures, mean HF parameters were significantly lower (P=0.035); while mean LF parameters and LF/HF ratio were significantly higher (P=<0.001) in the patient group when compared with the control group. As regard left ventricular function, there was no significant difference between cases and controls regarding all standard echocardiographic parameters. Using standard Doppler and tissue Doppler, there was evidence of subclinical left ventricular

dysfunction among epileptic children as evidenced by elevated myocardial performance index (MPI) (P=0.001). Finally, there was no significant correlation between duration of treatment or frequency of seizures with any of cardiac abnormalities.
CONCLUSIONS: children with drug-resistant epilepsy showed significant cardio-autonomic and subclinical left ventricular dysfunctions. These abnormalities were independent from duration of epilepsy, frequency, and type of seizures.
KEYWORDS: Epilepsy

45. Challenges Associated With Enrolling Pediatric Patients With Treatment-Resistant Epilepsy Aged 2–5 Years in a Clinical Trial and Lessons Learned for Future Trials

Segal E B (Hackensack, NJ), Wheless J W, Zafar M, Shih E, Ngo L, Rabinowicz A, Carrazana E

OBJECTIVE: We identified study-population challenges for a clinical trial evaluating diazepam nasal spray as immediate-use antiseizure medication for seizure clusters in patients aged 2–5 years. We also examined approaches to improve future study designs. Diazepam rectal gel is approved in the US for this age group; diazepam nasal spray is approved for patients aged ≥6 years.
METHODS: We retrospectively reviewed protocol amendments, screen-rate data, and blood-draw requirements to identify study-population challenges.
RESULTS: Identified challenges included protracted enrollment, elevated screen-failure rate, and need for multiple blood draws. In the original protocol, sequential cohorts aged 4–5 and 2–3 years were to be enrolled, which accounted for 2 screening failures and limited enrollment (n=5) over 12 months across 12 sites. The 2-cohort limitation was removed, allowing for more rapid enrollment (n=30) over the subsequent 12 months while achieving similar-sized final cohorts (2–3 years, n=18; 4–5 years, n=17). Several patients could not return to the site during the 21-day window between screening and baseline (eg, due to illness). In future trials, an increased screening window and consideration of exclusion criteria to allow mild nonfebrile illnesses may mitigate this. Particular challenges associated with very young patient age and multiple blood draws were preemptively mitigated using "sparse sampling" plus pharmacokinetic modeling to reduce draws per patient and the total number of patients needed.
CONCLUSIONS: Identification of challenges associated with enrollment of young children provides clarity for shaping protocols to address recruitment barriers, prevent discontinuation, and minimize protocol amendments.
KEYWORDS: Epilepsy, Education

46. Responsive Neurostimulation in Pediatric Drug Resistant Epilepsy: A Retrospective Case Series

Purosky I (Grand Rapids, MI), Bercu M M

OBJECTIVE: Epilepsy, affecting 470,000 children in the United States, presents a substantial healthcare challenge, with 20% experiencing drug-resistant epilepsy(DRE)1-3. The consequences of DRE include an elevated risk of premature mortality from seizure-related accidents, status epilepticus, and sudden unexpected death in epilepsy2. While deep brain stimulation(DBS) and responsive neurostimulation(RNS) have demonstrated efficacy in the adult epilepsy population, their use in children lacks approval from the Food and Drug Administration(FDA).
METHODS: We performed a retrospective(IRB approved) chart review on pediatric DRE patients (n = 31) who were treated with the RNS System at Helen Devos Children's Hospital(Grand Rapids, MI). All patients included in the study were treated for six or more months. Seizure reduction percentages were calculated via comparison of patients' observed seizure frequency at pre-implantation and their most recent follow-up visit post-implantation. The determination of seizure frequencies at baseline and post-implantation are from patient, parent, and clinical observation histories
RESULTS: Bilateral RNS systems were placed in 4 patients, while 27 patients only had one RNS placed. Among the 31 patients, 74% experienced a seizure reduction of 50-100% via calculated seizure reduction. Within those patients, 26% had >90% seizure reduction, with some even experiencing total seizure freedom. This population had 45% of patients verbalize noticeable improvement in quality of life.
CONCLUSIONS: Acknowledging potential long-term consequences of pediatric epilepsy on brain growth, this study explores RNS as a less invasive and safe surgical technique for both focal and generalized epilepsy, emphasizing dual benefits of seizure freedom and possible superior cognitive outcomes when compared to the untreated population.
KEYWORDS: Epilepsy, Neurodevelopmental Disorders, Behavioral Neurology

47. Ethosuximide: Drug Induced Lupus and Systemic Lupus Erythematosus in Children

Geraldino E (Dallas, TX), Sandhu S, Sirsi D

OBJECTIVE: Describe the clinical presentation of ethosuximide drug-induced lupus (DIL) and systemic lupus erythematosus (SLE) in children.
METHODS: A single-center retrospective study was conducted on pediatric patients with epilepsy who developed lupus-like symptoms while taking ethosuximide. We describe the demographics, clinical presentation, rheumatologic work-up, and clinical course.
RESULTS: Ten patients were identified, 50% with DIL and 50% with SLE. The median age was 5 years (range: 2-12 years). Most were female (80%) and Hispanic (70%). The most common indication for ethosuximide was Childhood Absence Epilepsy (60%). The median ethosuximide dose was 23 mg/kg/day (range: 14-26 mg/kg/day), with a median blood level of 70.5 ug/mL (range: 36-109 ug/mL) at the time of symptom onset.
The most common symptoms at presentation were arthralgias (60%) and gastrointestinal symptoms (40%). The median time from the start of ethosuximide to symptom onset in DIL was 2.25 months (range: 0.25-12 months), compared to

12 months (range: 3-72 months) in SLE. Autoantibodies present were Anti-Histone (100%), ANA (80%), and Anti-dsDNA (70%). Two-thirds of those diagnosed with DIL had positive dsDNA antibodies that later became negative.
Ethosuximide was discontinued in all patients, and symptoms resolved in those diagnosed with DIL. However, 90% of patients diagnosed with SLE continued to experience flares and remained on chronic immunosuppression.
CONCLUSIONS: Children presenting with lupus-like symptoms while taking ethosuximide should be evaluated for drug-induced lupus (DIL). Ethosuximide can also unmask clinically silent systemic lupus erythematosus (SLE) and screening for SLE and rheumatology referral is indicated. The association noted in Hispanic patients needs further investigation.
KEYWORDS: Epilepsy

48. Seizure Management of Infants with Hemimegalencephaly Undergoing Transarterial Embolization

Gumayan R L F (Washington, DC), Buraniqi E, Ruffini L, Tsuchida T, Pearl M, Anwar T

OBJECTIVE: Hemimegalencephaly is a congenital brain malformation associated with early-onset intractable epilepsy with longer seizure duration correlated with worse neurodevelopmental outcomes. Serial transarterial embolization (TAE) is an effective treatment for neonates and infants with hemimegalencephaly who are too young for surgical hemispherectomy. This study describes the institutional practice for seizure management of infants with hemimegalencephaly during staged embolizations.
METHODS: We performed a retrospective electronic chart review of patients who underwent TAE from 8/2018 to 11/2023. We reviewed their clinical presentation and summarized seizure management through the stages of embolizations.
RESULTS: Eight neonates met the criteria for TAE. The mean age of seizure onset was 10 days old (0-28 days) with the average age of first embolization at 49 days old (13-71 days). Seven neonates had diffuse hemispheric cortical involvement while one had multilobar involvement; four had a pathogenic variant in the mTOR pathway genes. Four patients underwent 3 stages of embolization. Four patients required more due to greater hemispheric enlargement or residual arterial supply.
The most common medications on admission included phenobarbital, levetiracetam, and vigabatrin. Patients were on 8 different antiseizure medications during peak seizure burden, staggered every 2-3 hours. Midazolam infusion was used transiently during embolizations. Following the final procedure, seizure control was achieved in seven patients, while one was discharged to hospice. Most were discharged on 3-4 medications, most commonly levetiracetam, phenobarbital, vigabatrin, and oxcarbazepine.
CONCLUSIONS: Neonates and infants undergoing TAE for hemimegalencephaly require many seizure medications transiently but after the final TAE are rapidly decreased to more typical refractory epilepsy polytherapy.
KEYWORDS: Epilepsy, Neonatal Neurology, Neurocritical Care

49. Five-Year Outcomes of Pediatric NCL2 Patients Treated with Cerliponase Alfa: A Retrospective Case Series

Halabi M (Irvine, CA), Lynskey C, Pedroza S, Sponberg R, Fote G, Wang R, Olaya J, Steenari M

OBJECTIVE: Neuronal ceroid lipofuscinosis type 2 (NCL2), characterized by deficiency of the enzyme tripeptidyl peptidase 1, manifests in childhood and leads to progressive neurological decline, including seizures, motor regression, and cognitive and visual impairment. Cerliponase alfa, an enzyme replacement therapy (ERT), has shown to significantly reduce motor and language function decline when compared with the natural history of NCL2. The long-term clinical outcomes of patients on ERT remain insufficiently documented. In this single-center case series, we describe the 5-year outcomes of 5 patients with NCL2 treated with cerliponase alfa.
METHODS: A retrospective review was completed on 5 patients with NCL2 on cerliponase alfa at a single pediatric hospital. Data was collected on each patient's presentation and clinical course before and after starting cerliponase alfa including seizure burden, vision changes, language and motor regression, and movement disorders.
RESULTS: All patients presented with seizures of varying semiology around age 3. The majority had global atrophy with cerebellar predominance on brain MRI around the time of NCL2 diagnosis. After initiating cerliponase alfa, parents reported a subjective improvement of symptoms. Following several years of therapy, all patients required several antiseizure medications and exhibited movement disorders, including dystonia, myoclonus, spasticity, and chorea.
CONCLUSIONS: Despite experiencing subjective improvement in seizure burden and initial improvement in motor and language function upon initiating cerliponase alfa, patients show evidence of disease progression after several years on the therapy. While ERT helped to slow the disease process, further work on other treatments such as gene therapy is critically needed to stop NCL2 disease progression.
KEYWORDS: Epilepsy, Neurodevelopmental Disorders, Neurometabolic

50. An Examination of Ketogenic Diet Patients and Initiations in Home vs Hospital Settings: Effects on Outcomes

Stillman C (Denver, CO), Silveria L, Kennedy K, Oliver J, Conley A

OBJECTIVE: The ketogenic (KETO) and modified Atkins (MAD) diets are used for treating refractory epilepsy with efficacy and safety initiating diets IP (inpatient) or OP (outpatient). Our aim was to assess if diet initiation setting corelates with outcomes and laboratory values
METHODS: We performed a retrospective analysis of 157 patients 2007 - 2022. We documented the setting of diet initiation (IP/OP), the diet type (KETO vs. MAD),

bicarbonate levels, demographics, ketone levels, seizure reduction, presence of a gastrostomy-tube and ratio each visit.
RESULTS: The IP cohort had a higher rate of starting Keto (99%) compared to OP (58%). Diet ratios at visit 1 (V1) varied between the IP (>50% >3.5) and OP groups (9% >3.5)G-tube rates were higher for IP (46%) than OP (24%). Seizure improvement at V1 occurred in 75.9% of IP vs. 38.9% from OP . Excluding MAD, 75.6% of IP reported seizure improvement vs. 45% of OP. At visit 3 there was no statistical difference in seizure improvement between the groups. Ketone levels (V1) were higher (p=0.003) for patients initiating IP [median IQR 4.09 (2.73, 6.15)] compared to those who started OP (median IQR 2.46 [1.03, 4.93]). Bicarbonate levels were not significantly different
CONCLUSIONS: We found that patients were more likely to report seizure improvement if they initiated diets in an IP setting. This improvement dissipates by visit 3. The IP groups was more likely to be on KETO, have higher ketones, higher ratio and more likely to have gastrostomy tube. Bicarbonate values were not different
KEYWORDS: Epilepsy, Lifespan Manifestations of Childhood Onset Conditions

51. Implications of Family Exchanges on Outcomes and Laboratory Values for Children Treated with a Ketogenic Diet

Stillman C (Denver, CO), Oliver J, Silveira L, Conley A, Kennedy K

OBJECTIVE: The ketogenic (KETO) and modified Atkins (MAD) diets have been used as effective ways to treat refractory epilepsy for years. Our aim was to assess if communication in the 1st month of diet (defined as number of exchanges between families and Keto team) (RD or APP) within the first month on diet correlated with outcomes.
METHODS: We performed retrospective review of 157 patients who started ketogenic diet 2007 - 2022. We counted the number of exchanges occurring in the first month after initiation. We documented the setting of diet initiation (IP/OP), duration on diet, presence of gastrostomy tube, the diet type (KETO vs. MAD), total length on diet, bicarbonate levels and ketone levels.
RESULTS: Exchanges were higher for patients on KETO (median IQR 7 (4-12.5) than MAD (median IQR 3 (1-5) (p=0.001). There was no association between exchanges and setting of diet initiation (p=0.289) or presence of gastrostomy tube (p=0.408). There was a significant correlation between length of time on diet and reduced number exchanges [rho (95%CI) -0.28 (-0.43, -0.12)]. The number of exchanges (vV1) was not related to age child (p=0.152), bicarbonate level (p=0.884) or ketones levels (0.148)
CONCLUSIONS: amilies reached out more when children were initiated on KETO as compared to MAD. Families that remained on diet longer, reached out less . The number of exchanges does not correlate with bicarbonate of ketone levels. Gastrostomy presence does affect exchanges (at V1).
KEYWORDS: Epilepsy

52. Vagal nerve stimulation with rapid titration for treatment of super refractory status epilepticus in febrile illness in a pediatric patient: a case report

Jbarah A (Atlanta, GA), Lin J, Bhalla S, Kannan V, Wolf D, Holt P, Chern J

OBJECTIVE: Febrile Infection-Related Epilepsy Syndrome (FIRES) is a subtype of new-onset refractory status epilepticus with fever. Standard treatments include antiseizure medications (ASM), immunotherapies, immunomodulators, and ketogenic diet. Although neuromodulation is utilized in chronic intractable epilepsy, there is less known about its efficacy for status epilepticus. We describe a case of FIRES that was managed with vagal nerve stimulation (VNS) which was refractory to standard therapies.
METHODS: Chart review was performed.
RESULTS: A 4-year-old female with bicuspid aortic valve, repaired aortic coarctation, and ventricular septal defect presented with fever, seizures, and altered mental status. Semiology was left eye deviation, blinking, nystagmus, and right-sided mouth pulling. EEG showed multifocal polyspike waves with subclinical bifrontal seizures. Brain MRI showed mild diffuse atrophy. Seizures were refractory to multiple ASMs, midazolam, ketamine, and pentobarbital infusions, plasmapheresis, steroids, IVIg, anakinra, and ketogenic diet. VNS was turned on upon implantation on hospital day (HD) 31. VNS was titrated to 2.5 mA output current in 10 days (HD 40) and 58% duty cycle by 13 days (HD 43) after implant. Ketamine and midazolam drips were weaned off on HD 36 and 81, respectively. Seizures decreased over course. The patient was extubated and transferred to inpatient rehab and discharged home after 5 months on 5 ASMs and 4: 1 ketogenic diet.
CONCLUSIONS: The case demonstrates the effectiveness of rapid VNS titration for FIRES in a pediatric patient with a significant cardiac history without adverse effects. VNS can be a potential therapy for acute management of super-refractory status epilepticus.
KEYWORDS: Epilepsy, Neuroimmunology

53. Using the Electronic Health Record to improve seizure treatment in a pediatric hospital

Hickman E T (Washington, DC), Safari P, Abera S, Badh R, Vasiliadis A, Harrar D, Saha A, Wells E

OBJECTIVE: 1) Develop a reporting system that identifies inpatients at risk for seizures and 2) Implement a seizure rescue medication orderset to facilitate ordering PRN antiseizure medications.
METHODS: A Seizure Trigger tool was developed through iterative work between neurology investigators and informatics specialists using HealtheIntent. The program uses ICD10 codes compiled by clinical investigators to identify patients at risk for seizures through the Electronic Health Record and also identifies whether a PRN seizure rescue medication is ordered. Following the implementation of the Seizure Trigger tool in December 2021, a Seizure Rescue Medication orderset was implemented and incorporated into the existing Hospitalist Admit Plan and PICU Admit Plan with Acute

Care and ICU specific dosing for seizure rescue medications, respectively. Efforts to educate providers about the plans are ongoing with the goal of increasing orderset utilization.
RESULTS: Following implementation in February 2022, the orderset was utilized 24 times in the next month. One year later from February-March 2023 the orderset was utilized 43 times in the same time period, an increase of 1.8 fold. Utilization has increased by an average of 8% per month due to ongoing education.
CONCLUSIONS: The HealtheIntent Seizure Trigger Report enables fast, systematic identification of inpatients at risk for seizures. It has been used to evaluate and enhance the efficacy of the Seizure Rescue Medication orderset implemented in February 2022. Tracking rescue medicine ordering across units and care teams has enabled development of targeted interventions to improve safety and outcomes for at-risk inpatients.
KEYWORDS: Epilepsy, Practice Parameters

54. Identifying Cell-Type Specific Somatic Variants in Focal Cortical Dysplasia Causing Intractable Epilepsy

Huynh C L (Columbus, OH), Mashburn-Warren L, Rivaldi A, Navarro J, Strawser C, Koboldt D, Ostendorf A, Miller K, Bedrosian T

OBJECTIVE: Malformations that affect as low as <1% of the brain cell population, such as focal cortical dysplasia (FCD), can have drastic effects including developmental delay, intellectual disability, and epilepsy. FCDs are associated with at least half of drug-resistant epilepsy cases, requiring surgical intervention to relieve the seizures. About half of the surgically resected lesions have identified pathogenic somatic variants, However, over half have no identified mutation in the resected FCD tissue or blood. Therefore, we aimed to utilize a novel approach to identify and characterize potential variants.
METHODS: Current methodologies utilize whole exome sequencing (WES) on bulk tissue, often resulting in inadequate detection of low-frequency somatic variants. Our approach selectively enriches cell types-–neurons, astrocytes, and oligodendrocytes-–and performs deep WES to increase the probability of variant detection. We validated this using a patient sample (JLE-50) harboring a known somatic variant (PTPN11) as a control.
RESULTS: In the case of JLE-50, the level of somatic variance in PTPN11 differed among the enriched cell types. Notably, oligodendrocytes exhibited a higher expression (8.25% variant allele frequency) compared to neurons and astrocytes. By employing a sample with a known mutation, our approach successfully validated the enrichment and detection of low-frequency somatic variants in oligodendrocytes.
CONCLUSIONS: The differential expression across cell types underscores the importance of cell-type specificity in understanding molecular mechanisms of disease. Enhanced detection of cell-type specific candidate somatic mutations enables a deeper understanding of drug-resistant epilepsy and FCD-related diseases. This advancement in genomic analysis holds promise for advancing personalized therapies and improving patient care outcomes.
KEYWORDS: Epilepsy, Neurogenetics, Neurodevelopmental Disorders

55. Caregiver-Reported Seizure Outcomes With Real-World Use of Cannabidiol (CBD) in Tuberous Sclerosis Complex (TSC): Interim Results From the BECOME-TSC Survey

Wheless J W (Memphis, TN), Koenig M-K, Wilson S ML, Samanta D, Krueger D, Meitzler S, Kaye C, Leary L, Danese S, Saurer T, Simontacchi K, Rajasekaran K

OBJECTIVE: BEhavior, COgnition, and More with Epidiolex® in TSC (BECOME-TSC) is an ongoing caregiver survey quantifying effect of CBD on seizure and nonseizure outcomes in people with TSC. Here we report preliminary seizure-related outcomes of the survey.
METHODS: Caregivers of people with TSC using CBD (Epidiolex®, 100 mg/mL oral solution) for ≥6 months completed an online survey, rating their impressions of change using a symmetrical Likert scale (worsening–improvement).
RESULTS: At this analysis, 17 caregivers had completed the survey. Mean (SD) patient age: 14.6 (8.1) years. Median (IQR) age at seizure onset: 6 (4–12) months. History of infantile spasms: 59% of patients. At CBD initiation, the greatest proportion of patients experienced focal onset seizures with impaired awareness (41%) and focal to bilateral tonic–clonic seizures (41%); respondents rated these seizure types as most frequent (29% each) and severe (29% each). Median CBD dose: 21 mg/kg/d. The most common concomitant ASM: everolimus (35%). Improvements in overall seizure frequency and severity were reported by 88% of respondents each; 6% reported worsening in seizure frequency. Seizure freedom (for ≥the past month) was reported by 55%. Improvements were commonly reported in frequency of seizures that involve movement or stiffening of both (71%) or one side (67%) of the body, infantile spasms (67%), and status epilepticus (67%). Most respondents reported decreased rescue medication use (80%), occurrence of seizure-related injuries (76%), and hospitalizations (71%).
CONCLUSIONS: In this preliminary report, caregivers of people with TSC perceived improvements in seizure frequency and severity and had more seizure-free days/week since initiating CBD.
Funding: Jazz Pharmaceuticals
KEYWORDS: Epilepsy

56. Does electroencephalography help predict long term outcomes after withdrawal of antiseizure drugs in seizure-free patients: a retrospective study

Ghawji M (Dallas, TX), Al Nimir H, Talai A

OBJECTIVE: Patients with epilepsy who have been in seizure remission for two years might consider discontinuing antiseizure medication (ASM) which carries risk of seizure recurrence and refractory epilepsy. The objective of our study is to identify whether abnormal electroencephalogram (EEG) at time of withdrawal of ASM would predict seizure

recurrence and if so, looking at which epileptiform abnormality is more likely to be associated with seizure recurrence.
METHODS: We reviewed 106 charts of 1095 available pediatric epilepsy patients who were weaned off ASM following two years of seizure freedom thus far. Data extracted from charts to identify patient background, epilepsy parameters, genetic testing and treatment modalities. Data analysis was based on individual variables. Survival curves were computed.
RESULTS: Preliminary data of patient charts reviewed showed a seizure recurrence of 23% and EEG abnormality was not a predictor of seizure recurrence or time to seizure recurrence. Further analysis of features of epileptiform abnormality on EEG based on prevalence and location did not show statistical difference in rate of seizure recurrence.
CONCLUSIONS: According to the results of this study, EEG at the time of withdrawal cannot be used as a predictor of seizure recurrence. The main limitations of these results were that they were based on a retrospective chart review and a small sample size; however, we aim to review all 1095 charts.
KEYWORDS: Epilepsy, Practice Parameters

57. Caregiver-Reported Nonseizure Outcomes With Real-World Use of Cannabidiol (CBD) in Tuberous Sclerosis Complex (TSC): Interim Results From the BECOME-TSC Survey

Wheless J W (Memphis, TN), Wilson S ML, Koenig M-K, Samanta D, Krueger D, Meitzler S, Kaye C, Leary L, Danese S, Saurer T, Simontacchi K, Rajasekaran K

OBJECTIVE: BEhavior, COgnition, and More with Epidiolex® in TSC (BECOME-TSC) is an ongoing caregiver survey to quantify effect of CBD treatment on seizure and nonseizure outcomes in people with TSC. Here we report preliminary nonseizure behavioral and cognitive outcomes from the survey.
METHODS: Caregivers of people with TSC treated with CBD (Epidiolex®, 100 mg/mL oral solution) for ≥6 months completed an online survey, rating their impressions of change using a symmetrical Likert scale (worsening–improvement).
RESULTS: At this analysis, 17 caregivers had completed the survey. Mean (SD) patient age: 14.6 (8.1) years. Median (IQR) age at seizure onset: 6 (4–12) months. History of infantile spasms: 59% of patients. Median CBD dose: 21 mg/kg/d. The most common concomitant ASM: everolimus (35%). Most frequently diagnosed co-occurring conditions: developmental delay (71%) and autism spectrum disorder (65%). Severe–profound intellectual disability was reported in 65% of patients; 6% had fluent verbal language. Compared with the pre-CBD initiation period, respondents most commonly reported definite improvements (for ≥the past month) in a patient's ability to be happy (71%), look up or smile when someone says their name (69%), communicate they want more of something (67%), learn new things (63%), be aware of surroundings (63%), and communicate they are uncomfortable (63%). Definite worsening was reported by ≤2 respondents in domains that included restriction in patient activities, difficulties with eating, using repetitive words/phrases, repetitive behaviors, impulsivity, and overactivity/hyperactivity.
CONCLUSIONS: These preliminary results show that caregivers of people with TSC perceived improvement in outcomes related to TSC-associated neuropsychiatric disorders since initiating CBD.
Funding: Jazz Pharmaceuticals
KEYWORDS: Epilepsy

58. Characterization of Epilepsy in Children with Septo-Optic Dysplasia

McCarty G (Louisville, KY), Iyer M, Danieli H, Karakas C, Singer E

OBJECTIVE: Septo-optic dysplasia (SOD) is a heterogenous neurodevelopmental condition characterized by the triad of optic nerve hypoplasia, absence of the septum pellucidum, pituitary hormone abnormalities and/or dysgenesis of the corpus callosum. SOD can be associated with seizures, but the presentation is not well-described. This study aims to characterize epilepsy in children with SOD.
METHODS: Children (<21 years) diagnosed with SOD (n=52) between 2018 and 2023 were identified through chart review.
RESULTS: We identified 22 (42%) patients with a history of seizure and SOD. MRI findings in addition to SOD triad included schizencephaly (n= 8), ventriculomegaly (n= 6) and polymicrogyria (n= 3). The mean age of seizure onset was 3.14 years (SD: 4.61, range nine days to sixteen years). Seizure types included focal (n=17) and generalized (n=5). Four patients (18%) had a history of infantile spasms. EEG showed diffuse slowing (n=6), focal epileptiform discharges (n=16), generalized epileptiform discharges (n=2) and normal findings (n=4). Thirteen patients were taking ≥ 2 anti-seizure medications at the last follow up. One patient tried a ketogenic diet for drug-resistant epilepsy (DRE). No patients had any surgical intervention for DRE. The average follow-up duration was 4.5 years (SD: 2.9). Eight patients (36%) have been seizure free for at least one year, ten (45%) have been seizure free for less than one year (range 2 weeks to 9 months), and four (18%) continue to have seizures.
CONCLUSIONS: Children with SOD are at risk of developing DRE. Neurologists should be aware of common structural comorbidities and epilepsy presentations in patients with SOD.
KEYWORDS: Epilepsy, Neurodevelopmental Disorders

59. Time to Targeted Treatment and Cognitive Outcomes in Rasmussen Syndrome.

O' Keeffe Donohue J (Boston, MA), Martino D, Cortina C, Zhang B, Ailion A S, Stredny C M

OBJECTIVE: Rasmussen syndrome (RS) is a unihemispheric inflammatory disorder typified by hemiplegia, epilepsy, and neurocognitive deterioration. Earlier surgical or targeted medical intervention may be associated with improved outcomes, but data is limited and conflicting in some series. Hence, we

aim to assess the effects of time to targeted medical and surgical treatment on outcomes in RS at our institution.
METHODS: We retrospectively investigated 16 patients diagnosed with RS between 2003 and 2024 who underwent neuropsychological assessment (NPA), including 3 non-surgical, 4 focal resection/ablation, and 9 hemispherectomy cases. Nine patients had 2 or more NPAs, which in 2 focal resection and 3 hemispherectomy cases included both pre- and post-operative NPA. The age-appropriate Wechsler IQ measure was given for most patients (WISC-4 or 5 n=16; WAIS-4 n=3; WPPSI-4 n=6; DAS-2 n=3), and the most recent measure was used in the analysis for those with serial testing. We performed statistical analyses investigating predictors of cognitive outcomes.
RESULTS: Longer duration from diagnosis to surgery was associated with lower verbal IQ (rho=-0.714,p=0.047). Use of IVIg (n=12) was associated with higher full scale IQ (median (IQR) (SS=76 (74 - 87) versus SS=38.5 (33 - 44),p=0.038) and verbal IQ (SS=81 (78 - 93) versus SS=49 (43 – 55),p=0.045). Time to targeted medical management was not significantly associated with IQ scores.
CONCLUSIONS: Time to surgery and the use of IVIg were associated with cognitive outcomes in our cohort. Larger studies powered to characterize these relationships and better identify predictors of outcome are needed in RS to improve the trajectory of the disease.
KEYWORDS: Epilepsy, Neuroimmunology

60. Reducing Diagnosis and Treatment Delays in Hospitalized Patients Monitored on EEG Using Quality Improvement Methodology

Albor L (Atlanta, GA), Cavallo M, Wood E, Selawski R, Lamar M, Algee S

OBJECTIVE: In our high-volume tertiary academic center, staffing limitations require outsourcing of EEG technologists and epileptologists to maintain consistent, 24/7 monitoring and diagnosis of inpatients on EEG. Outsourced staff monitor remotely from across the country. These factors create barriers to communication and may cause delays in care. Patient safety events reported through our notification system are classified as 'D' or greater when delays in diagnosis or treatment led to temporary patient harm or worse. The objective of this quality initiative was to reduce the incidence of these events in our hospitalized neurology patients monitored on EEG.
METHODS: We implemented several interventions to reduce such safety events: standardization of documentation for patient check-ins, education for EEG technologists and providers on staying vigilant during night shift, increase in communication between EEG technologists and providers during shift changes, and utilization of EEG software tools. Interventions were assessed using PDSA cycles.
RESULTS: At baseline, our center reported an average of four serious patient safety events annually. After implementing our interventions, there were no D level events involving diagnosis and treatment in EEG patients reported between October 2022 and March 2024.
CONCLUSIONS: Diagnosis and treatment delays affecting hospitalized patients on EEG significantly impact quality of care and status epilepticus is a neurologic emergency. Breakdowns in communication and shift changes were the primary drivers for these delays, which can be difficult to target with interventions. Despite this, strategies to encourage communication and accountability resulted in a 16 month period with no diagnosis or treatment delays resulting in patient harm.
KEYWORDS: Epilepsy

61. Presurgical Brain Network Analysis via Interictal EEG Predicts Seizure Outcomes after Corpus Callosotomy in Children

Ntolkeras G (Boston, MA), Pimenta de Figueiredo V L, Makaram N, Stone S, Pearl P, Rotenberg A, Grant E, Tamilia E

OBJECTIVE: Corpus callosotomy (CC) is a palliative surgical procedure for drug-resistant epilepsy (DRE) aiming to reduce severity/frequency of generalized seizures by disconnecting the two cerebral hemispheres. However, seizure outcomes after CC are variable and difficult to predict. We tested whether the analysis of pre-CC epileptogenic brain networks, obtained by interictal EEG recordings, predicts post-surgical seizure outcomes in children.
METHODS: We analyzed interictal scalp EEG from 30 children (median age: 10.7 years, IQR: 6.6-14,) with DRE who underwent CC with known seizure-reduction outcome (Excellent: >90%, Intermediate: 50-90%, Poor: <50%). We estimated brain functional connectivity in 6 frequencies (delta, theta, beta, alpha, gamma, broadband) and computed: within-hemisphere connectivity (WH-connectivity), between-hemisphere connectivity (BH-connectivity) and inter-hemispheric asymmetry. We tested whether these EEG network characteristics correlate with patient's outcome (Spearman correlation) and predict the likelihood of excellent seizure-reduction (ROC-curve analysis; Excellent vs. Intermediate/Poor).
RESULTS: Gamma-network characteristics directly correlated with post-CC seizure reduction: the greater the asymmetry and the BH-FC, the greater the reduction (R=0.4; p<0.05). BH-connectivity, WH-connectivity and asymmetry of the gamma-network were able to predict dichotomized outcome with an area-under-ROC-curve (AUROCC) of 87-88% and accuracy of 83%. Additionally, high WH-FC and high BH-connectivity in the alpha network predicted dichotomized outcomes with an AUROCC of 85-86% and accuracy of 77-80%.
CONCLUSIONS: Presurgical brain network analysis, through interictal scalp EEG, predicts post-CC seizure outcomes in children with DRE. We found that disrupting over-connected brain networks with high interhemispheric asymmetry may underlie the efficacy of CC and predicts excellent post-CC seizure reduction. Future studies comparing post-CC connectivity changes may help support these findings.
KEYWORDS: Epilepsy

62. Clinically meaningful reduction in drop seizures in patients with Lennox-Gastaut syndrome treated with cannabidiol (CBD)

Specchio N (Rome, Italy), Auvin S, Greco T, Lagae L, Nortvedt C, Zuberi S

OBJECTIVE: Evaluate threshold for a clinically meaningful reduction in drop seizures associated with Caregiver Global Impression of Change (CGIC) scores of 'slightly improved'/better or 'much improved'/better in patients with Lennox-Gastaut syndrome (LGS) receiving CBD.

METHODS: Post hoc analysis of RCTs (NCT02224560; NCT02224690) in patients with LGS receiving 10 or 20 mg/kg/d plant-derived highly purified CBD (Epidiolex®; 100 mg/mL oral solution). Drop seizure frequency reduction from baseline and CGIC scores at end of treatment were analyzed using receiver operating characteristic and distribution-based methods to quantify the clinically important response (CIR) and minimal clinically important difference (MCID) in seizure reduction thresholds, which were anchored to CGIC ratings of 'slightly improved'/better (scores 1–3) or 'much improved'/better (scores 1–2).

RESULTS: Of 215 patients, 129 (60%) reported 'slightly improved'/better and 67 (31%) 'much improved'/better. Spearman's correlation between CGIC scores and monthly drop seizure reduction was 0.47 (P<0.001). Best CIR thresholds for drop seizure reduction were −30.6% for CGIC 'slightly improved'/better (accuracy: 72%) and −49.6% for 'much improved'/better (accuracy: 69%); MCIDs (half standard deviation) were −21.0% and −18.4%, respectively. CIR thresholds were consistent between subgroups (eg, age or clobazam use) and the overall population. Based on best-fit CIR thresholds, 124/215 patients (58%) had 'slightly improved'/better and 87/215 (40%) had 'much improvement'/better response.

CONCLUSIONS: Based on a 'slightly improved'/better CGIC, the best fit threshold was approximately −30% for a CIR and −20% for MCID in seizure reduction. Anchoring between drop seizure change and CGIC may be appropriate (correlation >0.30) for defining clinically meaningful thresholds and warrants further research.

Funding: Jazz Pharmaceuticals

KEYWORDS: Epilepsy

63. Predictors of the Transition from Pediatric to Adult Epilepsy Care

Sondhi J (Pittsburgh, PA), Ali E, Trivedi K, DeCarvalho S, Kazmerski T, Kirkpatrick L

OBJECTIVE: To identify predictors of discussion about transition from pediatric to adult care, transfer to adult care, and retention in adult care among people with epilepsy.

METHODS: We reviewed medical records for individuals with epilepsy age ≥15 years seen outpatient by pediatric neurology in 2019. We evaluated whether they had documentation of transition discussion, if they transferred to adult care, and/or if they were retained in adult care (defined as ≥1 appointment/year and ≥1 year from transfer to study end) from 2019-2022. Excluding individuals who died or were discharged, we performed logistic regression for transition discussion, transfer, and retention, adjusting for sex, age, race/ethnicity, distance from institution, zip code median household income, rurality, drug-resistant epilepsy (DRE), intellectual disability (ID), and technology-dependence.

RESULTS: We tracked 274 individuals (50% female, median age 18, 84% white, 1.5% Hispanic, 24% DRE, 25% ID). Excluding 14 who died and 28 who were discharged, 57/226 (25%) had a documented transition discussion and 115 (51%) transitioned (median age 20 years). Of 95 eligible individuals, 77 (81%) were retained in adult care. Predictors (p<0.05) of transition discussion included older age (aOR 1.44, 95% CI 1.22, 1.70) and absence of ID (aOR 4.17 [1.51, 11.11]). Predictors of transfer included older age (aOR 1.19 [1.02, 1.39]), documented transition discussion (aOR 3.25 [1.48, 7.13]), and DRE (aOR 2.41 [1.10, 5.28]). We identified no significant predictors of retention.

CONCLUSIONS: Discussion of transition promotes transfer to adult care among people with epilepsy. Interventions may improve transition for this population, especially those with ID.

KEYWORDS: Epilepsy

64. Predictors of epilepsy surgery outcome among children with Infantile Epileptic Spasms Syndrome

Sun J B (Los Angeles, CA), Nariai H, Rajaraman R, Salamon N, Sankar R, Mathern G, Fallah A, Hussain S

OBJECTIVE: Infantile epileptic spasms syndrome (IESS) is a severe form of epileptic encephalopathy, often associated with medication refractoriness and adverse cognitive/behavioral outcomes. For select patients, surgical resection of epileptogenic brain regions can be curative. However, prediction of post-surgical outcome is challenging, and prior studies offer conflicting data as to which factors best predict post-surgical outcome. We set out to identify predictors of seizure freedom among a large, single-center cohort of children with IESS.

METHODS: We conducted a retrospective cohort study of children with IESS who underwent epilepsy surgery. Using bivariate logistic regression, we evaluated candidate predictors of 1-year postoperative seizure freedom, including lateralization/localization of MRI, FDG-PET, and EEG abnormalities, as well as etiology, age at surgery, presence of other seizures, and resection size.

RESULTS: We identified 96 children with IESS who underwent surgical resection, median (interquartile range) age of onset of IESS and surgical resection were 5.8 months (2.7–7.9) and 27.7 months (17.1–75.1), respectively. Twenty-nine (30%) children exhibited seizure recurrence within 1 year. Seizure recurrence was associated with presence of contralateral abnormalities on interictal EEG (OR 4.0; 95% CI 1.5–10.6; p<0.01), MRI (OR 3.9, 95% CI 1.5–10.4, p<0.01), and PET (OR 3.5; 95% CI 1.4–8.8; p=0.01). Of note, 14 (15%) cases exhibited seizure freedom at 1 year despite having contralateral abnormalities on EEG or neuroimaging.

CONCLUSIONS: Discordance of EEG and neuroimaging abnormalities appear to be key predictors of short-term post-surgical epilepsy outcomes. Further study is warranted to

evaluate longer-term outcomes, including developmental and behavioral endpoints.
KEYWORDS: Epilepsy, Early Stage Investigator

65. The EEG microstate alteration in children with febrile seizures

Jang H N (Seoul, Republic of Korea), Ahn S-H, Kim S, Jeong D-H, Moon J-H

OBJECTIVE: Febrile seizures are the most common seizure disorder in childhood. Children with simple febrile seizures (SFS) usually have a good prognosis, while complex febrile seizures (CFS) are associated with a higher risk of temporal lobe epilepsy, and cognitive dysfunctions. Microstate analysis of EEG can reflect the temporal dynamics of brain signals and the dynamic synchronization of brain neural networks. This study is aimed to analyze the topographical alteration in patients with SFS and CFS using microstate analysis.
METHODS: This study was performed with patients with febrile seizures in Soondchunghyang Cheonan Hospital from Mar 2023 to April 2024. Patients' stage II sleep EEG data were subjected to EEG microstate analysis. The microstate mean duration, frequency per second, and time coverage were analyzed using Mann-Whitney U-test.
RESULTS: A total of 27 patients were enrolled in this study, SFS (n=13), and CFS (n=14), there were no differences in age of patient group and sex. The Time coverage and the mean duration of microstate D in the SFS were higher than that of the CFS and microstate B ($P<0.01$) in SFS was lower than that of the CFS ($P<0.05$). The occurrence of microstate D was higher in the SFS group than in the CFS ($P<0.05$).
CONCLUSIONS: This study found a significant microstate alteration between the SFS and the CFS patients. These topological alterations might be applied to early detection of epilepsy in children who previously experienced febrile seizures, using machine learning in the future.
KEYWORDS: Epilepsy

66. School Supports in Pediatric Epilepsy Care

Miyanji H H (Winston Salem, NC), Thibodaux L K, Reisinger D L, Wikel K, Curtin M

OBJECTIVE: Pediatric epilepsy has a ~0.6% frequency and is associated with neurocognitive deficits even after seizure control. Early intervention of academic support may positively impact cognitive functioning to maximize academic potential. We describe a hospital-based school program's (HBSP) impact in acquiring school supports (Individualized education plan [IEP], Section 504 Accommodation Plan [504]) for patients with seizures or epilepsy.
METHODS: HBSP data were collected within a midwestern children's hospital during 2021-2022 and 2022-2023 years, yielding 48 unique patients with seizures or epilepsy. Approximately 27.9% of the patients had >1 HBSP consult during this period. Patients' demographics were collected: sex (male 52.1%, female 47.9%), race (white 68.8%, black 29.2%, Asian 2.1%), ethnicity (~17% Hispanic/Latinx).
RESULTS: Prior to 2021-2022, 27 patients had existing supports (IEP N=24; 504 N=3). Following HBSP contact, 7 patients received support recommendations (IEP N=2, 504 N=5). Patients who identified as Asian were statistically more likely to receive a 504 recommendation $X2(4, N=68)=30.267$, $p<0.001$. Statistically significant differences by medical team [504 $X2(16, N=68)=43.178$, $p<0.001$ and IEPs $X2(16, N=68)=35.841$, $p=0.003$] and patients with/without a true epilepsy diagnosis [504 $X2(2, N=67)=21.121$, $p<0.001$ and IEPs $X2(2, N=68)=13.885$, $p<0.001$] regarding recommendations were seen.
CONCLUSIONS: Prior to the study, patients had a high IEP/504 rate, but 10% of patients received recommendations for school support during the study. Limitations include small sample size without existing school supports and lack of clarity regarding HBSP role in existing support group (N=27). Based on current literature, many children with epilepsy would benefit from academic supports; engagement with an HBSP may support attainment.
KEYWORDS: Epilepsy, Education, Practice Parameters

67. Predictors of Autism at Onset of Epilepsy in Children: Results from a Population-Based Study

Saify M-S (Rochester, MN), Katusic M-K, Myers S-M, Voigt R-V, Nickels K-N, Wirrell E-W

OBJECTIVE: To identify factors correlating with higher risk of autism in children presenting with new-onset epilepsy, utilizing a population-based birth cohort.
METHODS: The Olmsted County birth cohort included children whose mothers were resident in Olmsted County, Minnesota at the time of the child's birth (1976-2000) and through 3 years of age. School and medical records were reviewed for autism, using a research definition (ASD-R), and the cohort was also screened for epilepsy diagnosed before 19 years of age. Characteristics of epilepsy in children with and without ASD-R were compared.
RESULTS: Of 30,490 individuals in the birth cohort, 257 (0.84%) had a diagnosis of epilepsy. Of these, 55 (21.4%) met criteria for ASD-R. At initial presentation, children with coexistent epilepsy and ASD-R versus epilepsy alone had younger age at epilepsy onset ($p=0.003$), higher likelihoods of structural vs other etiology ($p<0.001$), lesional focal epilepsy or Developmental and Epileptic Encephalopathy (DEE) versus other epilepsy type ($p=0.001$), status epilepticus ($p=0.013$), intellectual disability ($p<0.001$) and abnormal neurological examination ($p<0.001$) and were more likely to have a history of prenatal ($p=0.014$) and perinatal ($p=0.013$) complications. Furthermore, they had a higher likelihood of generalized slowing on initial EEG ($p<0.001$) and significant abnormality on MRI ($p=0.04$).
CONCLUSIONS: Coexistent ASD in epilepsy may be predicted by early age of epilepsy onset as well as several factors indicative of higher likelihood and greater degree of underlying brain pathology. Children with these risk factors should undergo early and rigorous screening for autism as they are at high risk of this comorbidity.
KEYWORDS: Epilepsy, Neurodevelopmental Disorders, Lifespan Manifestations of Childhood Onset Conditions

68. Caregiver Measures of Stress in Recollection of Childhood Seizure Events

Ray C (Atlanta, GA), O'Banion D, Diaz A

OBJECTIVE: Some patients having seizures do not remember the event but develop psychological sequelae. Little is known about the psychological sequalae of caregivers witnessing their child experience serious health events. It is possible that a single seizure is traumatic enough to induce PTSD symptoms in caregivers; therefore, we expect health implications for caregivers and repercussions on the child from caregivers with PTSD.

METHODS: During clinical histories in a child neurology clinic visit, caregivers' autonomic responsivity to stress was assessed with galvanic skin response (GSR) measures. Quiet baselines and recordings during the caregivers' retellings of events were obtained. GSR peaks above baseline were compared between groups presenting with seizure and groups presenting with headaches. There are 30 cases and 30 controls. Follow-up interviews were conducted using a PTSD symptom scale assessing for symptoms after the event.

RESULTS: In a similar study, skin conductance maximum value minus average baseline value were found to be predictive of PTSD. Preliminary analysis with 30 cases and 14 controls does not reveal trauma symptoms in caregivers recalling their child's seizure. Around 10% of these caregivers were shown to screen positive for PTSD. Controls' data is limited with data collection ongoing.

CONCLUSIONS: The lack of trauma symptoms may be due to environment of outpatient setting with prior study collecting data in the emergency department closer to time of trauma. Our study raises concern of probable PTSD in 10% of caregivers given the remarkable seizure frequency in children. Early intervention for caregivers and trauma-informed care need to be considered in seizure clinics.

KEYWORDS: Epilepsy, Lifespan Manifestations of Childhood Onset Conditions

69. Clinical Validation of SCN1A variant-phenotype association tool

Carson R (Boston, MA), O' Keeffe Donohue J, Valentine R, Ruiz I, Moufawad El Achkar C

OBJECTIVE: Early diagnosis of pathogenic variants in the sodium channel alpha 1 subunit (SCN1A) gene has significant management implications. The most common phenotypes associated with Loss of Function of SCN1A are Dravet Syndrome (DS) and Genetic Epilepsy with Febrile Seizures Plus (GEFS+), but it can be difficult to determine the phenotype early in the disease course. A prediction tool was published by Brunklaus in 2022 using age of seizure onset and genetic variant. The goal is to validate this tool in our patient population and examine additional clinical variables to aid in early diagnosis.

METHODS: We performed a retrospective review of patients with SCN1A variants at Boston Children's Hospital. Inclusion criteria included having a pathogenic, likely pathogenic or VUS in SCN1A and meeting modified delphi criteria. SNC1A variants were examined with the novel prediction tool. Additional early manifesting clinical variables were examined.

RESULTS: Of the 121 patients identified, 73 met inclusion criteria (50 DS and 23 GEFS+). The prediction tool had a sensitivity of 1, specify of 0.43, positive predictive value of 0.79, and negative predictive value of 1 for diagnosing DS in our population. Changing the threshold for DS diagnosis significantly alters these characteristics. Additional early variables of significance: history of status epilepticus (SE), SE before 24 months of age, and multiple seizure characteristics.

CONCLUSIONS: The prediction tool published by Brunklaus in 2022 has low specificity for diagnosing DS in our population. Changing the threshold for DS diagnosis changes performance characteristics. Additional consideration of other early markers could improve performance.

KEYWORDS: Epilepsy, Neurogenetics, Early Stage Investigator

70. A retrospective analysis of complex febrile seizures at one tertiary children's hospital

Gupta D (Orange, CA), Crawford J, Schweig M, Kalawi A, Totoiu M, Pearson R, Fernandez A

OBJECTIVE: Complex febrile seizures (CFS) were initially treated with anti-seizure medications in the 1950s. We now know complex febrile seizures have a slightly higher risk of epilepsy than the general public but do not require seizure medications for treatment. We performed a retrospective study to better evaluate the risk of epilepsy in patients with CFS, the acute management, and those that were misdiagnosed.

METHODS: Cases with a diagnosis code of CFS were analyzed from the years 2012 to 2022 that presented to one tertiary children's hospital. Several investigators individually analyzed charts of patients; evaluating demographics, diagnosis, work up, and follow up of a group of patients. Information was separated into different diagnoses groups. Student's T-test, chi square analysis and logistic regression were utilized to evaluate trends.

RESULTS: 345 patients were part of the final analyses set. The median age of patients was 21 months with 58% males and 39% females. 253(73%) of patients met the diagnosis of CFS based on diagnostic criteria. 116 had follow up after first visit. 36(31%) patients went on to have a confirmed epilepsy diagnosis. 92(23%) patients were misdiagnosed with complex febrile seizures and had a concurrent diagnosis of developmental delay.

CONCLUSIONS: With this retrospective data collection, CFS were studied to better understand risk factors of epilepsy as well as its management. This study shows a higher percentage of progression to epilepsy than previously noted. Patients with developmental delay were often also misdiagnosed with CFS showing the importance of consensus in diagnostic criteria.

KEYWORDS: Epilepsy, Practice Parameters

71. Characterization of Seizures in Children and Adolescents with B-Cell Acute Lymphocytic Leukemia: A Single Institutional Retrospective Study

Trivedi A M (San Diego, CA), Unwalla D, Montenegro M A, Gold J, Zimbric M, Bui J, Sahagian M, Kim McManus O,

Frederick A, Guido-Estrada N, Jindal A, Wiegand S, Rismanchi N, Yang J, Sweat M, Dove K, Nespeca M, Rho J, Sattar S

OBJECTIVE: This study aims to characterize seizure patterns and outcomes in patients diagnosed with B Cell Acute Lymphocytic Leukemia (B-ALL).
METHODS: This was a retrospective study conducted at a tertiary care hospital. Inclusion criteria were age at B-ALL diagnosis younger than 18 years-old; diagnosis of B-ALL and seizures at any point after B-ALL diagnosis. Exclusion criteria involved seizures before B-ALL diagnosis, those with other cancer types and those with non-epileptic spells.
RESULTS: 27 patients (8F, 19M) were included. The age at the time of leukemia diagnosis ranged from 5 months to 16 years (median age = 4 years, mean age = 5.9 years). The interval between B-ALL diagnosis and presentation of first seizures ranged from 0 to 16 years (median = 10.5 months; mean = 34 months). 20/27 patients (74%) presented with provoked seizures and 7/27 (26%) presented with unprovoked seizures in a presumed diagnosis of new onset epilepsy. From the group of patients with provoked seizures, 3/20 (15%) developed epilepsy, and of those, two cases were intractable (10%) with one receiving temporal resective epilepsy surgery. In the group with unprovoked seizures, 3/7 (43%) developed drug resistant epilepsy and one patient underwent implantation of a neurostimulation device
CONCLUSIONS: Our data shows that most seizures presented by patients with B-ALL happen both during acute treatment or remission. Most seizures were provoked and resolved. A minority of provoked seizures progressed to epilepsy; however, 50% (5/10) of the patients with new onset epilepsy after B-ALL diagnosis will develop drug-resistant epilepsy.
KEYWORDS: Epilepsy, Neuro-oncology

72. Impact of English Proficiency on Emergency Room Visits for Seizures

Plaza F I (New York, NY), Velez D, Karkare S, Kothare S

OBJECTIVE: This study aims to investigate the impact of language barriers on emergency room utilization for seizure-related events (emergency room visits for seizures (ERVS)) among pediatric patient populations. Drawing on the extensive background research demonstrating the challenges faced by non-English Language Preferring Speakers (NELPS) in accessing healthcare services, particularly in emergency settings, numerous studies have highlighted the disparities experienced by NELPS in healthcare access and outcomes. By examining the specific impact of language barriers on emergency room utilization for seizure-related events among pediatric patients, this study aims to contribute to a deeper understanding of the complexities surrounding healthcare access and outcomes in linguistically diverse populations.
METHODS: A retrospective chart review of about 5,000 pediatric ERVS patients at a large medical center in a metropolitan area from May 2013 until November 2020 compares the number of emergency room visits per patient and the primary language used. Due to the low number of NELPS at this time from the data collected, a Mann-Whitney U Test was used to compare the data.
RESULTS: Preliminary results of the chart review demonstrate that there is no significant difference between emergency department visits in primarily English-speaking patients (n=389, mean=2.91) and NELPS (n=23, mean=2.74), (z-score=0.14237, p-value=.88866). Data is still being collected to compare ERVS and language.
CONCLUSIONS: Preliminary results demonstrate that there is no difference between ERVS in patients with different primary languages. The research is still early and may still demonstrate a difference. Regardless, proper discharge instructions given with correct interpreter usage are important in mitigating the number of ERVS.
KEYWORDS: Epilepsy, Diversity, Equity, Inclusion

73. Physical activity in young people with Epilepsy: co-design and development of a web app

Astorga G H (Toronto, ON, Canada), Brown D, Ronen G M

OBJECTIVE: Being physically active is beneficial to the health of young people with Epilepsy (YPE). Recent work has found that YPE are interested in physical activities aligned with their preferences but may need guidance on participation. With input from YPE, their parents, and healthcare providers, this knowledge translation project developed a web app to promote safe engagement in physical activities.
METHODS: The study followed the Toronto Translational Framework to frame the context, ideate the design and test the prototype. A total of 73 specialists and providers in Child Neurology/Epilepsy in the USA, Canada, Israel, and Turkey completed a CNS-survey on their approaches to discuss physical activity with YPE. Content Analysis of the survey responses using the themes identified in previous work as codes informed the app prototype design.
RESULTS: Child-neurology professionals indicated the need for accessible, easy-to-use online tools to discuss physical activity in YPE. They identified 23 activities YPE prefers and suggested the tool should provide safety and accommodation guidelines, enable social connection and support, assist with setting goals, and reinforce advice discussed in clinical visits. The tool features align with the insights from YPE and their parents, identified in the previous study. Conversely, other respondents noted that the lack of resources and time during clinical visits prevents discussions of physical activities, which the online tool can address.
CONCLUSIONS: A web app accessible on phones and computers is under development. By creating a user-friendly tool addressing physical activity concerns, providers can support promoting an active lifestyle for YPE and their families.
KEYWORDS: Epilepsy, Education, Telemedicine

74. Modified titration schedule utilized in the phase 3, randomized, double-blind, placebo-controlled TrustTSC trial evaluating adjunctive ganaxolone for treatment of patients with tuberous sclerosis complex (TSC)-associated seizures

Flatt J (Radnor, PA), Koenig M K, Aimetti A, Miller I, Hulihan J

OBJECTIVE: Drug-resistant seizures are commonly reported in patients with TSC. In a phase 2 trial, TSC-associated seizure frequency decreased with ganaxolone treatment. The phase 3 TrustTSC study (NCT05323734) will assess the safety and efficacy of adjunctive ganaxolone versus placebo for seizures in children and adults with TSC.
METHODS: The study will enroll patients aged 1-65 years with confirmed diagnosis of TSC and inadequately-controlled seizures (≥8 countable seizures/month after exposure to ≥2 anti-seizure medications). Patients will undergo a 4-week baseline phase followed by a double-blind treatment phase (4-week titration and 12-week maintenance period). Ganaxolone will be titrated using a new titration schedule to a maximum daily dose of 63 mg/kg (patients weighing ≤28 kg) or 1800 mg (patients weighing >28 kg). This updated 4-week titration schedule is intended to reduce somnolence-related adverse events (SRAEs) by using a more gradual rise in plasma ganaxolone concentrations compared to the titration schedule used in prior studies. The primary endpoint is the change from baseline in 28-day seizure frequency during the double-blind phase. Efficacy (responders, seizure-free duration, Clinical Global Impression of Improvement), non-seizure outcomes (neurobehavioral symptoms, mood, sleep, quality of life), and safety (adverse events, physical/neurological/developmental examinations and others) will also be assessed.
RESULTS: Approximately 128 patients will be enrolled by spring 2024. Results will be available in fall 2024.
CONCLUSIONS: Results from this study will describe the efficacy and safety of ganaxolone for treatment of seizures associated with TSC. The modified titration schedule is anticipated to decrease SRAEs and improve treatment response.
KEYWORDS: Epilepsy

75. A deep dive comparing the diagnostic yield and clinical actionability from exome sequencing and multigene panel testing for epilepsy

Pineda-Alvarez D E (San Francisco, CA), Williams T, Ting Y, Hamilton S, Chen E, Facio F, Aradhya S,

OBJECTIVE: Genetic testing for epilepsy has diagnostic, prognostic, and therapeutic implications. Recent guidelines favor exome sequencing (ES) because of its higher diagnostic yield (MolDx) compared to multigene epilepsy panel testing (MGPT). Here, we compare the MolDx and clinical actionability (CA) in patients with epilepsy identified by ES or MGPT.
METHODS: Patients were referred for diagnostic ES or MGPT for epilepsy between December 2015-December 2023. Variants were classified using a validated variant classification framework based on ACMG/AMP guidelines. CA was defined as having specific treatment or actions that could impact disease management or prevention in patients with a diagnostic finding in certain genes. This list of genes was curated from published literature and/or expert opinion. Odds ratios (OR) and p-values were calculated using G-Tests; p-values<0.05 were considered statistically significant.
RESULTS: The overall MolDx in patients was higher in the ES cohort (459/1,582; 29.0%) versus MGPT (9,054/76,575; 11.8%) (OR 3.0, p<2.2x10-16). Diagnostic findings were identified by ES and MGPT in 303 and 209 genes, respectively, with 103 (25.2%) genes overlapping. Among patients with a diagnostic finding identified by ES and MGPT, 175/459 (38.1%) and 4,977/9,054 (55.0%), respectively, had results in genes with CA (OR 1.98, p=1.6x10-12).
CONCLUSIONS: MolDx was higher in patients with epilepsy tested using ES compared to MGPT, as expected. However, MGPT had a higher rate of results with CA. Factors like turn-around-time and cost should be considered. Additional studies are needed to understand the differences in gene findings and healthcare cost-per-CA finding.
KEYWORDS: Epilepsy, Neurogenetics

76. Etiologies and Genetic Pathway Analysis Reveals Prognostic Insights in Infantile Epileptic Spasms Syndrome (IESS): A Multicenter Retrospective Study

Chanvanichtrakool M (Bangkok, Thailand), Samanta D, Singh R, Christopher Y, Knupp K, Pasupuleti A, Shrey D, Madan-Cohen J, Keator C, Grinspan Z, Bhalla S, Bhatia S, Mytinger J, Naik S, Numis A, Lopour B, Hussain S, Ciliberto M, Neville K, Hyslop A, Takacs D, Sirsi D, Gropman A, Chen W-L

OBJECTIVE: We explored if categorizing infantile epileptic spasm syndrome (IESS) by genetic pathways predicted short-term remission and transition to Lennox-Gastaut syndrome (LGS).
METHODS: Retrospective data from 560 children with new-onset IESS from 20 US sites (2016–2020) as part of the NIMBIS (National Investigation of Multi-modal Biomarkers for Infantile Spasms) study and additional 29 children from Children's National Hospital. Key data points for this study included etiology, clinical remission of infantile spasms, and transition to LGS. Using the Cytoscape for gene set enrichment analysis (GSEA) from databases including KEEG, WikiPathways, GO biological process, and Reactome facilitated the identification of biological pathways. The clinical outcomes of different pathways were compared using a two-sided chi-square test.
RESULTS: 217 (37%) of 589 had a genetic etiology, consisting of monogenic disorders (69%), structural variants (30%), and presumed genetic etiology (1%). Children identified with pathogenic monogenic gene variants were enriched in the following pathway: BDNF signaling pathway (n=47), mTOR pathway (n=44), regulation of synaptic plasticity (n=22), neuronal migration (n=21), and axon extension (n=15) pathways. Individuals with variants in the neuronal migration pathway have a higher likelihood for developing LGS (p=0.008). On the other hand, individuals involved in the mTOR pathway have a higher likelihood of responding to first treatment (p =0.02) and have a lower risk of developing LGS (p =0.006).
CONCLUSIONS: This study highlights the utility of GSEA to compare the clinical outcome of individual with IESS. Grouping etiologies by genetic pathway appears to be a useful

marker of short-term electroclinical remission and potential transition to LGS.
KEYWORDS: Epilepsy

77. Intrathecal Rituximab Use in Rasmussen's Encephalitis Improves Unilateral Brain Atrophy and Reduces Seizure Burden

Scholz A (St. Louis, MO), Keefe S, Benzinger T, Glasser M, Landre R, Mar S, Mian A, Tomko S, Weisenberg J

OBJECTIVE: We report a previously healthy 11 year old girl with 5 months history of explosive onset, medically refractory focal motor seizures, aphasia, hemiparesis, and unilateral atrophy on serial brain MRI scans. Brain biopsy was consistent with Rasmussen's encephalitis, a rare and devastating neuroinflammatory condition. Immunosuppression has been used to target the presumed inflammatory nature of the condition, but many cases require hemispherotomy. In this case, we discuss the novel use of intrathecal (IT) rituximab, and demonstrate correlation with reduced seizure burden and improved brain atrophy.
METHODS: The seizures were refractory to numerous antiseizure medications at escalating doses. She was treated with IV methylprednisolone, plasmapharesis, IV immunoglobulins, and tocilizumab without clear clinical impact. Given experience in other neuroinflammatory conditions, the patient was treated with IV and IT rituximab (4 weekly doses) simultaneously. Serial continuous EEGs and brain MRIs were analyzed before and after IT rituximab.
RESULTS: Administration of IT rituximab was correlated with cessation of epilepsia partialis contina and significantly reduced seizure frequency within 48 hours, with improvement in right side hemiparesis, stable aphasia, and improvement in brain atrophy over time, most notably in the left temporal and cingulate lobes, but also in parietal and occipital lobes.
CONCLUSIONS: This report demonstrates a temporal correlation of IV and IT rituximab with improvement in seizure frequency, neurologic exam, and brain atrophy. The duration of these effects or long-term patient outcome is unknown, however this case provides support for a well tolerated and potentially efficacious treatment for this devastating condition.
KEYWORDS: Epilepsy, Neuroimmunology, Neuroimaging

78. Caregiver Versus Investigator Clinical Global Impression-Improvement Ratings in Fenfluramine Clinical Trials

Sullivan J (San Francisco, CA), Knupp K, Cross J, Scheffer I, Devinsky O, Auvin S, Thiele E, Wirrell E, Lagae L, Langlois M, Lothe A, Nabbout R

OBJECTIVE: To compare caregiver and investigator Clinical Global Impression-Improvement (CGI-I) scale ratings from the fenfluramine (FFA) clinical trial program of Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS).
METHODS: The proportion of patients rated as having clinically meaningful improvement ("much improved" or "very much improved") at last visit on CGI-I in the DS and LGS randomized controlled trials (RCTs) and open-label extension (OLE) studies is reported; a separate post-hoc analysis evaluated a subset of adults who enrolled in the DS OLE de novo. Descriptive statistics were used.
RESULTS: Ratings from 4 RCTs (3 DS and 1 LGS) and 2 OLE studies (1 DS and LGS each) were reported, including from 2 dosage groups in 3 of the RCTs. In 6/9 assessments, the proportion of investigators who rated patients as having clinically meaningful improvement after FFA was higher vs caregivers. In the 9 assessments, median proportions of clinically meaningful improvement ratings were 41.0% (range, 20-64.6) by investigators and 35.2% (range, 27.1-62.5) by caregivers. Of the adults who enrolled in the DS OLE de novo, 20/28 caregivers and 21/28 investigators rated patients as having clinically meaningful improvement after FFA.
CONCLUSIONS: In the DS and LGS FFA clinical trials, clinically meaningful improvement ratings on CGI-I at last visit were aligned among caregivers and investigators. Caregiver scores likely reflect achievement of goals most important to families and highlight the need to capture both caregiver and investigator CGI-I scores in clinical trials.
KEYWORDS: Epilepsy

79. Safety and Effectiveness of Adjunctive Fenfluramine in an Open-Label Extension Study of Children (2 to Under 6 Years Old) With Dravet Syndrome

Sullivan J (San Francisco, CA), Nabbout R, Lagae L, Devinsky O, Auvin S, Thiele E, Wirrell E, Specchio N, Pringsheim M, Imai K, Lock M, Langlois M, Healy P, Lothe A, Scheffer E E

OBJECTIVE: Phase 3 studies and interim open-label extension (OLE) analyses have shown profound, durable reduction in median monthly convulsive seizure frequency (MCSF) in patients with Dravet syndrome (DS) treated with fenfluramine. This final OLE analysis describes long-term safety and effectiveness of fenfluramine in patients 2 to <6 years old with DS.
METHODS: Safety was reported for patients who received ≥1 dose fenfluramine. The effectiveness endpoint in modified intent-to-treat (mITT) patients was median percentage change in MCSF from randomized controlled trial baseline to overall OLE. Caregivers and investigators rated patients on the Clinical Global Impression—Improvement (CGI-I) scale. Descriptive statistics and Wilcoxon signed-rank test were used.
RESULTS: As of January 27, 2023, 375 patients enrolled; 92 were 2 to <6 years old and received ≥1 dose fenfluramine (median treatment duration, 2.5 years). Of patients who did not complete the OLE (n=80), 61 transitioned to another study or commercial product, 5 withdrew due to lack of efficacy, and 2 had sudden death in epilepsy. In the mITT population (n=85), median MCSF change from baseline during the overall OLE was -74.2%, P<0.001. Clinically meaningful improvement (much improved or very much improved) was reported by 69.0% (58/84) of caregivers and 66.7% (56/84) of investigators. The most common treatment-emergent adverse events were pyrexia (n=42) and nasopharyngitis

(n=38). There were no cases of valvular heart disease or pulmonary hypertension in this population.
CONCLUSIONS: Patients with DS aged 2 to <6 years treated with fenfluramine have sustained reduction in seizures with clinically meaningful improvement in condition severity.
KEYWORDS: Epilepsy

80. Reducing Time to Second-Line Treatment in Pediatric Status Epilepticus Patients

Diehl E A (Seattle, WA), Dervan L, Barry D, Fenstermacher S, Walsh L, Morgan L

OBJECTIVE: Status epilepticus (SE) is a life-threatening neurologic emergency. Treatment delays are associated with more frequent respiratory failure, intensive care unit admission, and long-term complications. Despite national and international guidelines, many patients receive rescue medications later and at lower doses than recommended. We aimed to reduce the time to treatment and increase adequate dosing for second-line SE treatment by adding levetiracetam to the ED Omnicell (LEV-Omnicell). We compared these treatment factors and short-term clinical outcomes between patients receiving LEV-Omnicell vs. pharmacy-provided second-line agents.
METHODS: This retrospective cohort study included patients with SE who received a second-line medication (intravenous levetiracetam, valproate, fosphenytoin, phenobarbital, or lacosamide) in the Emergency Department (ED) from 10/3/2020-7/31/2023. After 7/14/2021, LEV was available in the ED Omnicell. Generalized linear models assessed differences.
RESULTS: Among 149 patients, 57 (38%) received SE medications from central pharmacy and 92 (62%) received LEV-Omnicell. Patients receiving LEV-Omnicell received treatment 9 minutes earlier (9.6 vs 19 minutes, p=0.03) and received the recommended dose more often (84% vs 95%, p=0.046). Patients receiving LEV-Omnicell had a significantly shorter ED length of stay (median 284 vs 185 minutes, p=0.03), though were more likely to undergo endotracheal intubation in the ED (34% vs. 16%, p=0.02); this difference was confounded by pre-hospital factors including number of benzodiazepines and seizure duration.
CONCLUSIONS: Omnicell levetiracetam availability resulted in decreased time to second-line treatment, improved dosing, and decreased ED length of stay.
KEYWORDS: Epilepsy, Practice Parameters

81. Epilepsy Monitoring Unit to Epilepsy Surgery Conference Cycle Time Reduction Using Quality Methodology

Cavallo M (Atlanta, GA), Encalarde T, Wood E, Ganote J, Bearden D

OBJECTIVE: Our goal was to reduce the amount of time between our patients' discharge from the epilepsy monitoring unit (EMU) following long-term video EEG monitoring and their initial presentation at our epilepsy surgery conference (ESC).
METHODS: Prior to patients' first ESC presentation following their EMU stay, a variety of procedures are completed to ensure they are appropriate epilepsy surgery candidates. Procedures typically include neuropsychological evaluation, PET scan, and MRI, among others, each requiring insurance approval that can delay completion. To manage this, our team created a standardized process to increase efficiency between EMU and initial ESC presentation while providing tailored care for each patient. Our intervention included 27 patients, 63% of which completed epilepsy surgery between January and June 2022.
RESULTS: At baseline, it took an average of 135 days from patients' discharge from EMU to their initial presentation at ESC. Insurance authorization caused the greatest delay. Following the implementation of our intervention, we reduced the average wait time to 94 days.
CONCLUSIONS: Epilepsy surgery has the potential to reduce seizure burden and improve quality of life. Decreasing wait time from EMU discharge to initial ESC presentation results in timelier care for patients. In our study, we reduced wait times from EMU to ESC while providing tailored care that ensured optimal assessment of patients' candidacy for epilepsy surgery, which can be used as a model for other pediatric hospitals.
KEYWORDS: Epilepsy, Practice Parameters

82. Etiological Heterogeneity of Infantile Epileptic Spasms in a Single-Center Cohort: Expanding the Genetic Landscape

Singh A (Milwaukee, WI), Abushanab E, Adams S, Jozwik J, Andrade-Machado R, Pollock S, Bass N

OBJECTIVE: To evaluate the diverse etiologies of infantile epileptic spasm syndrome (IESS) in a single-center cohort to inform prognosis & treatment responsiveness based on etiology.
METHODS: A retrospective review of IESS patients (Aug 2022 to April 2024) at a tertiary care center was conducted, analyzing demographic, clinical & genetic data.
RESULTS: Among 61 patients, 41% (n=25) had an acquired etiology, 46% non-acquired (n=29) and 13% (8) unknown (non-syndromic) etiology. Notable acquired causes included hypoxic ischemic injury (8), prematurity with grade 4 intraventricular hemorrhage(7), perinatal stroke(4), congenital CMV (2), abusive head trauma(2) and meningitis(2). Non-acquired causes were diverse, including tuberous sclerosis(2), other monogenic disorders(9), chromosomal rearrangements(4), Trisomy 21(3), lissencephaly(2), cortical malformation(3), congenital CMV(2), Aicardi syndrome(1) and undetermined(3, syndromic). MRI was abnormal in 57%(n=35). Among patients without an acquired etiology (36), chromosomal testing revealed etiology in 6 (17%), single gene testing in 2 patients (6%, 1 TSC, 1 NF with clinical suspicion). Gene-panel was done in 61% (n=21) with 33% yield and whole exome sequencing was done in 33%(12) with a 50% yield. Five among non-acquired group had novel variants in these genes: PAFAH1B1, DYRK1A, EPG5, IRF2BPL & FRRS1L. Movement disorder occurred in 27.5% with non-acquired

etiology. Patients with unknown etiology had higher responsiveness to first-line standard medications (87.5%), vs 38% in acquired and 36% in non-acquired group (p=0.021). Neonatal seizures were reported in 23% (14), majority with structural (86%, 12) etiology.
CONCLUSIONS: IESS demonstrates heterogeneous etiologies with implications for prognosis. The genetic etiology pool is rapidly expanding highlighting need for further research to elucidate underlying mechanisms.
KEYWORDS: Epilepsy, Early Stage Investigator

83. Payor Coverage for Epilepsy: Broader Coverage for Exome Sequencing Compared to Multigene Panels

Sassaman A (San Diego, CA), Soto S

OBJECTIVE: Studies and professional societies support exome sequencing (ES) for individuals with epilepsy. Since payor coverage can impact genetic testing access, we compared coverage for broad multigene panels (MGPs) and ES and coverage requirements for ES for individuals with epilepsy in the outpatient setting.
METHODS: We reviewed publicly available coverage policies from 10 national payors, regional payors, State Medicaids, and laboratory benefit managers (LBMs).
RESULTS: Most payors/LBMs (n=9) evaluated have coverage for ES for individuals with epilepsy; however, most payors/LBMs (n=6) have no explicit policies for MGPs. For ES there is variability in criteria for coverage across payors. For clinical features, 2 policies cover ES for epilepsy at any age, 3 only for epileptic encephalopathy with an onset <3 years of age, 3 require an additional clinical finding, and 1 has non-specific criteria of neurodevelopmental disorders. For provider restrictions, most policies require a specialist with expertise in clinical genetics. Many policies also have a counseling requirement. Some payors have a specific form to complete.
CONCLUSIONS: Currently, for the indication of epilepsy in the outpatient setting, there is broader payor coverage for ES than MGPs based on medical coverage policies. Lack of explicit policies for MGP leads to provider and patient uncertainty regarding coverage. Review of ES policies demonstrate extremely variable and complicated criteria for coverage. There is a need for provider engagement with payors to broaden and simplify ES coverage, so individuals with epilepsy can access the genetic tests that improve their care and management.
KEYWORDS: Epilepsy, Diversity, Equity, Inclusion

84. Epilepsia Partialis Continua following alemtuzumab treatment: first report following solid organ transplant and the first in a pediatric patient

Papas S S (Chapel Hill, NC), Gibson K, Sanderson K, Westreich K, Bradford K, Diaz M, Dujmovic Basuroski I, Shiloh-Malawsky Y

OBJECTIVE: We report a child presenting with epilepsia partialis continua (EPC) following alemtuzumab for immunosuppression for solid organ transplant, and response to immunomodulatory treatment.
METHODS: Case report and review of published literature.
RESULTS: A 10 year old male with bilateral renal hypoplasia received alemtuzumab and tacrolimus for immunosuppression induction following kidney transplant. Two weeks after the first cycle of alemtuzumab he presented with recurrent right arm clonic jerking, right hand weakness and aphasia. Electroencephalogram (EEG) revealed left fronto-parietal seizures . Seizures were refractory to antiseizure medications including levetiracetam, lacosamide and fosphenytoin, and showed only transient improvement following general anesthesia with midazolam and ketamine. He was diagnosed with EPC. Brain imaging and cerebrospinal fluid were normal including negative serum and cerebrospinal fluid autoimmune encephalitis antibody panels. Four published cases of EPC following alemtuzumab for multiple sclerosis had responded to immune modulating treatments. The patient received five days of high dose methylprednisolone, IVIG, plasmapheresis and rituximab which led to rapid seizures resolution and marked improvement in hemiparesis, aphasia and EEG abnormalities. He was found to have a likely pathogenic variant in MT-TF mitochondrial gene.
CONCLUSIONS: To our knowledge this is the first report of EPC following alemtuzumab in a child, and the first report of EPC following alemtuzumab used for immunosuppression induction for solid organ transplant. The response to immunotherapy suggests an autoimmune etiology of EPC in our patient. MT-FT variant might have contributed to decreased seizure threshold. This case adds to the literature of EPC in patients receiving alemtuzumab and expands its clinical setting.
KEYWORDS: Epilepsy, Neuroimmunology

85. Reducing Wait Time From Main Admissions Arrival to Scheduled Admission in the Epilepsy Monitoring Unit Using Quality Methodology

Gisler S (Atlanta, GA), Kilgore T, Cavallo M, Ganote J, White M, Richardson M, Lamar Y

OBJECTIVE: Long wait times for patients in main admissions pending room availability for scheduled admission to the epilepsy monitoring unit presents a patient safety concern, as patients weaned off or taking sub-optimal medication to capture specific seizures are at increased risk of seizing while not under medical supervision. This quality improvement project was implemented to reduce this wait time.
METHODS: To reduce wait times, we changed how patients are placed in beds and our communications between clinical staff and patient families. Calls were placed to patient families communicating availability the day of their appointment. We also implemented a new bed tracking system to streamline interdepartmental communications These interventions reduced inbound call volumes to our transfer center, reduced gaps in communication and allowed us to share updates with patient families regarding bed availability and placement in real time.
RESULTS: At baseline, patients on average waited 65 minutes from the time of their arrival until they were placed in a bed. Following our interventions, we reduced wait time to 39 minutes. This led to increased satisfaction for patient families and our staff.

CONCLUSIONS: Our system experiences some of the highest patient volumes in the country, leading to a variety of challenges in access to care and patient wait times. Bed availability being limited due to high patient census impacts the timeliness and quality of care we can provide. More efficient communication between providers and patient families, as well as amongst providers, allowed us to better utilize available resources.
KEYWORDS: Epilepsy

86. Approach to Anti-Seizure Medication Treatment of Pediatric Epilepsy with Eyelid Myoclonia in a Case Series

Kronfol C A (Austin, TX), Chinthaparthi S

OBJECTIVE: To analyze anti-seizure medication (ASM) treatment of epilepsy with eyelid myoclonia (EEM) in a case series.
METHODS: Retrospective chart review of ASM treatment in four patients meeting diagnostic criteria for EEM.
RESULTS: Levetiracetam was the first-line ASM in three patients. It showed improvement or resolution of seizures in these patients. It was discontinued in two patients due to behavioral side effects. In the fourth patient it was tried after failure of previous medications early in the course of treatment and stopped for unclear reasons. It was later restarted in conjunction with clobazam. This patient had brief improvement in seizure frequency but later required addition of zonisamide. Other medications tried included clobazam, valproic acid (VA), lamotrigine, and ethosuximide. VA showed efficacy in two patients but was discontinued in one patient for gait disturbances and cognitive slowing. Lamotrigine was tried in two patients. It was effective in one and stopped in the second patient due to photosensitivity. Other medications showed minimal efficacy.
CONCLUSIONS: Levetiracetam was the most commonly used medication and efficacious in three out of four patients. Given it has minimal side effects, it is a good first-line medication to consider in EEM. However, behavioral disturbances associated with levetiracetam may lead to discontinuation as seen in two of these patients. Use levetiracetam with caution in patients with baseline behavioral difficulties. The other medications we recommend are VA and lamotrigine which showed good seizure control. Given their mood stabilizing effects, they are good subsequent choices for patients who fail levetiracetam due to behavioral issues.
KEYWORDS: Epilepsy, Practice Parameters, Education

87. Implementation of a standardized treatment and follow up pathway for patients with Infantile Spasms Syndrome improves their quality of care and clinical outcomes.

Bhalla S (Atlanta, GA), Grychowski L, Carr G, Devine S, Cavallo M, Encalarde T, Wood E, Wolf D

OBJECTIVE: Infantile spasms syndrome (ISS) is an early-life epileptic encephalopathy that can cause long-term neurodevelopmental disabilities and epilepsy. This quality improvement project aimed to streamline clinical management for new onset ISS patients and reduce the time from treatment initiation to the first electro-clinical follow up appointment with an encephalogram (EEG) and a provider.
METHODS: We conducted retrospective chart review to track treatment and follow-up for our patients. Interventions included creating and implementing an evidence-based ISS management protocol and coordinating the first follow-up visit in our epilepsy monitoring unit (EMU) instead of an outpatient EEG and clinic appointment.
RESULTS: Since implementation of protocol, we achieved 100% adherence for using standardized medications. From January 1, 2022, to September 1, 2022, the baseline average wait time from admission to first follow-up visit was 25.2 days (for 27 patients). Despite our diligent coordination of care interventions, our outpatient follow-up EEG and clinic visits post-treatment were tracking at average of 24 days from October 1, 2022, to August 1, 2023. Since September 2023, we changed our process to establish follow up in our EMU and our average time from treatment initiation to follow up in EMU has reduced by 30.6% to 17.5 days.
CONCLUSIONS: Close follow-up monitoring is crucial for evaluating treatment response and relapse in ISS patients, directly affecting their clinical outcomes. By adopting an evidence-based treatment protocol, we have standardized care. Prompt follow-up in the EMU is practical, approved by health insurers, and allows epileptologists to adjust treatment plans as needed, ultimately enhancing overall clinical outcomes.
KEYWORDS: Epilepsy, Practice Parameters, Education

88. Efficacy of Felbamate and Ganaxolone for Pediatric Febrile Infection-Related Epilepsy Syndrome (FIRES)

Kung M S (Orange, CA), Gupta D, Arellano J, Liu V

OBJECTIVE: FIRES (Febrile Infection-Related Epilepsy Syndrome) is neurologically devastating condition with poor outcomes; morbidity reportedly as high as 9-18% in the acute phase, 90% develop refractory epilepsy, and cognitive issues are common in surviving patients. Novel anti-seizure regimens not previously described in literature were utilized to optimize seizure control and outcome. Given presumed autoimmune etiology of FIRES, there is compelling rationale to trial anti-seizure medications with immunosuppressive properties.
METHODS: Three patients who met criteria for clinical diagnosis of FIRES were identified and treated with immunotherapies per NORSE/FIRES international consensus guidelines. FIRES subjects were identified from the last two years at a tertiary children's hospital. 1) Felbamate was trialed during acute phase of illness and continued as maintenance regimen. 2) Ganaxalone was trialed off-label for one severe case of FIRES.
RESULTS: Patients (n=3) had a mean age (7 years +/- 3), gender (2 males, 1 female) and presented with refractory focal/multifocal seizures in the setting of elevated CSF Interleukin-2 or Interleukin-6. Patient 1 had normal MRI brain, Patient 2 with subtle T2 hyperintensities in the temporal operculum, and Patient 3 had bilateral cortical and basal ganglia abnormalities. Both Felbamate and Ganaxalone medication trials decreased ICU duration compared to cases

described in prior NORSE/FIRES literature and exhibited no recurrence of seizures to date.
CONCLUSIONS: This institutional experience with pediatric FIRES suggests that utilizing Ganaxalone and Felbamate during acute hospitalization and continuing maintenance dose outpatient may facilitate improved outcomes as defined by seizure control and relatively short ICU duration.
KEYWORDS: Epilepsy, Neuroimmunology, Neuroinfectious Disease

89. Hyperconnectivity During Sleep Increases with Longer Duration of Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS)

Vasitas M E (Palo Alto, CA), Goad B S, Lee-Messer C, Baumer F

OBJECTIVE: Children with Self-Limited Epilepsy with Centrotemporal Spikes (SeLECTS) have elevated connectivity both during periods with spikes and during spike-free periods. It is unclear if connectivity abnormalities are static or worsen over time. Here, we assess whether connectivity increases as epilepsy duration increases.
METHODS: Spike-free epochs of sleep and wakefulness were segmented from 63 clinical electroencephalograms (EEGs) of children with SeLECTS (30 with epilepsy of short duration <6 months since diagnosis; 33 with long duration of >6 months) and 41 age- and sex-matched controls. The average connectivity of each electrode with the other 18 electrodes was measured using the weighted phase lag index, a metric robust against volume conduction. We investigated whether connectivity differed between the control, short-duration, or long-duration epilepsy groups after adjusting for age, sex, and antiseizure medication use.
RESULTS: The short-duration group had a SeLECTS diagnosis for .059+/-.010 years whereas the long-duration group had been diagnosed for 2.90+/-.331 years. Connectivity during sleep but not during wakefulness was significantly elevated in children with SeLECTS compared to controls, more so in those with longer epilepsy duration. Compared to controls, sleep connectivity was elevated in 1 of 19 electrodes in the short-duration group versus 15 of 19 electrodes in the long-duration group. Mean sleep connectivity at every electrode was greater in the long-duration group versus the short-duration group, but differences were not significant.
CONCLUSIONS: Hyperconnectivity during spike-free periods of sleep increases with longer duration of epilepsy, suggesting that spike exposure may lead to progressive changes in brain function over time.
KEYWORDS: Epilepsy, Lifespan Manifestations of Childhood Onset Conditions, Neurodevelopmental Disorders

90. Brought Back to Life: Pediatric Patient Survives Near-SUDEP Without Resuscitation

Abdelmoity L (Overland Park, KS), Kostreva J, Ojha K, Ilyas M

OBJECTIVE: We describe a rare case of Ictal Asystole in a patient with Generalized Epilepsy
METHODS: A retrospective review of a single pediatric case at a tertiary care center
RESULTS: 16-year-old male with a history of recurrent blackouts with stiffness, on Levetiracetam, presented to the epilepsy monitoring unit for characterization of events. A seizure was captured during which he became limp, had asymmetric body jerks and made gasping sounds. Electrographically, it had an abrupt onset with runs of generalized sharps with evolution, followed by diffuse background attenuation and diffuse high amplitude slowing. However, during the seizure he also became bradycardic and had around 30 seconds of ictal asystole. It reverted to his baseline sinus rhythm without any intervention. Subsequent telemetry and ECHO were unrevealing. MRI Brain was unremarkable. A leadless pacemaker was implanted in the patient, given prolonged ictal systole without any complications. He has done well since then, with no further episodes.
CONCLUSIONS: Ictal asystole1, has been described in patients with focal epilepsy but has rarely been reported in patients with generalized epilepsy. The asystole, in this case, was likely caused by the acute and high vagal tone during the seizure. It can be a self-limiting phenomenon different from postictal asystole noted after bilateral tonic-clonic convulsions with risk for SUDEP (Sudden Unexpected Death in Epilepsy). Permanent pacemaker implantation is recommended when AED optimization has failed or if the ictal asystole lasts longer than 6 seconds2.
KEYWORDS: Epilepsy, Education, Early Stage Investigator

91. 4-Phenylbutyrate Protects Against Seizure Related Events In a Mouse Model of Dravet Syndrome

Ziobro J M (Ann Arbor, MI), Daddo N, Jahagirdar S, O'Malley H, Isom L, Parent J

OBJECTIVE: Dravet Syndrome (DS) is a severe developmental and epileptic encephalopathy caused by pathogenic loss-of-function variants in the voltage-gated sodium channel gene, SCN1A. Despite the availability of several newer medications, seizures remain medically refractory for many DS patients. 4-phenylbutyrate (PBA) is an FDA approved compound for the treatment of urea cycle disorders. It is also known to be a chemical chaperone and histone deacetylase inhibitor, hypothesized to improve trafficking of functional proteins to the cell surface. We therefore sought to explore PBA as a potential therapeutic agent in a mouse model of DS.
METHODS: Scn1a+/- DS mice received daily intraperitoneal injections of 400 mg/kg PBA or an equal volume of 0.9% normal saline and monitored for spontaneous deaths from postnatal day (P)18-40. Surviving mice were exposed to hyperthermia to induce seizures. Brains were harvested for immunohistochemistry (IHC) and Western blot.
RESULTS: Spontaneous death occurred in 30% of saline treated mice (n=31) versus 10% of PBA treated mice (n=30) during the study period. Hyperthermic seizures were observed in 28% of surviving saline-treated mice versus 8% of PBA treated mice. Preliminary IHC studies suggest increased levels of Nav1.1 at the cell surface of cortical interneurons of PBA-treated mice.
CONCLUSIONS: Preliminary results suggest that PBA may be protective against spontaneous seizures that lead to SUDEP and provoked seizures in a mouse model of DS. PBA may increase Nav1.1 targeting to the plasma

membrane. Further studies are needed to fully evaluate this effect and to better elucidate the mechanisms of PBA as a potential therapeutic agent.

KEYWORDS: Epilepsy, Experimental Therapeutics, Neurogenetics

EXPERIMENTAL THERAPEAUTICS

92. Optimizing Database Development and Management in a Multi-Site, International, Randomized, Investigator-Initiated Interventional Neonatal Seizure Clinical Trial

Lee M (Minneapolis, MN), Faanes B, Ramey E, Coleman C, Reiner G, Sharpe C, Wang S

OBJECTIVE: Managing clinical trials for neonatal seizures involves unique challenges due to the sensitive population and the need to integrate complex, multi-source data. The prime study team has developed a database and data management strategy that ensures high data integrity, meets regulatory cross-institutional standards, and facilitates effective analysis of clinical trial data for neonatal seizures.

METHODS: NEOLEV3 is an FDA-funded, Investigational New Drug Phase 2 Dose Escalation Study of Levetiracetam in the Treatment of Neonatal Seizures recruiting from five hospitals across the USA and New Zealand with Data Safety Monitoring Board (DSMB) oversight. We developed a robust database system using REDCap, featuring real-time data entry validation, automated audit trails, data resolution workflows, and secure electronic health record integration.

RESULTS: The implemented database system reduces errors and inconsistencies by using advanced conditional logic, form logic display, Data Access Groups, field validations, limited free text fields, real-time alerts, and data locking. This uniformity in data management aligns with DSMB expectations.

CONCLUSIONS: The database system facilitates streamlined data entry while adhering to all local and federal compliance regulations. Initial challenges included navigating setup and training at diverse international sites unfamiliar with the interface. Critical support from the Clinical Data Manager and REDCap Administrators effectively addressed these issues while complying with Good Data Management Clinical Practice. This initiative sets a benchmark for future neonatal trials and demonstrates the feasibility of managing complex data in challenging multi-site international settings. It lays the groundwork for optimizing neonatal seizure protocols and improving long-term neurodevelopmental outcomes.

KEYWORDS: Experimental Therapeutics, Neonatal Neurology, Neurocritical Care

93. NNZ-2591, A Novel, IGF-1-Related Treatment for Neurodevelopmental Disorders Demonstrates Efficacy for Children and Adolescents with Phelan-McDermid Syndrome

Berry-Kravis E (Chicago, IL), Neumeyer A M, Holder Jr J L, Srivastava S, Glass L, Jones N, Squires L

OBJECTIVE: The effects of treatment with NNZ-2591 (an analog of an IGF-1 dipeptide metabolite) on symptoms of Phelan-McDermid syndrome (PMS) were examined in a phase 2, multisite, open-label clinical trial of children and adolescents (aged 4–13 years).

METHODS: Participants (n=18) were titrated to 12 mg/kg twice daily and were treated for a total of 13 weeks. Safety and tolerability were assessed by adverse events (AEs) and findings on electrocardiograms, physical examinations, ophthalmic examinations, and laboratory values. Clinical benefit was assessed based on a range of efficacy measures evaluating clinically important symptoms of PMS (clinician and caregiver measures).

RESULTS: NNZ-2591 was well tolerated and demonstrated a good safety profile. Most AEs were mild or moderate, and there was no pattern of laboratory, vital sign, ophthalmic, or ECG abnormalities identified. There was only 1 Serious AE (gastroenteritis) which was unrelated to the study drug. This AE occurred during the safety follow-up period after the end of treatment.

Statistically significant improvement was assessed by both clinicians and caregivers across multiple efficacy measures. For 10 of 14 efficacy endpoints, improvement from baseline on overall/total scores was statistically significant (Wilcoxon signed rank test $P<0.05$). Improvements were consistently seen across clinically important aspects of PMS, including communication, behavior, cognition/learning, and socialization.

CONCLUSIONS: NNZ-2591 appeared to be safe and well tolerated in children and adolescents with PMS. Statistically significant improvement was observed by both clinicians and caregivers from treatment, across multiple efficacy measures. Improvements were consistently seen across many of the core PMS characteristics.

KEYWORDS: Experimental Therapeutics, Neurodevelopmental Disorders

94. Interim Results from the HELIOS Trial: A Phase 2, Open-Label Study Evaluating an Oral, Fixed-Dose Combination of Sodium Phenylbutyrate and Taurursodiol in Wolfram Syndrome

Urano F (St. Louis, MO), Marshall B, Hurst S, Viehoever A, Ahmadi S, Hershey T, Van Stavern G, Cruz Bravo P, Powers Carson J, Erpelding N, Cottrell K, Leinders M, Mehta L

OBJECTIVE: Wolfram syndrome (WS) is a rare, fatal genetic disorder characterized by childhood-onset diabetes mellitus, optic atrophy, deafness, diabetes insipidus, and neurodegeneration. The oral, fixed-dose combination sodium phenylbutyrate (PB) and taurursodiol (TURSO) has demonstrated preclinical efficacy in patient-derived cell and mouse WS models. The phase 2, open-label HELIOS trial is evaluating the safety/tolerability of PB&TURSO and its effects on endocrinological, neurological, and ophthalmologic function.

METHODS: Adults with a definitive genetic WS diagnosis, insulin-dependent diabetes mellitus, and stimulated C-peptide ≥0.2ng/mL were enrolled from one U.S. site and will receive PB&TURSO for ≤96 weeks. The primary efficacy endpoint is change from baseline in C-peptide at Week 24, using a 0-240-minute mixed meal tolerance test.

Secondary efficacy endpoints include measures of glucose control, best-corrected visual acuity, and global impression of change.

RESULTS: As of March 2024, 8/12 participants had completed Week 24 and are included in this analysis. Average Week 24 C-peptide production was higher compared with Screening. Shorter time to peak C-peptide at Week 24 vs Screening was also observed in 7/8 participants. Compared to baseline, mean hemoglobin A1C was lower at Week 24; visual acuity also demonstrated improvement amongst 5/8. All participants showed disease stability or improvement at Week 24, as measured by clinician and participant global impression of change. PB&TURSO was generally well-tolerated with diarrhea the most common adverse event.

CONCLUSIONS: Preliminary results show potential improvement of pancreatic β-cell function, visual acuity, and overall symptom burden post-PB&TURSO treatment in WS. Analyses once all 12 participants have completed Week 24/48 assessments will provide more insight.

KEYWORDS: Experimental Therapeutics, Neurogenetics, Lifespan Manifestations of Childhood Onset Conditions

95. The NINDS Approach to Therapeutic Development for Ultra-Rare Neurological Disorders, Bridging Translational and Clinical Frontiers in Gene-based Therapy

Farhat N (Bethesda, MD), Cho H J, Hartman A, Boshoff C, Cudkowicz M, Videnovic A, Coffey C, Tamiz A, Wright C

OBJECTIVE: Approximately 70% of rare genetic disorders present in childhood, and most have an identified genetic origin that serves as a potential target for the emerging field of gene-targeted treatments.

METHODS: The Ultra-Rare Gene-based Therapy (URGenT) network was launched by the National Institute of Neurological Disorders and Stroke (NINDS) in 2021, supporting the late-stage pre-clinical development of gene-based therapies for ultra-rare neurological diseases. NINDS recently expanded the network to include clinical trial resources through the Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT). NeuroNEXT conducts high-quality neuroscience clinical studies, and consists of a Clinical Coordinating Center, Data Coordinating Center, and geographically distributed clinical sites. NeuroNEXT established the Gene Therapy Consortium (GTC) to provide guidance on issues unique to gene-based therapy trials, thus facilitating the transition of promising assets from the pre-clinical to the clinic. The review process is designed to launch trials within six to nine months of the initial application.

RESULTS: The URGenT network will assist at different stages of awards including manufacturing, IND-enabling studies, and IND submission. Four active pre-clinical projects are developing gene-based therapies for Menkes disease, Prion disease, ALS, and Aspartylglucosaminuria. NINDS recently published a Research Opportunity Announcement (ROA) for URGenT trials. Applicants outside of the URGenT pre-clinical program may apply to this ROA.

CONCLUSIONS: The NINDS model aims to accelerate development of gene-based therapeutics for ultra-rare diseases. Throughout the URGenT network, NINDS will engage with academic researchers, industry partners, patient advocacy groups, and other stakeholders to deliver novel therapeutics safely and quickly to children with ultra-rare neurological disorders.

KEYWORDS: Experimental Therapeutics, Neurogenetics

96. Ecopipam Does Not Adversely Affect Metabolic Parameters in Pediatric Patients With Tourette Syndrome (TS): Results From a Phase 2b Randomized, Placebo-Controlled Trial (RCT) With a 12-Month Open-Label Extension (OLE)

Gilbert D L (Cincinnati, OH), Atkinson S D, Karkanias G B, Munschauer F, Wanaski S, Cunniff T

OBJECTIVE: Dopamine-2 receptor antagonists are efficacious for moderate/severe TS, but they increase the risk of metabolic syndrome symptoms (eg, weight gain, hypertension, hyperglycemia, and dyslipidemia). This trial explored whether ecopipam, a selective dopamine-1 receptor antagonist, was associated with the emergence of clinical features suggestive of metabolic syndrome in pediatric patients with TS.

METHODS: A total of 153 patients with TS aged 6-18 years (mean, 12.8 years) entered the phase 2b RCT, and 121 patients entered the OLE. Assessments included changes in weight, blood pressure (systolic [BPs]; diastolic [BPd]), HgbA1c, total cholesterol, triglycerides, and z-scores for BMI derived from age- and gender-matched CDC data. Changes during the phase 2b RCT were assessed via a mixed model for repeated measures, and a paired t-test was used to assess changes during the OLE.

RESULTS: In the phase 2b, 12-week RCT, no significant differences (ecopipam – placebo) in mean change for weight (0.07 kg, P=0.97), BPs (1.49 mmHg, P=0.39), BPd (1.65 mmHg, P=0.28), HgbA1c (-0.08 %, P=0.11), total cholesterol (-0.07 SI units, P=0.38), or triglycerides (0.02 SI units, P=0.86) were observed. During the 12-month OLE, there were no significant changes in BPs (0.26 mmHg, P=0.85), BPd (0.91 mmHg, P=0.44), HgbA1c (0.03 %, P=0.60); total cholesterol (0.20 SI units, P=0.14), or BMI z-scores (0.05, P=0.35).

CONCLUSIONS: Ecopipam, a selective D1 receptor antagonist, significantly improved YGTSS-TTS scores in a 12-week phase 2b RCT and its 12-month OLE without adversely affecting weight, BMI, HgbA1c, lipids, or BP, indicating the drug does not increase the risk of metabolic syndrome.

KEYWORDS: Experimental Therapeutics, Movement Disorders

97. Effect of Ecopipam, a Selective Dopamine-1 Receptor Antagonist, on Tic Characteristics as Assessed by the YGTSS: Results From the Phase 2b Randomized, Double-blind, Placebo-controlled Clinical Trial in Tourette Syndrome

Gilbert D L (Cincinnati, OH), Karkanias G B, Atkinson S D, Munschauer F, Wanaski S, Cunniff T

OBJECTIVE: Ecopipam, a first-in-class selective dopamine-1 receptor antagonist, is in development for Tourette syndrome

(TS). Whether features of tics are more or less responsive to treatment is unknown. The study aim was to assess the effect of ecopipam treatment on motor and phonic/vocal tic characteristics comprising the Yale Global Tic Severity Scale-Total Tic Score (YGTSS-TTS: number, frequency, intensity, complexity, and interference) in individuals aged 6 to <18 years.
METHODS: Patients were randomized 1: 1 to ecopipam (n=76) or placebo (n=77). This post-hoc analysis of a phase 2b trial examined YGTSS-TTS characteristics at baseline and weeks 4, 6, 8, and 12, utilizing a mixed model for repeated measures analysis of change from baseline.
RESULTS: For motor tics, the largest reductions were in intensity scores (ecopipam – placebo least-squares means [LSM] difference of -0.48 [95% CI, -0.79 to -0.17]; P<0.01) followed by interference, frequency, and number (ecopipam – placebo differences ranging from -0.43 to -0.34; all P<0.05). For phonic tics, the largest reduction was in complexity scores (ecopipam – placebo LSM difference of -0.48 [95% CI, -0.91 to -0.06]; P=0.03). Differences in reduction in motor tic complexity scores and all other phonic tic subscores fell short of statistical significance.
CONCLUSIONS: Ecopipam significantly reduced both motor and phonic tics. Of the 5 motor tic characteristics, only complexity was not significantly reduced. Of phonic tic characteristics, only complexity was significantly reduced. Lower baseline phonic tics scores may limit power to identify statistical differences. The current analysis increases our understanding of ecopipam's effects on tic characteristics.
KEYWORDS: Experimental Therapeutics, Movement Disorders

98. Treatment-emergent adverse events (TEAE) in children with Ataxia-Telangiectasia treated for one year with intra-erythrocyte dexamethasone sodium phosphate (EryDex

Horn B (San Francisco, CA), Thye D, Roden M

OBJECTIVE: Corticosteroids are indicated in many neurological disorders; however, their use is limited by side effects. EryDex releases dexamethasone gradually from erythrocytes to tissues over a one-month period, which reduces toxicity by eliminating peak levels. We present treatment-emergent adverse events (TEAEs) in children with ataxia-telangiectasia treated with EryDex (NCT 02770807) to ameliorate neurological complications, and compare them to placebo control.
METHODS: AEs reported during a one-year treatment of ataxia-telangiectasia patients with EryDex, were coded using MedDRA version 24.0. TEAEs reported in >10% of treated patients (N=116) and placebo control (N=19), are presented.
RESULTS: TEAEs reported in >10% of EryDex-treated patients were pyrexia (29.3%; 15.8% placebo), vomiting (20.7%; 15.8% placebo), cough (19.8%; 31.6% placebo), nasopharyngitis (18.1%; 26.3% placebo), positive bacterial test from the product not resulting in bacteriemia in patients (17.2%; 21.1% placebo), upper respiratory infection (14.7%; 5.3% placebo), diarrhea (12.1%; 26.3% placebo), pruritis (11.2%; 0% placebo) and headache (11.2%; 10.5% placebo).
CONCLUSIONS: Reported TEAEs were similar between treated patients and placebo control with an exception of pruritis, which was noted only in treated patients, and is a well-known complication of intravenous dexamethasone. Side-effects typical of prolonged steroid use, well described in the literature, such as Cushingoid features, erythema, central obesity, hirsutism, striae, increased weight or abnormal behavior, were not reported in EryDex-treated patients. While the efficacy of EryDex and dose equivalence with standard corticosteroids requires further studies, observed safety profile makes it a suitable investigational agent for clinical trials in children requiring chronic steroid use to control their disease.
KEYWORDS: Experimental Therapeutics, Movement Disorders

99. Reduction of heparan sulfate (HS) exposure in cerebrospinal fluid (CSF) correlates with improved long-term cognitive function in patients with mucopolysaccharidosis IIIA (MPS IIIA) following treatment with UX111 gene therapyReduction of heparan sulfate (H

Lau H A (Novato, CA), Patra K, Wolf M, Smith N, Couce M, Rajan D, Truxal K, de Castro M, Fuller M, Monteagudo E, Dougherty L, del Toro M, Flanigan K

OBJECTIVE: MPS IIIA is a rare, childhood-onset neurodegenerative lysosomal storage disease resulting in toxic accumulation of HS in the brain leading to irreversible neurocognitive decline and early death. UX111 is an AAV9 viral vector encoding human SGSH being investigated for efficacy and safety in children with MPS IIIA.
METHODS: UX111-CL301 (NCT04088734) is an ongoing, open-label phase 1/2/3 trial. Children received a single UX111 IV injection and were followed for 24 months (parent study) then for ≥5 years after administration for long-term follow up (NCT04360265). Data are analyzed when all children reached ≥24 months post-treatment and include data from both studies.
RESULTS: At the last data cut, the mITT group (3.0x1013 vg/kg UX111 and ≤24 months old or >24 months old with a baseline Bayley cognitive DQ >60) included 17 children. Baseline mean (SD) age was 22 (10) months. At Month 1, mean (SD) CSF HS decreased 58% (14%) relative to baseline with sustained reduction in CSF HS exposure (median follow up of ∼2 years). At baseline, mean (SD) BSITD-III cognitive raw score was 47.6 (22.2). Scores were stable or improved over time for most patients. Estimated yearly change in BSITD-III cognitive raw score strongly correlated to CSF HS exposure (Spearman's correlation coefficient −0.72, P=0.0011). The only treatment-related adverse event ≥grade 3 was one event of increased alanine aminotransferase that resolved.
CONCLUSIONS: Rapid and sustained reductions in CSF HS exposure after a single UX111 administration showed strong correlation with stabilized or improved cognitive function. The newest data cut will be presented.
KEYWORDS: Experimental Therapeutics, Neurodevelopmental Disorders

100. An Open-label Phase I/II Study of Batten-1 (miglustat) for the Treatment of CLN3-Related Juvenile Batten Disease: 12-month Safety, Biomarker, and Efficacy Results

Clark G D (Houston, TX), Dang Do A, Porter D D, Augustine E, Mink J, Kiser M, Sebille M, Rein W

OBJECTIVE: Juvenile Batten Disease is a rare, fatal, lysosomal storage disease primarily affecting the nervous system. This 18-month open label study in 6 affected patients (≥ 17 years) assessed the safety, biomarker trends and efficacy of Batten-1 (oral miglustat) up to 600mg/d.

Batten-1 inhibits glucosylceramide synthase blocking the accumulation of glycosphingolipids (GSL), and it has anti-inflammatory effects.

METHODS: Safety assessment: incidence of treatment emergent adverse events (TEAEs) and serious adverse events (SAEs), safety labs, neurological examination. Biomarkers: Neurofilament light chain (NFL, serum and CSF) reflecting neurodegeneration, and serum GB3, a GSL accumulating in Juvenile Batten Disease. Efficacy: modified physical assessment subscale of the UBDRS.

RESULTS: Seven participants were screened and 6 participants (5 males and 1 female, mean age 18.8 ± 0.98 years) enrolled.

Safety: no treatment related SAEs, 6/6 patients reported diarrhea and weight loss, 2/6 appetite decrease, muscular weakness, and reduced platelet counts.

Biomarkers: Serum NFL decreased 17% at 6 and 32% at 12 months, CSF NFL decreased 64% at 12 months. Serum GB3 decreased 25% at 6 and 45% at 12 months.

UBDRS: No major progression of the modified Physical Assessment scores after 12 months: Baseline 32.83±4.64, 6 months 32.83±5.27, 12 months 33.83±5.47.

CONCLUSIONS: The safety profile of Batten-1 is consistent with the known profile in other indications. Both biomarkers show a marked decrease after 12 months of treatment and the physical assessment scores do not show expected progression.

Results after 18 months of treatment will be available at the time of presentation.

KEYWORDS: Experimental Therapeutics, Neurogenetics, Neurometabolic

101. Intrathecal Baclofen for the Management of Pediatric Intractable Bladder Spasms: A Case Series

Islam N (Portland, OR), Garavatti E, Siedeman C, Austin C, Sayama C, Wilson J

OBJECTIVE: The intrathecal baclofen pump is used to treat severe spasticity.1 Improvements in bladder spasms have been observed in some patients with baclofen pumps placed for spasticity. We present two pediatric patients with medically intractable bladder spasms successfully treated with intrathecal baclofen.

METHODS: The medical records were reviewed for two patients whose primary indication for baclofen pump placement was intractable bladder spasms.

RESULTS: Patient #1, 16-year-old female with severe neurogenic bladder due to caudal regression syndrome requiring multiple admissions for pain management, had an intrathecal baclofen pump placed delivering 40mcg/day. She had complete relief from bladder spasms until she was readmitted 3 years later for spasms from urinary tract infections. Her pump was increased gradually to 395mcg/day with resolution of spasms and discontinuation of patient-controlled analgesia after switching to bolus mode. Similar to Vaidyanathan et al,2 we found that the addition of boluses treated breakthrough spasms for Patient #1.

Patient #2, 17-year-old female with transverse myelitis, presented with intractable bladder spasms refractory to all previous interventions and received an intrathecal baclofen pump in 2023, titrated to 150 mcg/day with resolution of bladder pain and improvements in spasticity.

CONCLUSIONS: We report two children with primary baclofen pump placement for a novel indication, medically intractable bladder spasms, both with remarkable benefit. From these findings, we suggest that intrathecal baclofen should be considered for treating refractory bladder spasms.

KEYWORDS: Experimental Therapeutics, Neuromuscular

FETAL NEUROLOGY/ NEONATAL NEUROLOGY

102. Perinatal neurologic complications associated with COL4A1/A2 variants – A patient registry cohort study

Pandey S (San Francisco, CA), Boyce D, Monetti S, Gould D, Vassar R

OBJECTIVE: Individuals with COL4A1/2 variants or those carrying fetuses with known/suspected COL4A1/2 variants are often recommended to undergo Cesarean section to decrease theoretical risk of intracranial hemorrhage. However, no studies have assessed tolerance of vaginal delivery in individuals or fetuses with COL4A1/2. This study uses patient registry data to preliminarily assess how fetal intracranial abnormalities may influence delivery type in individuals with COL4A1/2 variants. Additionally, we aim to explore associations between delivery type and postnatal neurologic complications in children with COL4A1/2 variants.

METHODS: Data was analyzed from surveys collected through the Gould Syndrome Foundation Registry, completed by patients or parents of patients with COL4A1/2 variants. Associations between delivery type and neurologic diagnoses were measured using Chi-squared tests, with statistical significance defined as $p<0.05$.

RESULTS: Of the 98 survey respondents, 71 children had known birth status, including 44/71 (62%) born vaginally. In utero stroke was identified in 10 (14%) of cases; an additional 4 had other fetal brain abnormalities. In utero stroke was associated with increased likelihood of C-section delivery ($p=0.036$). Of all children ($n=71$), neurologic complications of COL4A1/2 were common, including cerebral palsy (54%), seizures (69%), and stroke (33%), but vaginal delivery was not associated with increased risk of these diagnoses.

CONCLUSIONS: Data from this largest-to-date COL4A1/2 cohort suggest that method of delivery is not associated with

increased risk of adverse neurologic outcomes. Future studies on the natural history of individuals with COL4A1/2 should systematically document delivery type and perinatal complications to inform optimal management while avoiding unnecessary C-section delivery.
KEYWORDS: Fetal Neurology, Neurogenetics

103. Socioeconomic Characteristics of Patients Seeking Fetal Consultation for Neurological Disorders: A Retrospective Study

Ahmed A (Erie, PA), Shoaib A

OBJECTIVE: This retrospective review sought to determine the differences between the socioeconomic and demographic profiles of patients seeking fetal consults at a tertiary academic center compared to the population of the area served by this center.
METHODS: 125 patients who sought fetal consults for neurological conditions from 2019-2023 were identified. Information on insurance type (public vs. private), median income of the patients' zip code, primary language (English, Spanish, or other), and race were collected from medical records. These measures were compared to US Census data of our county, including the median income, race (white, black, Hispanic, or other), and the percentage of English speakers.
RESULTS: Of our sample, 124 patients had insurance. 65 had private insurance. The average median income of our sample was $90,105.79, which was higher than the median salary in our county, $70,732.00 ($p < 0.01$). In addition, 102 patients noted English being their preferred language, 19 noted Spanish, and 4 noted another language. This was not statistically different from the overall population. Of the patients who disclosed their race, 32 identified as white, 25 identified as black, 40 identified as Hispanic, and 17 identified as other. This was not significantly different from the overall population.
CONCLUSIONS: The patients that sought fetal consultations for neurological conditions had a mix of races and languages similar to the general population in our county. 57.58% had public insurance. However, our patients, on average, lived in areas where the median income was statistically higher than the median income of the county at large.
KEYWORDS: Fetal Neurology

104. Regional Brain Growth Differences in Fetuses with Low Socioeconomic Status and Congenital Heart Disease

Brumfield O (Brookline, MA), Pujols K H, Hart N, Waring K, Rofeberg V, Wypij D, Gholipour A, Rollins C

OBJECTIVE: Socioeconomic status (SES) is known to be associated with brain structure differences in-utero. Congenital heart disease (CHD) is also associated with altered fetal neurodevelopment. We used fetal magnetic resonance imaging (MRI) to investigate associations between SES and brain volumes in fetuses with CHD and healthy controls.
METHODS: We included pregnant persons aged 18-45 years and fetuses 24-36 weeks gestation, with and without CHD, and with no known congenital/genetic abnormalities. Predictors were income-to-needs ratio (INR, low income being INR<1) and maternal education (low being less than a college degree). Primary outcome was total fetal brain volume, with regional volume analyses carried out secondarily. Linear regression using generalized estimating equations adjusting for gestational age (linear and quadratic terms), sex, and CHD status (control vs hypoplastic left heart syndrome/transposition of the great arteries vs other CHD) was used to evaluate relationships between brain regions and both INR and maternal education.
RESULTS: Both groups of CHD fetuses (n=97) had generally smaller brain volumes than controls (n=60). Low income was not associated with total brain volume, but was associated with smaller proliferative compartments (beta -0.5, 95% CI [-0.8, -0.1]; p=0.008). Lower maternal education was associated with smaller subcortical gray matter (-0.3, [-0.4,-0.-1]; p=<0.001) and cerebellar volumes (-0.5, [-0.8, -0.1]; p=0.02).
CONCLUSIONS: Low SES was not associated with global measures of the fetal brain but both income and education were associated with region-specific differences. These findings suggest that distinct mechanisms may underlie associations between unique elements of SES and regional fetal brain development.
KEYWORDS: Fetal Neurology, Neuroimaging, Diversity, Equity, Inclusion

105. Serum Biomarkers for Early Prediction of Intraventricular Hemorrhage in Preterm Neonates: A Prospective Study

Ibrahim AI (Ismailia, Egypt), Ahmed M A, Zekry O Z, El-kelany A E

OBJECTIVE: This study aimed to investigate the potential role of serum biomarkers for the early detection of premature neonates at high risk of intraventricular hemorrhage
METHODS: This prospective longitudinal case-control study included 75 preterm neonates with gestational ages between 28 and 32 weeks. Serial cranial ultrasounds were conducted postnatally. Subjects were divided into case 28 (37.3%) and control 47 (62.7%) groups according to whether they developed IVH or not. Serum erythropoietin, S100B, and activin A were measured for all preterm newborns in the first 24 hours.
RESULTS: Serum erythropoietin, activin A, and S100B proteins concentrations were significantly higher among the IVH group (38.9 ± 12.9, 1.42 ± 0.23 μg/L, 0.19 ± 0.06 μg/L) than among the control group (22.6 ± 14.9, 0.71 ± 0.2 μg/L, 0.07 ± 0.02 μg/L) ($P = 0.001$ for all comparisons). Activin A and S100 proteins were positively correlated with the degree of hemorrhage. At a cutoff value of 1.2 μg/L, serum activin A had a sensitivity of 85.7% and a specificity of 92.4%. Serum S100B protein showed a sensitivity of 75.0% and a specificity of 94.6% at a cutoff value of 0.15 μg/L, and serum erythropoietin had a sensitivity of 81.3% and a specificity of 66.7% at a cutoff value of 37 mIU/mL. The combination of both activin A and S100 proteins improves sensitivity and specificity to approximately 100%.
CONCLUSIONS: Serum erythropoietin, S100B, and activin A proteins are valuable biomarkers for early detection of IVH

in preterm neonates prior to clinical and radiological diagnosis.
KEYWORDS: Neonatal Neurology

106. School-Age Neurodevelopmental Outcome after Provoked Neonatal Seizures

Glass H C (San Francisco, CA), Sturza J, Lemmon M E, Wusthoff C, Soul J, Chu C, Thomas C, Massey S, Benedetti G, Berl M, Anwar T, Numis A, McCulloch C, Franck L, Shellhaas R

OBJECTIVE: To characterize school age outcome after acute provoked neonatal seizures.
METHODS: Nine-center, prospective cohort of neonates with acute provoked seizures assessed at five years using WPPSI-IV, Vineland-2, Behavior Assessment System for Children-3 (BASC), Behavior Rating Inventory of Executive Function (BRIEF), and Social Responsiveness Scale (SRS). Latent class analysis (LCA) was used to define outcome clusters.
RESULTS: Among 144 children, median WPPSI was 97 (IQR 79,112) and Vineland 94 (IQR 80,102). Twenty percent had cerebral palsy; 28% had diagnosed attention deficit hyperactivity disorder (ADHD) or significant BASC attention/hyperactivity ratings; 17% had diagnosed autism spectrum disorder (ASD) or significant SRS; 14% had epilepsy.
LCA revealed three distinct profiles: 1) Typical Development in 65%; 2) Behavioral/Social Dysregulation in 18% (low likelihood of physical disability and normal or mild/moderately impaired cognition, but high likelihood of ADHD/ASD/impaired executive function); 3) Multi-Domain Disability in 17% (high likelihood of moderate/severe impairment across physical, cognitive, and behavioral domains, as well as epilepsy).
Regression analysis revealed neonatal characteristics (severely abnormal EEG, ≥ 2 anti-seizure medications, and abnormal neurologic examination), and infant characteristics (impaired development, CP, and epilepsy at two years) associated with childhood profile.
CONCLUSIONS: Among children with provoked neonatal seizures, most had typical development and function at school age. Children with disability were equally likely to have multiple domains affected or preserved cognitive and physical function with behavioral, executive and/or social dysregulation. Neonatal/infant characteristics associated with neurodevelopmental impairment can help inform predictive modeling of outcome and interventions to promote typical development.
KEYWORDS: Neonatal Neurology, Neurodevelopmental Disorders, Epilepsy

107. Congenital Syphilis Presenting with Intracranial Hemorrhage and Ischemic Stroke in a Preterm Neonate

Yao L (Houston, TX), Das A, Ankar A, Fisher K

OBJECTIVE: Congenital syphilis is a well described entity affecting 57 per 100,000 births yearly in the US, though newborns are often asymptomatic. Herein, we present the case of a preterm neonate presenting with thromboembolic stroke and intraparenchymal hemorrhage in the setting of placenta vasculitis with fetal vasculature hemorrhage indicating vertical transmission.
METHODS: N/A
RESULTS: Patient is a 6-day old female born at 33-week gestation via C-section due to non-reassuring fetal heart tracing. Prenatal history was notable for fetal growth restriction and maternal history of previous intrauterine fetal demise due to in-utero syphilis. Maternal serology revealed nonreactive RPR, reactive treponema antibody, and reactive TPPA. However, the patient's RPR was nonreactive. CSF studies were notable for negative VDRL with an elevated protein. Placental pathology revealed chronic villitis with proliferative hemorrhagic vasculitis consistent with maternal syphilis. Patient started a 10-day course of penicillin given concerns for congenital syphilis. Head ultrasound revealed a left occipital intraparenchymal hematoma. This was redemonstrated on her brain MRI, though MR angiography and venography were normal. Repeat brain MRI performed 1 week later revealed a new right putamen infarct. Echocardiogram revealed both atrial and ventricular septal defects. Thrombophilia evaluation was negative, and no residual venous thrombi was discovered.
CONCLUSIONS: This case demonstrates intraparenchymal hemorrhage and ischemic stroke in the immediate postnatal period as sequelae of vertical transmission of syphilis in a premature neonate due to suspected infectious vasculitis with corroborating placental findings. While CNS manifestations of congenital syphilis are rare, head ultrasound and MRI may be indicated in screening for vascular neurologic complications.
KEYWORDS: Neonatal Neurology, Neuroinfectious Disease, Stroke

108. A Seat at the Table: Family Conferences for Infants with Neurologic Conditions

Young K A (Durham, NC), Field N K, Nanduri N, Glass H, Bansal S, Lemmon M

OBJECTIVE: We aimed to characterize parents' perspectives on the value of and opportunities to improve conferences between parents of critically ill infants and the healthcare team.
METHODS: Parents of infants with neurologic diagnoses in the ICU at an academic medical center participated in longitudinal interviews about decision-making. Parents were included if they had an upcoming family conference to discuss goals of care or neurologic prognosis. Interviews occurred post-conference, at hospital discharge and six months post-discharge. A codebook was developed to characterize interview themes, which were derived using a conventional content analysis approach.
RESULTS: Fifty-two parents (n=37 mothers, n=15 fathers) of 37 infants completed 123 interviews. Approximately half of infants (49%) were born prematurely (< 37 weeks gestation), 32% experienced seizures, and 27% were diagnosed with a brain malformation. Parents described how family conferences offered opportunities to 1) receive decision-relevant education and ask questions, 2) discuss the "big picture" trajectory of care and important decisions, 3) foster

consensus between parents and the care team, and 4) process emotions. Parents identified several opportunities to improve family conferences, including: 1) having the care team assume responsibility for calling regular meetings, 2) summarizing meeting content for parents and documenting discussions for clinicians and 3) prioritizing attendance of consistent and supportive team members.
CONCLUSIONS: These findings demonstrate a valuable role for family conferences in the care of infants with neurologic conditions. Future studies should explore the feasibility and impact of regularly scheduled family conferences, accessible meeting summaries, and attendees dedicated to parent support on therapeutic alliance and communication quality.
KEYWORDS: Neonatal Neurology, Neurocritical Care, Ethics

109. The role of aEEG and continuous conventional EEG in the diagnosis of seizures in infants with moderate to severe hypoxic ischemic encephalopathy

Balasubramaniam S (Wilmington, DE), Talekar K, Adeniyi-Jones S, Carola D, Solarin K, Aghai Z

OBJECTIVE: This study aims to investigate the correlation between aEEG, cEEG and clinical seizures in infants with moderate to severe HIE receiving therapeutic hypothermia.
METHODS: The study analyzed retrospective data on newborns born over 35 weeks gestation who were admitted to the NICU between April 2017 and August 2022 for moderate to severe HIE and received therapeutic hypothermia. Using cEEG seizures as a gold standard, statistical parameters of clinical and aEEG seizures were calculated.
RESULTS: A total 82 infants were included in the analysis, 18 infants (21.9%) had clinical seizures, 19 infants (23.2%) had seizures on aEEG and only 9 infants (11%) had seizures on cEEG. The cEEG confirmed electrical seizures only in 6 out of 19 infants (31.6%) who had seizures on aEEG. Similarly, cEEG detected electrical seizure only in 5 out of 18 infants (27.8%) with clinical seizures. The cEEG also diagnosed electrical seizure in 3 additional infants who had no seizure activity on aEEG and 4 infants who had no clinical seizures. Only 5 infants (6.1%) had concurrence clinical, aEEG and cEEG seizures.
CONCLUSIONS: Relying on aEEG and clinical seizures will over treat and under diagnose electrical seizures in neonates with HIE undergoing therapeutic hypothermia. Continuous conventional EEG can play a crucial role in both diagnosis and management of seizures in neonates with HIE. Promoting the use of cEEG and considering its integration into standard of care can greatly improve the diagnosis and management of neonatal seizures, ultimately improving the outcomes.
KEYWORDS: Neonatal Neurology, Epilepsy, Practice Parameters

110. Life After Neonatal Seizures: Characterizing the Longitudinal Parent Experience.

Field N K (Durham, NC), Franck L S, Shellhaas R A, Glass H, Young K, Dhar S, Hamlett A, Pilon B, Means K, Soul J, Massey S, Wusthoff C, Chu C, Thomas C, Rogers E, Berl M, Anwar T, Benedetti G, Lemmon M

OBJECTIVE: To characterize the parent experience of caring for children impacted by neonatal seizures, including longitudinal assessment across childhood.
METHODS: This prospective, observational, multicenter study was conducted at Neonatal Seizure Registry (NSR) sites in partnership with the NSR Parent Advisory Panel. Parents completed surveys at discharge, 12-, 18-, 24-months, 3-, 4-, 5-, 7-, and 8-years of age. Surveys included demographic information and several open-ended questions targeting parent experience. A conventional content analysis approach was used to analyze qualitative data.
RESULTS: 320 caregivers completed at least one open-ended question. We identified three primary themes: (1) Personal Burden of Care: Parents experienced emotional distress, financial strain, physical demands, and fears for their child's unknown outcome and potential for seizure recurrence. (2) Managing Day-to-Day Life: Parents described difficulties navigating their parenting role, including managing their child's challenging behaviors and understanding their child's needs amidst neurodevelopmental impairment. (3) My Joys as a Parent: Parents valued bonding with their child, being a caregiver, and watching their child's personality grow. Though overall themes were consistent, the ways in which they manifested differed across ages, with parents of older children highlighting aspects of parenthood like physical demands, behavioral challenges, and the feelings of joy or loss that accompanied witnessing their child's developmental progress.
CONCLUSIONS: Parents of children impacted by neonatal seizures face both persistent and unique challenges over time, which are interwoven with the joys of being a parent. Our findings suggest that future interventions should acknowledge and promote parental resiliency and address caregivers' psychosocial needs longitudinally.
KEYWORDS: Neonatal Neurology, Epilepsy, Neurodevelopmental Disorders

111. Empiric Treatment for seizure-like Events in Neonates: Are We Better than a Coin Flip

Sullivan N (Birmingham, AL), Gaonkar M, Leahey E, Shukla V, Walker S, Rashid S

OBJECTIVE: The gold standard is to characterize seizure-like events on continuous video electroencephalogram (cvEEG) before administering anti-seizure medication (ASM). However, in many scenarios, an ASM is empirically administered before cvEEG confirmations of seizures. We analyzed data from a large tertiary care center's neonatal intensive care unit (NICU) to investigate the incidence of successful event capture on cvEEG and the probability of providers making correct decisions regarding empiric ASM administration.
METHODS: We retrospectively (June 2018- April 2024) identified 232 neonates placed on cvEEG (> 4-hour duration) for concerning events. We then identified a subset of these patients for whom cvEEG captured events. We further analyzed groups with typical events captured and classified as epileptic (seizures) vs. non-epileptic.

RESULTS: Of the 232, cvEEG only captured an event of concern in 41.8% of neonates. The correct empiric ASM administration was higher in patients with events of concern classified as epileptic seizures (60.9% vs. 33.3%; p= 0.007). These patients had additional seizures that did not correlate with their typical event (33.3% vs 7.8%; p= .002). Overall, the probability of correct decision was 62% (empiric treatment) vs. 65% (no empiric treatment).
CONCLUSIONS: Although the gold standard, when available, cvEEG did not capture the event of concern for the majority of patients. The low yield, resource-intensive nature, and lack of universal availability of cvEEG translates into clinical judgment remaining integral to ASM-related decision-making. Although far from ideal, providers performed better than expected by chance when choosing in favor or against empiric ASM use for typical neonatal events.
KEYWORDS: Neonatal Neurology, Epilepsy

112. The little brains' dilemma: a proposed neonatal seizure treatment algorithm

Roman Guzman A M (Lexington, KY), Thamann A, Torgalkar R

OBJECTIVE: Neonatal seizures are often difficult to identify and challenging to treat with a lack of data on ideal anti-seizure medication (ASM) regimens for this population . This enhances the need for standardized algorithms of neonatal seizure management to reduce seizure burden and improve effectiveness of the care process.
METHODS: Literature review in Pubmed and Cochrane "neonatal seizures", "incidence neonatal seizures ", "algorithm neonatal seizures", "antiepileptic drugs in neonatal seizures".
RESULTS: Inclusion criteria for this neonatal seizure pathway includes neonates with suspected seizures. After identification of seizure(s), initiation of necessary workup, and EEG placement, we then propose a three-tier treatment protocol. First-line ASM treatment is with levetiracetam 60 mg/kg for short, self-limited seizures only while phenobarbital 20 mg/kg is first-line treatment for seizure >3 minutes, seizure requiring benzodiazepine rescue treatment, or multiple repeated seizures from onset. Second line treatment then proceeds as needed with fosphenytoin 15 mg/kg. Third line treatment ensues with either alternative second line medications or midazolam bolus then infusion with the option of pyridoxine trial for suspected neonatal epilepsies. Further workup should be obtained to determine etiology of seizures. Protocol also provides guidance for early ASM weaning prior to discharge for symptomatic neonatal seizures.
CONCLUSIONS: Neonatal seizures can be a challenging clinical dilemma, often with difficulty in choosing an ideal ASM escalation regimen. Here we present a treatment algorithm for neonatal seizures to provide a standardized approach in the NICU. Further data collection will be needed to assess effectiveness and clinical outcomes.
KEYWORDS: Neonatal Neurology, Neurocritical Care, Epilepsy

113. Effect of Clemastine Treatment on Long-term Motor Outcomes in a Mouse Model of Preterm White Matter Injury

Odell E (San Francisco, CA), Jabassini N, Green A, Chan J, Ostrem B

OBJECTIVE: Preterm white matter injury (PWMI) is the most common cause of brain injury in premature babies. PWMI involves a failure of myelination in the developing brain, and frequently results in motor delays and disability, including cerebral palsy. Clemastine was previously shown to rescue myelination deficits in a mouse model of PWMI, with a minimum effective dose (MED) of 7.5mg/kg/day. We sought to determine the effect of clemastine treatment on long-term motor outcomes, hypothesizing that clemastine treatment at the MED rescues motor deficits in young adult mice in a chronic sublethal hypoxia model of PWMI.
METHODS: Mouse pups were exposed to normoxia or hypoxia (10% FiO2) from postnatal day 3 (P3) through P10. Vehicle or clemastine at the MED was given orally to hypoxia-exposed mice, daily from P3 through P10. At 6 weeks of age, we performed motor testing with rotarod, pole and balance beam tests. We assessed oligodendrocyte differentiation and myelination by immunohistochemistry in the brain and optic nerves following motor testing.
RESULTS: Hypoxia exposure with vehicle treatment resulted in impaired motor performance compared to normoxia. Clemastine treatment rescued hypoxia-induced motor impairments. Normoxia-exposed and hypoxia-exposed, clemastine-treated mice also displayed improved myelination and increased density of differentiated oligodendrocytes at 10 weeks compared to hypoxia-exposed, vehicle-treated mice.
CONCLUSIONS: Clemastine treatment at 7.5 mg/kg/day from P3-P10 rescues motor and myelination deficits in young adult mice in a chronic sublethal hypoxia model of PWMI. These results demonstrate evidence of a durable response and suggest that clemastine might improve long-term motor outcomes in neonates with PWMI.
KEYWORDS: Neonatal Neurology, Cerebral Palsy

114. Parent Experience of Decision-Making for Infants with Neurologic Conditions in the Intensive Care Unit

Young K A (Durham, NC), Field N K, Nanduri N, Glass H, Lemmon M

OBJECTIVE: Existing literature demonstrates the importance of understanding parent preferences and experiences to facilitate shared decision-making. We aimed to characterize 1) how parents identified and weighed values in decision-making, 2) parent-perceived and preferred decision-making roles, and 3) parent perceptions of clinician recommendations.
METHODS: Parents of infants with neurologic diagnoses in the intensive care units at a large, academic medical center participated in interviews about decision-making from 2018-2020. Interviews were analyzed using a conventional content analysis approach. Two independent research team members analyzed data and resolved discrepancies via consensus.
RESULTS: Fifty-two parents (n=37 mothers, n=15 fathers) of 37 infants completed at least one interview. Parent median

age was 31 (range: 19-46) and half self-identified as Black. The most common infant neurologic diagnoses were seizures (32%) and brain malformations (27%). We identified 3 themes: 1) Identifying, balancing, and communicating values: Parents wanted the care team to elicit and explore their values, and reflected on how holding multiple values and communicating these values to clinicians was a challenge. 2) Experiences and perceptions of decision-making roles: Parents preferred being involved in decision-making and lack of involvement sometimes led to conflict with the team. 3) Perceptions of recommendations: Parents positively described how recommendations facilitated their involvement in decision-making and suggested clinicians "step into their shoes" when making recommendations.

CONCLUSIONS: We characterized the parent perspective of decision-making and identified parent-informed opportunities for clinicians to improve the parent experience. Future work should test the efficacy of these strategies in improving shared decision-making, therapeutic alliance, and parent satisfaction.

KEYWORDS: Neonatal Neurology, Neurocritical Care, Ethics

115. MRI Brain T2-Hyperintensity and Neurodevelopmental Outcomes in Neonatal Encephalopathy

Christensen R (Toronto, ON, Canada), Widjaja E, Kamino D, Mamak E, Ly L, Tam E

OBJECTIVE: Diffuse T2-hyperintensity on brain MRI is commonly seen with neonatal encephalopathy, however the clinical implications remain unclear. The objective of this study was to examine the association between brain T2-hyperintensity and neurodevelopmental outcomes after neonatal encephalopathy.

METHODS: A prospective cohort of neonates born >36 weeks postmenstrual age with neonatal encephalopathy underwent brain MRI. Scans were assessed for T2-hyperintensity and diffusion restriction, and graded using Kidokoro and Barkovich scoring. Regional T2-hyperintensity and diffusion restriction were assessed in the mamillary bodies and pons. The association between diffuse and regional T2 hyperintensity and Bayley-III cognitive, language and motor composite scores at 18-months and 3-years were examined using linear regressions adjusting for sex and Barkovich scores.

RESULTS: The cohort included 102 term infants (63% males) born at median 40 weeks (IQR: 1.9), with brain MRI at median 4 days of age (IQR: 1). Participants with moderate-severe encephalopathy (99%) were treated with therapeutic hypothermia. Diffusion restriction was present in 35% diffusely, 5% in the mamillary bodies, and 4% in the pons. T2-hyperintensity was present in 76% diffusely, 28% in the mamillary bodies, and 17% in the pons. T2-hyperintensity score and mamillary body T2-hyperintensity were not associated with cognitive, language and motor outcomes. Pons T2-hyperintensity was associated with worse motor outcomes at 18-months, controlling for diffusion restriction (β=-10.1; P=0.02).

CONCLUSIONS: Diffuse, and mamillary body T2-hyperintensity were common after neonatal encephalopathy, but not associated with neurodevelopmental outcomes. Pons T2-hyperintensity was associated with worse motor outcomes, and could be used as a neuroimaging biomarker for neuroprognostication.

KEYWORDS: Neonatal Neurology, Neuroimaging, Neurocritical Care

116. Classification System for Intracranial Hemorrhage Secondary to Neonatal Cerebral Venous Sinus Thrombosis

Christensen R (Toronto, ON, Canada), Krishnan P, Cizmeci M, Chau V, de Vries L, Moharir M

OBJECTIVE: Neonatal cerebral venous sinus thrombosis (CVST) is associated with intracranial hemorrhage (ICH) and brain injury. The presence of "severe" ICH poses a challenge for anti-coagulation treatment of CVST, as ICH can be highly variable. The objective of this study was to develop a standardized approach to classify the location and severity of ICH in neonatal CVST.

METHODS: This was a retrospective cohort study of term neonates with radiologically confirmed CVST (MRI/MRV or CT/CTV). Neonates were excluded if they were preterm and if CVST was diagnosed with cranial ultrasound. Scans were reviewed to confirm the location and severity of ICH and classified by incorporating previously published intracranial hemorrhage grading systems.

RESULTS: A total of 148 neonates with CVST were included. ICH secondary to CVST was categorized based on location (extra-axial, parenchymal, intraventricular, supratentorial, infratentorial) and severity (minor, major). Extra-axial hemorrhage was classified as minor for thin hemorrhage < 3mm and major for thick hemorrhage > 3mm or mass effect. Parenchymal hemorrhage was classified as minor for punctate and major for hematomas or mass effect. Intraventricular hemorrhage was classified as minor for grades 1-2, and major for grade 3 with or without periventricular hemorrhagic infarct, mass effect or hydrocephalus. Images characteristic of each type of hemorrhage were collated into an atlas.

CONCLUSIONS: A neonatal CVST ICH classification system allows for a comprehensive and standardized description of hemorrhage in neonates with CVST. The utility of a classification system for CVST associated hemorrhage includes stratification of at-risk neonates, identification of neonates eligible for anticoagulation therapy and neuroprognostication.

KEYWORDS: Neonatal Neurology, Stroke, Neuroimaging

117. Optimizing Regulatory Management in a Multi-Site, International, Investigator-Initiated Interventional Neonatal Seizure Clinical Trial

Ramey E (Minneapolis, MN), Faanes B, Lee M, Coleman C, Wang S

OBJECTIVE: Conducting an interventional clinical trial for neonatal seizures across multiple sites and countries presents significant regulatory challenges due to varying local and international laws, ethical standards, and operational hurdles.

Effective regulatory management is critical for ensuring compliance, trial integrity, and participant safety. Here, the study team for the NEOLEV3 trial introduces strategic regulatory practices to enhance trial efficiency and compliance.

METHODS: NEOLEV3 is an FDA-funded, Investigational New Drug (IND) Phase 2 Dose Escalation Study of Levetiracetam in the Treatment of Neonatal Seizures recruiting from five hospitals across the USA and New Zealand with Data Safety Monitoring Board (DSMB) and Clinical Trials Monitoring oversight. The study team streamlined ethical approval processes by developing standardization of documentation, and implementing a comprehensive training program on regulatory requirements for all site staff.

RESULTS: he NEOLEV3 study team's standardized regulatory framework includes: 1) Implementation of compliant electronic storage tools to electronically sign, manage, and store study documents (Florence eBinders and Box), 2) Coordination between the FDA IND, a USA central IRB (Advarra), and New Zealand's Health and Disability Ethics Committee, and 3) FDA Part 11 compliance (21 CFR Part 11) database management for electronic records and signatures. This regulatory framework provides for remote clinical trial monitoring, centralized audit trails, efficient identification of compliance and site performance issues that enhances overall data integrity.

CONCLUSIONS: Successful regulatory management in an interventional neonatal seizure clinical trial requires meticulous planning, a clear understanding of the regulatory landscape in each country, and effective communication and coordination among all stakeholders.[SW1]

KEYWORDS: Neonatal Neurology

118. Continuous Electroencephalography Monitoring for Neonatal Seizure Detection: Incidence and Outcomes in Cardiac Surgery Patients

Philliben R F (Salt Lake City, UT), Ostrander B, Keene J, Campbell K, Sandoval Karamian A, Hobbs R, Glotzbach K

OBJECTIVE: Perioperative brain injury is a potentially devastating complication after neonatal cardiac surgery. Seizures are a marker of brain injury and predict adverse outcomes. Neonatal seizures are frequently subclinical, making a brain injury diagnosis elusive without continuous electroencephalography (cEEG). This study's objective was to determine the incidence of neonatal seizures after implementation of a postoperative cEEG neuromonitoring program.

METHODS: Prospective, single center, cohort study including neonates (<30 days) undergoing cardiopulmonary bypass surgery between 2019 and 2021. Patients were given 48 hours of postoperative cEEG monitoring along with protocolized medical seizure treatment when indicated. Center standard anesthesia practice included intraoperative (pre-cardiopulmonary bypass) pentobarbital for operations requiring circulatory arrest or low-flow cerebral perfusion

RESULTS: 104 neonates underwent EEG monitoring (35% single ventricle). Median (IQR) age at surgery was 6 days (4,8), ICU and hospital length of stay were 14.4 (9.6, 22) and 25.3 (16.4, 33.5) days, respectively. 22% had major complications, including seizures. 1.9% (2 patients) had perioperative, electroclinical seizures (1 status epilepticus). Average time to seizure was 25.8 hours. 66% of the cohort received intraoperative pentobarbital (1 patient with seizure). Perioperative mortality was 4.8%. 6% of the cohort had a seizure prior to discharge, but outside the monitoring period.

CONCLUSIONS: The incidence of perioperative seizure incidence in this neonatal cohort was significantly lower than what is currently reported within the literature. The pharmacodynamic and developmental impact of intraoperative pentobarbital on seizure incidence remains unknown. Future study will be performed to include qualitative analysis of cEEG monitoring and its association with short- and long-term neurodevelopmental outcomes.

KEYWORDS: Neonatal Neurology, Neurocritical Care, Early Stage Investigator

119. Neonatal Mild Hypoxic-Ischemic Encephalopathy: Accelerated death of viable neurons is delayed until 2nd week post-injury

McNally M A (Boston, MA), Lau L A, Granak S, Hike D, Staley K

OBJECTIVE: Mild hypoxic-ischemic encephalopathy (HIE) is common in neonates with 30-40% of patients experiencing adverse long-term outcomes. Progression of injury is poorly understood, and no therapies are currently available. Thus, we developed a novel in vivo system to measure individual neuronal activity and death in real-time after mild hypoxia-ischemia (HI).

METHODS: After P1 intracerebroventricular injection (AAV1-Syn1-mRuby2-GCaMP6s) and P8 cranial window placement,P10 mouse pups underwent right carotid ligation and 15 minutes of hypoxia (FiO2 0.08) vs. sham. Chronic, awake two-photon calcium imaging of right parietal cortex was completed. Neuronal death was quantified using the fluorophore quenching assay. Ex-vivo 14T MRI was completed at P28.

RESULTS: Mild HI transiently suppresses cortical activity for hours post-injury (vs. sham, n=13 pups/group; $p<0.01$). No post-HI seizures are seen. By 24 hours, network activity recovers. Cortical rhythms remain intact for 11 days post-injury (n=8 pups/group; n.s.). Despite this, mild HI causes delayed, progressive neuronal loss maximal during the second week post-injury (n=8 pups/group; $p<0.01$). At baseline, 24-, and 48-hours post-HI, network participation of individual neurons destined to die is indistinguishable from those that survive (n=8 pups; n.s.). 2 weeks post-HI, no cortical or hippocampal atrophy was quantified on ex vivo MRI (n=3 pups/group; n.s.).

CONCLUSIONS: Like neonates with mild HIE, our model demonstrated re-constitution of cortical network activity, no post-HI seizures, and no moderate-severe injury on MRI. Mild HI causes accelerated neuronal death in the second week after injury. Critically, these neurons demonstrate multiple biomarkers of viability for days post-injury, suggesting their later death can be modified.

KEYWORDS: Neonatal Neurology, Early Stage Investigator

120. A Novel Question Prompt List for Parents of Neonates with Seizures.

Field N K (Durham, NC), Glass H C, Franck L S, Shellhaas R, Means J, Soul J, Massey S, Wusthoff C, Chu C, Thomas C, Rogers E, Berl M, Anwar T, Benedetti G, Lemmon M

OBJECTIVE: Existing data suggest parents of critically ill children may be unsure of what questions to ask when communicating with clinicians about their child's care. We aimed to develop a question prompt list (QPL) for parents of neonates with seizures to facilitate meaningful dialogue between parents and their baby's care team.

METHODS: This prospective, observational, multicenter study involved nine US-based Neonatal Seizure Registry (NSR) sites. Parents of children with acute provoked seizures completed surveys at discharge, 12-, 18-, 24-months, and 3-, 4-, 5-, 7-, and 8-years. We used 3 sources to create QPL content: (1) unanswered questions about their child's condition posed by 104 caregivers, (2) an existing QPL created for neonatal intensive care unit (NICU) parents, and (3) feedback from the NSR Parent Advisory Panel, which is comprised of community members and parents and provides input on all studies within the NSR portfolio.

RESULTS: The collation of data and subsequent collaborative refinement resulted in a QPL containing 21 questions. Questions were categorized into five topics: (1) Understanding my baby's seizure diagnosis (4 questions), (2) My baby's seizure medications (5 questions), (3) What to expect for my baby's future (5 questions), (4) What to do in case of seizures after my baby goes home (3 questions), and (5) Finding information and support (4 questions).

CONCLUSIONS: We present a novel, parent-informed tool to support parent-clinician communication about neonatal seizures. Next steps include implementation and evaluating the effectiveness of this QPL on quality-of-care outcomes such as parent question-asking, medical understanding, and well-being.

KEYWORDS: Neonatal Neurology, Epilepsy, Neurodevelopmental Disorders

121. Challenges in Consenting Critically Ill Neonates for Neuro-Interventional Clinical Trials

Coleman C (Minneapolis, MN), Faanes B, Ramey E, Lee M, Reiner G, Haas R, Gold J, Sharpe C, Wang S

OBJECTIVE: Obtaining informed consent for neuro-interventional clinical trials involving critically ill neonates presents unique ethical, legal, and practical challenges with the vulnerability of the patients, the time urgency of clinical situations and complexity of the consent process. We studied major challenges in securing informed consent in this setting.

METHODS: We collected feedback from neonatologists, neurologists, nurses, research staff, and families regarding the difficulties of obtaining informed consent in two neuro-interventional neonatal clinical trials: 1) Effects of Music-Based Intervention (MBI) on Neurodevelopmental and Pain Response in Preterm Infants, and 2) A Phase 2 Dose Escalation Study of Levetiracetam in the Treatment of Neonatal Seizures (NEOLEV3).

RESULTS: Three primary challenges were identified: 1) the urgent and emotionally distressing decision-making timeframe; 2) the overwhelming complexity of trial information for families; and 3) ethical dilemmas in proxy decision-making regarding risks and benefits. In the MBI trial, the more critically ill the neonate, the longer the time to consent (average 9.6-9.8 days) compared to more stable neonates (average 4.5-6.5 days), and the overall consent rate was approximately 15%. In the levetiracetam trial, due to the time-sensitive nature of neonatal seizures, consent was obtained within hours of birth, and thus far, has an overall enrollment rate of over 90%.

CONCLUSIONS: Effective strategies to improve consent include using simplified communication materials and enhancing training on consent practices. Future approaches should focus on promoting transparent and empathetic engagement with parents or guardians to ensure informed, ethical consent in high-pressure clinical settings.

KEYWORDS: Neonatal Neurology, Ethics, Neurocritical Care

122. A Phase 2 Dose Escalation Study of Levetiracetam in the Treatment of Neonatal Seizures (NEOLEV3)

Wang S (Minneapolis, MN), Gold J, Reiner G, Haas R, Sharpe C

OBJECTIVE: Neonatal seizures affect 1 in 300 infants with high rates of permanent disabilities such as cerebral palsy, global developmental delay and epilepsy. Mounting evidence indicates that seizures contribute to brain injury and neurodevelopmental disability; better treatment may improve long-term neurodevelopmental outcomes.

METHODS: Here, we present our FDA-funded NEOLEV3 clinical trial that aims to refine the standard clinical paradigm for neonatal seizure treatment by demonstrating a stratified approach; using Levetiracetam (LEV) with its significantly improved side effect profile, targeted at reducing mild to moderate seizure burden, reserving Phenobarbital (PHB) with its associated side effects for neonates with high seizure burden. We hypothesize that optimal dosing of Levetiracetam (LEV) to treat neonatal seizures is significantly greater than 60mg/kg.

RESULTS: A dose escalation and safety study is underway to determine the maximum safe tolerated dose of LEV (primary endpoint). Infants who continue to have seizures following standard dose LEV will receive either higher dose LEV or the control drug PHB, randomized in a 3: 1 allocation ratio. Dose escalation will proceed in 3 phases to the maximal LEV loading dose of 150mg/kg. A minimum of 10 subjects will be studied at each dosing level phase with evaluation of dose limiting toxicity. Secondary endpoints include: additional efficacy of higher doses of LEV, pharmacokinetics of high dose LEV in neonates, and the usefulness of Persyst neonatal seizure detection.

CONCLUSIONS: Successful completion of NEOLEV3 will result in optimization of a safe, non-toxic medication (LEV) for neonatal seizures and improvement of technologies for accurate immediate automated diagnosis of seizures.

KEYWORDS: Neonatal Neurology, Experimental Therapeutics

123. Acute and long-term neurodevelopmental complications faced by neonates requiring renal replacement therapy

Taylor S E (Cincinnati, OH), Schuh M, Taylor J M, Venkatesan C

OBJECTIVE: Characterize neurologic morbidity associated with dialysis during early life in neonates dependent on renal replacement therapy (RRT), including hemodialysis and peritoneal dialysis.

METHODS: A retrospective analysis was performed on all neonates prenatally diagnosed with congenital anomalies requiring initiation of RRT early in life (within the first 6 weeks). Their postnatal course was followed for the presence of neurologic morbidity, including acute neurologic events.

RESULTS: We identified 17 neonates born with congenital anomalies of the kidney or urologic tract and started on RRT within the first 6 weeks of life. Current ages range from 11 months to 6 years. Ten patients (58.8%) developed an acute neurological complication. The most common was seizures (n=9, 52.9%), followed by stroke (n=7, 41.2%), and posterior reversible encephalopathy syndrome (PRES) (n=2, 11.7%). There were two infants who had more than one stroke. Seizures occurred within the setting of stroke, infection, hyponatremia, PRES, or were cryptogenic. Four infants developed epilepsy. Nearly all patients had abnormalities on brain MRI (13 of 14, 92.8%). This included three who did not have an acute neurologic event, but whose MRI demonstrated global cerebral volume loss. Longer-term neurodevelopmental assessment in patients older than 2 years (n=10) showed that nine (90%) required gastrostomy-assisted feeding, four (40%) had cerebral palsy, and two (20%) were non-verbal.

CONCLUSIONS: Neurologic morbidity is frequently seen in neonates requiring RRT. Morbidity includes acute events like seizures or stroke, as well as long-term neurodevelopmental deficits. Counseling prior to initiation of RRT should review the high risk for neurological complications.

KEYWORDS: Neonatal Neurology, Stroke

124. Lacosamide as an adjunctive therapy in the management of refractory neonatal seizures: A retrospective study

Sah J P (Louisville, KY), Ritchie J, Jain S, Javarayee P, Karia S, Means M, Karakas C

OBJECTIVE: Neonatal seizures present significant treatment challenges, often requiring multiple antiseizure medications (ASMs). This retrospective study aims to evaluate the efficacy of lacosamide (LCM) as an adjunctive ASM in treating refractory neonatal seizures.

METHODS: The study included neonates treated with LCM within 44 weeks of corrected gestational age admitted to our hospital between January 2015 and December 2023. The collected data included demographic features, birth history, perinatal/postnatal complications, seizure etiology, seizure burden, and treatment details. The primary outcome was the response to LCM, assessed by quantitative changes in electrographic seizure burden pre- and post-24-hour LCM administration by reviewing raw video-electroencephalogram (v-EEG).

RESULTS: Eighteen out of 33 eligible neonates had available v-EEG data and were included in the study. The demographic and clinical characteristics of the neonates varied, including a range of etiologies including hypoxic ischemic injury, intracranial hemorrhage, brain infection, cortical malformation and genetic. The most common first-line ASM used was phenobarbital; an average of three ASMs were used before LCM use. The median loading dose of LCM was 6 mg/kg/day. In this cohort, 72% of neonates had a favorable response with >75% seizure burden reduction post-LCM use.

CONCLUSIONS: LCM may be a promising adjunctive ASM in treatment of refractory neonatal seizures. Further prospective studies are needed to confirm the effectiveness of LCM and explore its long-term outcomes and safety profile in this vulnerable patient group.

KEYWORDS: Neonatal Neurology, Epilepsy

125. Pilot of Bilateral Infant Stimulation Study (BLISS): a study of positive touch intervention on parent and infant biophysical stress response in the NICU

Islam N (Portland, OR), Garavatti E, Cimino C, Ondusko D, McEvoy C, Mackiewicz K

OBJECTIVE: Parent-child bonding is imperative during early infant development.1 Admission to the neonatal intensive care unit (NICU) creates decreased bonding opportunities and can have clinical impacts on parents, including symptoms of stress, anxiety, and depression.2,3 These can be improved through family-centered interventions.4,5 Our objective was to develop a methodology for studying physiologic stress response in parents and infants in NICU environment during a parent-provided positive touch intervention.

METHODS: Participants include parent-infant dyads in the NICU with infant eligibility criteria of >31 weeks gestation at birth and <4 weeks old, with an enrollment goal of 40. Infant physiologic data is collected from hospital monitors and parent data is collected through wearable heart rate devices. Parents completed surveys before and after intervention. Anxiety was measured with Visual Analog Scale for anxiety (VSA) and State Train Anxiety Inventory (STAI), distress with the Distress Thermometer, and emotional closeness with an analog scale.

RESULTS: 19 dyads did not fulfill all eligibility criteria on further screening, 13 declined participation, 12 enrolled, 4 discharged early, 1 had scheduling conflicts, and 7 completed study activities. Infant heart rate was unable to be collected for 2 sessions due to incompatibility of hospital monitor in off-unit housing of patients. Preliminary data shows that our intervention impacts parent anxiety (p=0.0124, p=0.0496) and feeling of closeness (p=0.0143) with their infant but not parent distress levels (p=0.0998).

CONCLUSIONS: This study is ongoing. Overall, preliminary data suggests study intervention improves parent anxiety and parent-infant bonding.

KEYWORDS: Neonatal Neurology, Experimental Therapeutics

126. Expanding the phenotypic understanding of MIRAGE syndrome to include neurologic involvement seen in two patients with SAMD9 mutations.

Cruz C (Portland, OR), Baiandurova A, Coryell J, Pettersson D, Boston B, Garavatti E

OBJECTIVE: We aim to document the phenotypic presentation of two patients with SAMD9 associated MIRAGE syndrome. There is a paucity of data on neurologic symptoms these patients experience and limited information about neuropathological features.

METHODS: Parental consent was obtained for inclusion in case reports. A clinical brain autopsy was obtained on one patient. Chart review was completed on both patients to identify clinical features of MIRAGE syndrome. A neuroradiologist reviewed all brain imaging obtained on these two patients.

RESULTS: These two patients demonstrated some shared clinical features of MIRAGE and neurologic involvement. Both patients demonstrated lenticulostriate vasculopathy on head ultrasound, progressive ventriculomegaly, and developmental venous anomalies.

CONCLUSIONS: These two cases demonstrate several typical features of MIRAGE and contribute to defining the neurologic phenotype that is underreported. This contributes to the recent understanding that the clinical phenotype is broader than when first described. The underlying neuropathologic process of the SAMD9 gene is yet to be understood. All data on cause of death that has been documented is related to infection or complications from myelodysplasia, our cases demonstrate features of progressive neurologic injury. Etiology of seizures may be related to gliosis or cortical malformations. Malignant hyperthermia has not been previously documented in patients with MIRAGE syndrome. Both patients experienced autonomic dysfunction leading to infectious rule-outs, consideration of balancing the need for infectious rule-out with possible autonomic dysfunction. Further research is needed to make clinical guidelines recommendations and appropriately counsel families.

KEYWORDS: Neonatal Neurology, Neuroimaging, Neurogenetics

127. Survey-based national exploration of parental holding practices in neonatal intensive care units

Garavatti E (Portland, OR), Calder T, Scottoline B

OBJECTIVE: We aim to explore current parental holding practices during various medical interventions used in NICUs across the United States. We aim to explore current parental holding practices during various medical interventions used in NICUs across the United States.

METHODS: This is an exploratory study, approved by our IRB. A NICU provider survey was created examining holding practices during various medical interventions, including EEG and therapeutic hypothermia, and asked about formal holding policies and who determines if holding will be offered. The survey was distributed through AAP's listserv for Section on Neonatal-Perinatal Medicine. The survey was modified for NICU nursing and was distributed through Vermont Oxford Network (VON) email listse, and was submitted for distribution through National Association for Neonatal Nursing (NANN).

RESULTS: There were 150 responses to provider survey through AAP, 18 responses to nursing survey through VON and 26 responses to nursing survey through NANN. Most responses (93% of provider and 100% of nursing) were based on level III or IV NICUs. Both providers and nursing staff report holding being more commonly allowed with infants with PICC (86% and 93%), on ventilator (41% and 43%), and with UVC (40% and 50%) and not allowed while on therapeutic hypothermia (42% and 36%), with chest tube in place (25% and 29%), and on high frequency ventilator (19% and 18%).

CONCLUSIONS: Primilinary results show similar trends in parental holding practices as compared to nursing. No interventioin was found to have uniform practices across country. Less holding is offered with therapeutic hypothermia, chest tubes, high frequency ventilation, and umbilical arterial catheters. Guidelines or protocol for parental holding are infrequently used.

KEYWORDS: Neonatal Neurology, Neurocritical Care, Practice Parameters

128. A Case Series of Neonates with Deep Medullary Vein Thrombosis

Barsh G R (Palo Alto, CA), Pal R, Dahmoush H, Mayne E

OBJECTIVE: Deep medullary venous thrombosis (DMVT) is characterized by the formation of blood clots within the deep medullary veins of the brain, often in neonates. Advances in MRI technology have improved detection of DMVT, but there is controversy about their etiology, clinical significance, and management.

METHODS: We identified children with medullary venous thrombosis identified on MRI between 2008-2023 at Stanford Children's Health. Charts were reviewed for clinical history, MRI findings, management, and neurodevelopmental outcomes.

RESULTS: Our analysis included 64 infants with DMVT. Maternal, delivery, and neonatal comorbidities were common, including advanced maternal age (30%)s, pre-eclampsia/eclampsia (11%), C-section delivery (42%), hypoxic ischemic encephalopathy (22%), and congenital heart disease (22%). Median age at presentation was 3 days, (IQR 1-8 days). Infants presented with seizure (45%), hypotonia (20%), encephalopathy (38%), and respiratory distress (31%). Most DMVT were bilateral (69%) and often associated with parenchymal ischemic (50%) or hemorrhagic injury (36%). 15/64 patients received intervention with hyperhydration (8/15), anticoagulation (3/15), or both (4/15). 81% of patients survived to discharge. Neurologic morbidity at first follow-up visit was common, including seizures (49%), weakness (15%), spasticity (21%), hypotonia (38%), and developmental delay (55%).

CONCLUSIONS: Symptomatic DVMT presents early in the neonatal period, commonly with seizures, encephalopathy, respiratory distress, and abnormal tone. Symptomatic DVMT is often bilateral and associated with concurrent

parenchymal injury. The majority of infants in our cohort had associated comorbidities. Notably, our cohort had high rates of neurodevelopmental morbidity on follow up, underscoring the need for continued research into DMVT causes and treatments.

KEYWORDS: Neonatal Neurology, Stroke, Neurocritical Care

129. Neurotransmitter metabolism after neonatal brain injury

Lammert D B (Baltimore, MD), Fernandez R F, Scafidi S, Scafidi J

OBJECTIVE: Apnea of prematurity leads to increased risk for cognitive deficits, cerebral palsy, and epilepsy. Glucose oxidation through the tricarboxylic acid (TCA) cycle is disrupted under hypoxic conditions. Glutamine (Gln), γ-amino-butyric acid (GABA), and glutamate (Glu) are derived from alpha-ketoglutarate, a TCA cycle intermediate. We aimed to elucidate the effects of intermittent hypoxia on Gln, GABA, and Glu homeostasis.

METHODS: Early postnatal mouse brain development is equivalent to third trimester humans. Pups were exposed daily to repeated brief cycles of hypoxia or normoxia from postnatal day 1 (P1) through P11 then sacked at P11, P17 and P30 by microwave fixation, which preserves metabolites and avoids dissection-associated metabolic changes. Hippocampal metabolites were measured using capillary electrophoresis-mass spectrometry. Enzymes and transporters involved in Gln-GABA-Glu cycling were analyzed by qRT-PCR, western blot, and functional activity assays.

RESULTS: Surprisingly, Gln, GABA, and Glu were unchanged after intermittent hypoxia at P11 and P17. However, branched-chain amino acids and citrate were increased. Gene expression, protein expression, and function of pyruvate carboxylase, which introduces new carbons into the TCA cycle for anabolism, were decreased.

CONCLUSIONS: Taken together, the data suggests neurotransmitter homeostasis is preferentially maintained after intermittent hypoxia, despite a decrease in pyruvate carboxylase expression and function. Therefore, branched-chain amino acids or fatty acids are utilized at the expense of growth and energy production to support neurotransmitter homeostasis. While our metabolomics data represents steady state neurotransmitter levels, ongoing studies utilizing labeled substrates will delineate carbon flux through the TCA cycle and Gln-GABA-Glu cycling at the synapse.

KEYWORDS: Neonatal Neurology, Neurodevelopmental Disorders, Neurometabolic

130. Neurodevelopmental Impact of Gut Microbiome Alterations after Neonatal Hypoxic-Ischemic Injury

Caretti V (Houston, TX), Korf J, Carerra M, McCullough L, Ganesh B

OBJECTIVE: Neonatal hypoxic-ischemic encephalopathy (nHIE) is a major cause of lifelong neurologic disabilities, including attention deficit hyperactive disorder. The gut microbiome influences brain development. nHIE induces acute alterations in the gut microbiome homeostasis; whether these changes persist longitudinally is unknown. This study examines whether nHIE-induced alterations in the gut microbiome extend into adulthood and whether they can be therapeutically modulated to mitigate neurobehavioral outcomes.

METHODS: Neonatal C57BL/6 mice (post-natal day 9) underwent nHIE induction (modified Rice-Vanucci model) or sham operation (n=5-8 per sex/group). Fecal samples were collected longitudinally for microbiome analysis via 16s rRNA sequencing. Behavioral deficits were evaluated before and after fecal microbiota transfers (FMT) from naïve mice (open field).

RESULTS: nHIE mice showed a lasting shift in gut microbiome diversity with a notable reduction in beneficial bacteria like Lactobacillus and Bifidobacterium into adulthood. This was shown by a persistent shift in β- (between samples) diversity in the microbiota of nHIE-pups vs. controls ($p = 0.037$, $R2 = 0.1$). Behavioral tests revealed hyperactivity in nHIE mice ($p < 0.01$). Post-FMT from naïve mice, nHIE mice exhibited normalized behavior ($P = 0.03$), while sham mice (controls) had no change. Conversely, naïve mice receiving nHIE -FMT developed hypoactivity ($P< 0.001$).

CONCLUSIONS: nHIE caused persistent alterations in the gut microbiome, which are associated with hyperactive behaviors. FMT from healthy- naïve donors reversed this phenotype, highlighting the potential of gut microbiota modulation for treating neurodevelopmental sequelae after nHIE. We are currently determining if FMT can ameliorate motor, cognitive, and social deficits after nHIE.

KEYWORDS: Neonatal Neurology, Stroke

GLOBAL NEUROLOGY

131. EEG differentiates the microbiologic etiology of febrile coma

Postels D (Washington, DC), Zelleke T, Harrar D, Zhang J, Zhang B, Barber J, Dasan R, Amoah N, Findorff O, Krieger S, Barrett E, Ray S, Andrews A

OBJECTIVE: In patients with febrile coma previously exposed to malaria, there may be diagnostic uncertainty of the illness's microbiological etiology due to overlap in clinical and laboratory features of viral, bacterial, and parasitic neuroinfections. In non-immune travelers to endemic areas or in areas with low malaria transmission rates, this is especially problematic as the coma and fever of cerebral malaria (CM) may occur before blood smears or malaria rapid diagnostic tests become positive. Validating non-laboratory biomarkers associated with the microbiological etiology of neuro-infections may aid clinicians in caring for children with febrile coma.

METHODS: We evaluated whether electroencephalogram (EEG) is a valid biomarker to differentiate the microbiological etiology of febrile coma in African children. We compared results of qualitative and quantitative EEG interpretations

from 203 children with CM to EEG results from 87 children with non-malarial febrile coma.
RESULTS: Either qualitative or quantitative EEG interpretation methods differentiate coma of malarial from non-malarial etiology. The area under Receiving Operating Curves (AUROC) using qualitative or quantitative EEG interpretation methods produced similar results with excellent discrimination of coma etiology using quantitative (AUROC curve of 0.85) or qualitative methods (AUROC of 0.86).
CONCLUSIONS: Either qualitative of quantitative EEG methods discriminate the microbiological etiology of coma (malaria vs. non-malarial) in children living in malaria endemic regions. Further studies are warranted to assess EEG's ability to aid clinicians caring for patients with febrile coma who have returned from travel in malaria endemic regions, or to adults living in areas of low or high transmission intensity.
KEYWORDS: Global Neurology, Neuroinfectious Disease, Early Stage Investigator

132. Associations between Total Body Parasite Burden and Malarial Retinopathy in Children with Cerebral Malaria

Nwanze C (Washington, DC), Muller D, Suleman P, Barber J, Seydel K, Postels D

OBJECTIVE: Of the severe malaria syndromes caused by Plasmodium falciparum infection, cerebral malaria (CM) carries the highest risk for mortality. About two-thirds of children with clinical CM develop retinal abnormalities termed malarial retinopathy, comprising macular whitening, vessel color changes or hemorrhages. The presence of malarial retinopathy confers a higher risk of mortality in children with CM. The pathogenesis of malarial retinopathy remains poorly understood but sequestration of parasitized erythrocytes in retinal vasculature has been previously hypothesized to produce vessel color changes observed on ophthalmoscopy. Our study aimed to investigate the association between individual components of malarial retinopathy and sequestration of parasitized erythrocytes in retinal vasculature of children with CM.
METHODS: Using clinical data and archived biospecimens from children 6 months – 13 years old admitted to Queen Elizabeth Central Hospital between January 2010 and March 2023, we estimated total body parasite burden using plasma levels of parasitic lactate dehydrogenase (pLDH) and quantitative histidine-rich protein 2 (qHRP2). We estimated sequestered parasite load using the difference between total body parasite burden and circulating parasite load.
RESULTS: Children with retinopathy-positive CM ($n = 172$) had significantly higher total ($p< 0.001$) and sequestered ($p< 0.001$) body parasite burdens compared to children with retinopathy-negative CM ($n = 42$). Macular whitening and vessel color changes positively correlated with total body parasite burden ($r=0.187$, 0.199) and sequestered parasite load ($r=0.158$, 0.152), as measured by qHRP2.
CONCLUSIONS: These findings provide evidence that higher intensity of sequestration is associated with malarial retinopathy and its individual components in children with CM.
KEYWORDS: Global Neurology, Neuroinfectious Disease

133. Using EEG to Assess Coma Etiology in Children with Retinopathy-Negative Cerebral Malaria

Takle M (Washington, DC), Andrews A, Riggle B A, Zelleke T, Harrar D, Zhang J, Zhang B, Wilson K, Taylor T, Seydel K, Postels D

OBJECTIVE: Children with cerebral malaria (CM) may be classified as retinopathy-positive or retinopathy-negative. Autopsy studies suggest that those with malarial retinopathy have high levels of cerebral parasite sequestration, while children with retinopathy-negative CM have possible non-malarial causes of death and less sequestration, implying concurrent asymptomatic parasitemia with a non-malarial coma etiology. However, subsequent epidemiological studies argue that both retinopathy-negative and -positive CM are caused by acute malaria infection. EEG differentiates coma of malarial and non-malarial origin. To evaluate the contribution of acute malaria infection to retinopathy-negative CM pathophysiology, we compared qualitative and quantitative EEG characteristics of children with retinopathy-negative CM, retinopathy-positive CM, and non-malarial coma.
METHODS: We compared qualitative and quantitative EEG characteristics from recordings of children ages 3 months to 14 years admitted between 2013 and 2019 to Queen Elizabeth Central Hospital in Blantyre, Malawi, with retinopathy-negative CM, retinopathy-positive CM, and non-malarial coma. The predictive performance of qualitative and quantitative EEG characteristics was quantified using area under receiving operating characteristic curve (AUROC).
RESULTS: Neither qualitative nor quantitative EEG interpretation methods can discriminate children with retinopathy-positive from retinopathy-negative CM. Conversely, quantitative EEG can readily differentiate children who have retinopathy-negative CM from those with non-malarial coma based on the measured AUROC of 0.67, 0.83 and 0.87, for qualitative, quantitative EEG and analyzed in tandem or combined, respectively.
CONCLUSIONS: EEGs of children with retinopathy-negative CM are similar to those with retinopathy-positive CM and significantly different from children with non-malarial coma, supporting the hypothesis that acute malaria infection is causative in the acute illness of retinopathy-negative CM.
KEYWORDS: Global Neurology, Neuroinfectious Disease

134. EEG conductive paste made from household supplies: a recipe for resource-limited settings

Hebert M (Atlanta, GA), Adanene A, Tefera S, Moges A, Yibe B, Deginet E, Abatkun M, Clarke A, Sankhla N

OBJECTIVE: Hospitals in Ethiopia and other resource-limited countries often experience shortages of medical supplies, including Electroencephalogram (EEG) conductive paste. EEG conductive paste is a water-soluble glue used to adhere electrodes to the scalp to record electrical signals

generated by the brain. Shortages of EEG paste may interfere with timely diagnostic evaluation and management of neurological conditions like epilepsy. The goal of this project was to produce EEG paste using common household materials for settings where commercial paste is not readily available or affordable.

METHODS: EEG paste was made by adding equal amounts of flour and salt to a small amount of oil and Arabic gum dissolved in water over gentle heat until a dough-like paste was formed. The homemade EEG paste was applied to patients at Black Lion Hospital in Addis Ababa, Ethiopia and compared to commercial product (Ten20 brand conductive paste).

RESULTS: We compared our homemade EEG paste to commercial paste and found that the quality of EEG tracings appeared the same. Sample EEGs were performed on patients at Black Lion Hospital using homemade paste and interpreted by an epileptologist. Tracings between left and right hemispheres on the same patient using homemade vs commercial pastes showed similar waveform amplitudes, frequencies, and morphologies. Total cost to make 8 ounces of homemade EEG paste is ~$2 USD. Ten20 brand EEG paste in Ethiopia ranges between $90-$300 USD.

CONCLUSIONS: In resource-limited settings, homemade EEG conductive paste using readily available household supplies is a practical, affordable, and effective alternative to commercial EEG paste.

KEYWORDS: Global Neurology, Epilepsy, Diversity, Equity, Inclusion

135. Neurodevelopmental outcomes of Colombian children with antenatal Zika virus exposure at school age during the COVID-19 pandemic

Mulkey S B (Washington, DC), Andringa-Seed R, Corn E, Williams M, Peyton C, Arroyave-Wessel M, Podolsky R, Msall M, Berl M, Cure C

OBJECTIVE: Evaluate multi-domain development of antenatal Zika virus (ZIKV)-exposed Colombian children without microcephaly compared to non-exposed controls at ages 5-6.

METHODS: Our prospective cohort study includes 48 ZIKV-exposed children (Cases) and two control groups of 118 non-exposed children. Control-1 children (n=63) were born prior to ZIKV entry to Colombia and Control-2 children (n=55) were born after the ZIKV epidemic. The younger Control-2 group was enrolled due to COVID-19-related delays in school entry experienced by Control-1 but not Cases likely affecting child outcomes; like Cases, Control-2 experienced no delays in starting school. Neurodevelopment was assessed in all groups at ages 5-6 years using the Behavior Rating Inventory of Executive Function (BRIEF), Adaptive Behavior Assessment System (ABAS), Movement Assessment Battery for Children (MABC), and the Wechsler Preschool and Primary Scale of Intelligence (WPPSI). Standard regression models were used to compare outcomes with close-to-normal distributions; proportional odds models were used for those without. P-values were adjusted using the Benjamini-Hochberg false discovery rate (FDR) (significance, $p<0.05$).

RESULTS: Cases were evaluated at mean±SD age 5.9±0.2 years; Control-1 at 5.9±0.3 years; Control-2 at 5.2±0.2 years. Control-1 BRIEF scores were elevated, and ABAS scores were lower compared to Control-2 and Cases ($p<0.001$). Control-2 MABC scores were lower than Control-1 and Cases ($p<0.001$). Case WPPSI full-scale IQ scores were lower than both controls ($p=0.002$), driven by differences in Visual Spatial Index ($p<0.001$).

CONCLUSIONS: Children with antenatal ZIKV exposure have differences in cognitive function at school age. Differential COVID-19 experiences in early childhood can affect pediatric research outcomes.

KEYWORDS: Global Neurology, Neurodevelopmental Disorders, Neuroinfectious Disease

HEADACHE

136. Tolosa-Hunt Syndrome Presenting with Oculomotor and Abducens Nerve Palsy in an Adolescent

Taskin DT (Jacksonville, FL)

OBJECTIVE: To report a case of Tolosa-Hunt syndrome presenting with oculomotor and abducens nerve palsies in an adolescent.

A 17-year-old previously healthy male presented with one week of headaches, painful eye movements, and diplopia. Examination revealed right-sided oculomotor and abducens nerve palsies, with neuroimaging showing thickening of the right cavernous sinus. Despite borderline elevated opening pressure (27 cmH2O) on lumbar puncture and elevated CSF white blood cells (WBCs to 7 with normal protein and glucose), extensive workup ruled out other etiologies. The patient responded well to steroid therapy, achieving full remission.

METHODS: Clinical examination, neuroimaging (MR BRAIN ORBITS with IV contrast and CTA HEAD with and without IV contrast), lumbar puncture, and rheumatology workup were performed to evaluate the patient's symptoms and identify the underlying etiology.

RESULTS: The patient exhibited right-sided oculomotor and abducens nerve palsies, with neuroimaging confirming thickening of the right cavernous sinus. Lumbar puncture revealed borderline elevated opening pressure, while rheumatology workup was negative.

CONCLUSIONS: Tolosa-Hunt syndrome should be considered in patients with cranial nerve palsies and cavernous sinus involvement. Prompt steroid treatment can rapidly improve symptoms. It's a rare diagnosis of exclusion with a dramatic response to steroids

KEYWORDS: Headache, Neuroimmunology

137. Migraine treatment at school: Patients' Barriers and Preferences

Hershey A D (Cincinnati, OH), Samaha M K, Shmuely S, asmar Y, Ironi A, Stark-Inbar A

OBJECTIVE: Migraine affects 1 in 10 adolescents and children. However, most schools mandate that medications be

administered by school nurses, often leading to delayed or missed treatment. Remote electrical neuromodulation (REN) is a smartphone-controlled device FDA-cleared for acute and preventive migraine treatment in patients 12 and older, which can be used discreetly. This study retrospectively evaluates students' treatment barriers, accessibility, and preferences.

METHODS: REN users across the United States under the age of 18, received an electronic study invitation. Eligible respondents, determined by a screening questionnaire, were prompted to fill an electronic survey asking about reasons for treatment discontinuation before being prescribed REN; treatment barriers at school; treatment preferences at school; and reasons for their preferences.

RESULTS: 332 adolescents participated, 80.4% female, aged 7-17 (15.5 $\pm$ 2.1). Patients previously discontinued migraine treatments mainly due to lack of efficacy (69.9% acute; 53.9% preventive), side effects (39.2% acute; 38.0% prevention), and/or intolerance to medications (15.1% acute, 12.0% prevention). Common treatment barriers at school were having to go to the nurse's office (66.6%), inability/unwillingness to leave class (41.9%), disliking to seem different (42.5%), and need for smartphone permission (23.2%). Of students who treat at school, 82.2% preferred REN alone or in combination with medications, citing reasons like not having to leave class (42.5%), discreet treatment (39.2%), gaining a sense of control (16.3%), and being allowed smartphone in class (12.0%).

CONCLUSIONS: This study highlights the challenges of managing migraine at school, while underscoring the importance of REN as an accessible, discrete, and effective migraine treatment at school

KEYWORDS: Headache

138. Survey on Migraine Counseling Patterns by Pediatric Neurologists

Park P S (New Haven, CT), Ionita C, Vassilopoulos A

OBJECTIVE: Pediatric migraine is prevalent and impactful, and effective treatment is necessary for improved outcomes. Guidelines exist, but no studies have evaluated whether pediatric neurologists' practice aligns with guidelines. This study aimed to investigate pediatric neurologists' perceptions and priorities for a variety of lifestyle and psychosocial domains in the treatment of migraines and explored clinical practice constraints.

METHODS: A self-report online survey was distributed and completed by 114 pediatric neurologists, assessing their personal history of headaches, headache visit durations, and availability of mental health clinicians in their practice. Respondents rank-ordered eight non-pharmacological management domains based on perceived importance for migraine management: sleep, psychosocial factors, functional impairments, hydration, abortive medication overuse, regular meals, exercise, and caffeine.

RESULTS: Most new headache visits were 45-60 minutes, follow-up visits were 20-30 minutes, and 62.3% reported a personal history of headaches. About 29.0% of practices had integrated mental health clinicians. Sleep was ranked as the most important counseling domain by 38.6% of respondents, followed by psychosocial factors (18.4%) and functional impairments (14.9%). Caffeine and exercise were considered the least important domains by 28.1% of respondents.

CONCLUSIONS: Pediatric neurologists prioritize non-pharmacological management domains differently in migraine counseling. Sleep, psychosocial factors, and functional impairments emerged as key foci, highlighting the need for comprehensive approaches to address migraine management within time constraints of clinic visits. Integrating mental health clinicians into practice may enhance comprehensive care of pediatric migraine patients through targeted health behavior interventions. Findings underscore the importance of individualized approaches to lifestyle counseling in pediatric migraine management.

KEYWORDS: Headache

139. Real-world Evidence of Remote Electrical Neuromodulation (REN) for the Acute Treatment of Migraine in Children Aged 6-11

Werner K W (Durham, NC), Gerson T G, Stark-Inbar A I, Shmuely S S, Ironi AI, Garas S G, Szperka CS, Hershey A H

OBJECTIVE: Remote Electrical Neuromodulation (REN) is a safe, effective, nonpharmacological wearable FDA-cleared device for acute and/or preventative treatment of migraine in patients 12 years or older. This study evaluated the real-world safety and efficacy of REN for the acute treatment of migraine in children 6-11 years old.

METHODS: Prospective real-world data from participants were collected through the REN device (Nerivio®) smartphone application following parental consent. Device safety was the primary endpoint. Secondary endpoints looked at efficacy 2-hours post-treatment.

RESULTS: This study enrolled 293 children aged 6-11 (median age 11, IQR=9-11), including 73.7% female, who performed 5,493 REN treatments. Less than a third of the participants discontinued therapy after 1-4 treatments (30.4%), 16.4% conducted 5-8 treatments, and 53.2% conducted 9 or more treatments. No adverse events were reported. Consistent efficacy 2 hours post-treatment in at least 50% of REN treatments was reported by 72.2% (13/18) of participants for headache pain relief, 36% (9/25) headache pain freedom, 83.3% (15/18) functional disability relief, and 38.9% (7/18) functional disability freedom. Complete freedom from migraine-associated symptoms observed at treatment baseline in at least 50% of REN treatments were reported by 70% (7/10) for nausea/vomiting, 50% (4/8) phonophobia, 22.2% (2/9) photophobia, and 63.6% (7/11) reported freedom from at least any associated symptom. REN was standalone in 45.4% of treatments; and was combined with over-the-counter medication and with prescribed medication in 34.4% and in 20.9% of treatments respectively.

CONCLUSIONS: REN may provide a safe and effective non-pharmacological acute treatment of migraine for children 6-11 years of age.

KEYWORDS: Headache

140. Pediatric Headache: Who Is Referred to Neurology?
Wignall E R (Birmingham, AL), Marcus L, Novara S

OBJECTIVE: To describe the patient population referred for tertiary neurology care in an underserved state and determine the impact of a headache referral checklist on the triage process.
METHODS: A headache triage checklist was developed to improve the quality and review of referral information. The checklist included three categories (special circumstances, acute treatments, preventative strategies). Retrospective chart review was performed on all patients referred to our institution for headache from December 2023 through February 2024. Patient demographics, time to appointment, and headache features were analyzed. In total, 128 referrals were reviewed. Return patients were excluded, leaving 88 new headache referrals for analysis.
RESULTS: Of our sample, 53% were female, 24% White, 24% Black, 7% Hispanic, 1% Asian, and 8% unknown race. The mean age was 12 years (range 3-17). Mean time from referral to appointment was 4.8 months (range 6 days-1 year). Of the 88 referrals, 55% included the headache referral checklist for analysis. The most common special circumstance reported was chronic daily headache (65%), the most common acute treatments were NSAIDs (92%), and the most common preventative strategy was lifestyle modifications (63%).
CONCLUSIONS: The use of the headache checklist had no discernable impact on the triage process. Only half of referrals included a checklist and the most common reason for referral was chronic daily headache. Most primary care providers reported trying acute treatments and preventative strategies prior to referral. In the future, more detailed review of the checklist could improve the triage process and thus patient care.
KEYWORDS: Headache, Practice Parameters

141. Is there an association between optical coherence tomography changes and increased intracranial pressure in pediatric patients with idiopathic intracranial hypertension?
Kirven N A (Farmington, CT), DiMario Jr. F J

OBJECTIVE: The clinical presentation of idiopathic intracranial hypertension in children is infrequent and differs from adults. We examined the relationships between clinical symptomatology, measured optical coherence tomography (OCT) and intracranial pressure (ICP) in children.
METHODS: We retrospectively identified all patients with a diagnosis of papilledema from January 2017- December 2023. We conducted a chart review and extracted symptoms, lumbar puncture opening pressures, OCT values and demographic information.
RESULTS: We identified 63 patients with the diagnosis of IIH, 33 of which had OCT values available. Among those 33 patients, there was a positive correlation between ICP and OCT r=0.523, (CI=0.219-0.734). All 66 patients with the diagnosis of IIH had a symptom score calculated. There was a positive correlation between ICP and symptom score r=0.364, (CI=0.121-0.565). The correlation between OCT and symptom score among the 33 patients with OCT values was r=0.134, (CI=-0.219, 0.456). Headache was present in 44 of 66 patients (67%), making it the most common symptom present at time of diagnosis, followed by visual changes (35%), and nausea (30%).
CONCLUSIONS: Childhood IIH presents with significant clinical variability. We identified a positive correlation between OCT values and opening pressures, providing evidence to aid in the diagnosis of childhood IIH. The presenting symptom score was less helpful in predicting increased ICP in IIH, affirming the significant clinical variability in children.
KEYWORDS: Headache

142. Efficacy and safety of remote electrical neuromodulation (REN) for migraine prevention in adolescents: Interim results of a real-world study
Lax D N (Bronx, NY), Rabany L, Shmuely S, Asmar Y, Stark-Inbar A, Ironi A, Monteith T

OBJECTIVE: Remote Electrical Neuromodulation (REN) is a clinically proven, FDA-cleared, non-pharmacological migraine prevention treatment for ages 12 and up. This real-world evidence interim analysis examined the safety and effectiveness of REN preventive treatment in adolescents.
METHODS: REN-naïve adolescents across the United States who were prescribed REN for migraine prevention by their healthcare provider and treated with the device once between July 2023-January 2024 were recruited. Following electronic screening, patients signed informed consent and answered baseline questionnaires. Participants were requested to treat for prevention and report symptoms daily via the Nerivio in-app electronic-diary for six months. MITT criteria: treatments ≥10 and reports ≥22 per month.
RESULTS: Twenty-one mITT participants aged 12-17 (mean 15.4±2.0) years were analyzed. The average number of monthly migraine days was reduced from 15.43 (±7.8) at baseline to 12.25 (±8.3) at month three, i.e., therapeutic gain of 3.18 days, p=0.042.
The mean patient global impression of severity (PGI-S) score was reduced from 4.81 (±0.73) at baseline, to 3.94 (±1.52) at month three, p=0.03. In the patient global impression of change (PGI-C), 72.2% of participants indicated at least some degree of improvement (5.56% very much improved, 33.33% much improved, 33.33% minimally improved), 11.11% reported no change, and 11.11% reported being worse.
Of 64 ITT participants, one reported mild device-related adverse events (DAEs). None reported moderate/severe DAEs.
CONCLUSIONS: The reduction in monthly migraine days and overall severity, coupled with strong safety profile support the safety and effectiveness of REN for migraine prevention in adolescents. The relatively small sample-size calls for further research.
KEYWORDS: Headache, Experimental Therapeutics, Early Stage Investigator

143. Visual Snow: A Pediatric Case Series

Soliz J N (Miami, FL), Arias J A, Warman R, Vasconcellos E

OBJECTIVE: Visual Snow (VS) is a rare neuro-ophthalmological entity characterized by the presence of continuous tiny dots, or static, across the entire visual field that often persist for years. Along with the snow, patients with VS syndrome (VSS) present with two or more additional visual symptoms. Despite a growing number of adult studies, only a few pediatric cases have been published in the literature. We aim to characterize the presentation and comorbidities of VS and VSS in pediatric patients.

METHODS: A retrospective chart review was conducted of patients presenting to a pediatric neurology center between March 2018 and April 2024 with diagnoses including visual disturbances or distortions.

RESULTS: Eight patients (7 females, mean age 14.5±2.45) were identified with VS (2/8 met criteria for VSS). Children with VS often had entoptic phenomena but did not meet criteria for VSS. All patients had unremarkable neurological and ophthalmological exams. 75% had migraine, 62.5% attention deficit hyperactivity disorder (ADHD), 37.5% anxiety disorder, and 25% autism spectrum disorder. Seven patients had EEG and neuroimaging, which were unremarkable except for one with VSS that had a subcentimeter FLAIR hyperintense lesion in the thalamus and a stable cervical internal carotid artery aneurysm felt to be unrelated to the VSS.

CONCLUSIONS: VS seems to be more prevalent in girls, and most pediatric patients with VS do not meet proposed criteria for VSS. As with adults, migraine was the most common comorbidity in our series but developmental disorders such as ADHD were also prevalent. Further pediatric studies are needed.

KEYWORDS: Headache, Neurodevelopmental Disorders

144. Efficacy of intravenous medications in relieving headache among youths in an infusion center

Victorio M C (Akron, OH), Ostrowski-Delahanty S

OBJECTIVE: Treatment of status migrainosus in adolescents typically consists of a combination of intravenous medications – diphenhydramine, antiemetic and ketorolac, commonly called "migraine cocktail". When this treatment does not resolve or relieve headache, other intravenous medications are used. This study's objective was to determine the impact of each infusion medication on patient pain scores.

METHODS: Charts of headache patients who received treatment in the infusion center from 2014-2017 were reviewed. Demographic information, headache diagnosis and self-report pain scores (scale 0-10) pre/post-infusion of each medication, and at discharge were collected. Success of infusion treatment was calculated as >50% reduction in self-reported pain score. For each line of treatment, change in pain scores were calculated.

RESULTS: 616 patients were seen, 51% received treatment for status migrainosus; 25.8% prolonged migraine. Mean intake pain score: 6.01 (SD=2.312). All patients received diphenhydramine, anti-emetic, ketorolac as 1st,2nd and 3rd line medications, respectively. Either or combination of MgSO4, valproate, methylprednisolone or DHE were given for those who had <50% pain reduction. Patients receiving 2nd line medication were 7.97 times more likely to report >50% pain reduction; and 1.2 times more likely to report >50% pain reduction after receiving 3rd line medication. Additional medications beyond the first 3 medications did not significantly add to self-reported pain reduction.

CONCLUSIONS: In adolescents with status migrainosus or prolonged headache, migraine cocktail may help reduce head pain by at least 50%. Although limited by retrospective design, findings suggest that additional intravenous medications given after the migraine cocktail may not significantly improve pain scores.

KEYWORDS: Headache

145. A single center retrospective study of the development and management of glioma in patients with Neurofibromatosis Type I

Jain A (Johns Creek, GA), Jandhyala N, Garcia M, Segal D, Yohay K

OBJECTIVE: To evaluate the prevalence and natural history of non-optic gliomas in a cohort of Neurofibromatosis Type I (NF1) patients.

METHODS: A retrospective chart review of 1373 NF1 patients followed at our institution from 2012-2023 was performed and we identified those with non-optic glioma(s). Patient demographics, clinical presentation, imaging findings, survival and progression-free survival (PFS), and treatment information was collected.

RESULTS: There were 178 patients with non-optic glioma, ranging from age 5-76 years at data collection. The median age at which gliomas were first noted was 7 years and most were asymptomatic. Gliomas were most frequently located in the midbrain (38.3%), followed by the cerebellum (16.2%). Of those who received treatment, 37 (20.0%) had surgery, 36 (19.0%) chemotherapy, and 13 (7%) radiation. Twenty-five patients received biopsies, with the majority of lesions categorized as pilocytic astrocytoma (72%), followed by glioblastoma (16%). The median PFS was 5 years and the majority of patients were alive at last known follow-up (174/178, 97.8%). The median OS of the 4 deceased patients was 16 years from diagnosis.

CONCLUSIONS: We describe the clinical course of a large cohort of NF1 patients with non-optic gliomas. In our cohort, the prevalence of non-optic gliomas was 12.9%, which were most commonly in the midbrain. Of lesions biopsied, most were low-grade. The median PFS was 5 years and 46% of patients required treatment beyond surveillance or ETV/VPS. Further delineation of the outcomes of patients with non-optic glioma can better inform treatment and follow-up.

KEYWORDS: Headache, Neuro-oncology

MOVEMENT DISORDERS

146. Experiencing Life with Tourette Syndrome: The Invisible Effects of Tics

Martindale J M (Winston Salem, NC), Carson J, Chapman L, Reilly K, Pring K, Higgs H, Storch E A, Daniel S, Salsman J M, Rapp S R, Mink J W

OBJECTIVE: Persistent Tic Disorders (PTD), including Tourette Syndrome (TS), are neurodevelopmental disabilities characterized by multiple motor and vocal tics for over a year affecting 1.4 million US individuals1. Although many disabilities are stigmatized, PTD/TS is unique because tics are audible and visible, causing unwanted attention and negative labeling. Stigma in TS impacts mental health, tic severity, and persistence2-6. Our objective was to evaluate how individuals with PTD/TS experience stigma.

METHODS: In-depth qualitative interviews were conducted for: 1) Individuals aged 8-30 with DSM-V-TR confirmed PTD/TS, 2) Caregivers/partners, and 3) medical providers or advocates. Youth had time to answer sensitive questions confidentially. Interviews were conducted in-person or via secure video-conferencing and lasted 45-90 minutes. Interviews were recorded, transcribed verbatim, and de-identified. Preliminary analysis was completed by rigorous and accelerated data reduction.

RESULTS: 27 qualitative interviews were conducted between March 2023 and March 2024. All cohort's felt PTD/TS was misunderstood at multiple levels and had difficulty navigating disability rights. Certain tics are less accepted, despite disability awareness, and can be met with discipline or negative reactions. When tics were perceived as offensive to other protected classes, seeing PTD/TS as a disability became unfavorable. Individual's faith, mental health, and support networks were impacted by ostracization from religious communities through implicit or explicit exclusion or more extreme beliefs of spiritual possession.

CONCLUSIONS: There is a broader impact of PTD/TS beyond tics. The impact of disability rights and religious community on these individuals should be further explored.

KEYWORDS: Movement Disorders, Ethics, Diversity, Equity, Inclusion

147. Characterization of Sensory Behaviors in Youth with Chronic Tic Disorder

Hendry E (Rochester, NY), Walsh N, Sapozhiknov Y, Mink J, Esposito E, Oakes L, Adams H, Ross A, Vermilion J

OBJECTIVE: To characterize sensory behaviors in youth with chronic tic disorder (CTD).

METHODS: We enrolled subjects ages 6 to 17 with CTD. Sensory profiles were determined by the parent-proxy reported Short Sensory Profile 2 or the self-reported Adolescent/Adult Sensory Profile, depending on age. Symptom severities for anxiety (Pediatric Anxiety Rating Scale), tics (Yale Global Tic Severity Scale-Total Tic Score), and premonitory urge severity (Premonitory Urge for Tics Scale) were assessed. Anxiety disorder diagnoses were determined using the Anxiety and Related Disorders-IV Child and Parent Interview. OCD and ADHD diagnoses were determined by DSM-5 criteria. Relationships between abnormal sensory profiles and co-occurring conditions were assessed with Fisher's exact test. Relationships between urge severity and sensory profile and tic severity and sensory profile were assessed by using Student's Two-Side T-Test.

RESULTS: Thirty-six subjects completed sensory profiles. Abnormal sensory profiles were reported in registration (n=16, 44%), seeking (n=18, 50%), sensitivity (n=19, 53%), and avoidance (n=18, 50%) categories. Presence of co-occurring OCD was associated with abnormal sensory avoidance (OR = 0.17, p-value = 0.04). Presence of co-occurring ADHD disorder was associated with abnormal sensory registration (OR = 0.10, p-value = 0.001) and abnormal sensory sensitivity (OR = 0.11, p-value = 0.01). Prescence of co-occurring anxiety disorder was associated with abnormal sensory registration (OR = 0.15, p-value = 0.03) and abnormal sensory sensitivity (OR = 0.18, p-value = 0.03). Urge severity and tic severity were not significantly associated with abnormal sensory profiles.

CONCLUSIONS: Youth with CTD, particularly those with co-occurring neuropsychiatric conditions, report abnormal sensory behaviors in various domains.

KEYWORDS: Movement Disorders

148. Unusual Presentation of Acute on Chronic Dopa-Responsive Dystonia (DRD)

Tanenbaum R (Memphis, TN), Guillen D, Wolters W

OBJECTIVE: To present an acute on chronic case of Dopa-Responsive Dystonia (DRD) and discuss necessary diagnostic work-up in her unique presentation.

METHODS: This is a female with frequent falls, toe-walking, and abnormal gait since 1 year of age. She had been seen at 4 years of age with noted mild appendicular hypertonia and had normal imaging studies. At age 5, she acutely presented with significantly worsening weakness and tightness in 4 extremities leading to inability to ambulate after streptococcus pharyngitis. Physical exam demonstrated motion activated dystonia in 4 extremities and decreased range of motion with 4-5 beats clonus in ankles. During her admission, symptoms were milder earlier in the morning.

RESULTS: She was admitted during the acute episode. Work up was only remarkable for CRP 46 mg/L.

CT head, MRI brain/total spine and CSF neurotransmitter all within normal limits. Genetic cerebral palsy spectrum and neurotransmitter panels showed VUS in KMT2B and TGM6, which can cause autosomal dominant dystonias but not previously reported in DRD. The patient was started on a low dose of levodopa-carbidopa with dramatic improvement. On follow up, her dystonia had resolved including her long standing symptoms prior to admission.

CONCLUSIONS: While acute worsening of DRD symptoms is rare, DRD ranges in clinical presentations. After ruling-out other structural/metabolic causes of acute on chronic weakness/worsening gait. This case emphasizes that it is imperative to consider DRD and start levodopa-carbidopa

trials in patients presenting with acute difficulty walking in association with increased tone.
KEYWORDS: Movement Disorders

149. Real-world Trofinetide Dosing for Rett Syndrome: The LOTUS Study

Cosand L (San Diego, CA), Abler V, Ryther R, Beisang A

OBJECTIVE: Trofinetide is approved by the US Food and Drug Administration for treating Rett syndrome (RTT) in patients aged ≥2 years. Trofinetide is recommended to be dosed twice a day following weight-banded dosing. Here, we present trofinetide dosing patterns in LOTUS, an observational, prospective, real-world online study of trofinetide in patients with RTT.
METHODS: Caregivers of patients who were prescribed trofinetide under routine clinical care were eligible to participate. Real-world dosing was reported weekly for the first 3 months of the study and then monthly using a caregiver-reported questionnaire.
RESULTS: In total, 101 respondents were included in this 5-month follow-up. Most participants (>75%) took trofinetide twice daily, while others took it 3 times per day (3.7—10.2%) or 4 times per day (1.7—2.0%). Trofinetide daily dosing (mL/day) increased over follow-up. The median dose (interquartile range [IQR]) reported at Week 1 was 48.3% (20.0—91.0) of target dose in label. By Week 10, the median dose (IQR) was 93.3% (76.0—96.0) of the target dose. Approaches to initial trofinetide dosing reported in this follow-up included initiation at target dose, increasing dose until the target dose was reached, dose reductions after the target dose was reached, and maintenance of dose that was lower than the target dose. Some of the dose adjustments reflect attempts to mitigate adverse events.
CONCLUSIONS: Based on this interim analysis, most patients initiate trofinetide at a lower dose than suggested in the label but increase their dose close to target dose by Week 10 of treatment.
KEYWORDS: Movement Disorders, Neurodevelopmental Disorders

150. Biofeedback-based Videogame Device to Treat Rage Attacks in Tourette Syndrome: A Pilot Study

Vermilion J (Rochester, NY), Wals N, Tae M, Kahn J, Peechatka A, Ragnio J, Stone E, Mink J

OBJECTIVE: To assess the feasibility of using a biofeedback-based videogame device, called Mightier, to improve rage attack severity in children with Tourette Syndrome.
METHODS: We recruited 10 children ages 6-12 years old with Tourette Syndrome and rage attacks into this 20-week trial. Parents tracked frequency, severity and duration of rage attacks for one month pre-intervention and post-intervention. For the intervention period, children were instructed to play Mightier games over a 12-week period. Feasibility was tracked by recruitment, retention, and engagement. Rage severity was evaluated pre -and post-intervention using the Clinical Global Impression-Rage (CGI-Rage) and Rage Outbursts and Anger Rating Scale (ROARS). We also assessed CGI-Improvement (CGI-I).
RESULTS: We enrolled 11 subjects over 18 months and have had one screen failure and one withdrawal due to medication changes. Currently, we have complete data for 8 subjects who have finished the study. Subjects had good engagement with the device, playing an average of 40 minutes per week. We also measured cooldowns, when the subject successfully calmed his or her heart rate during a game. Subjects had an average of 35 cooldowns per week. Median change in CGI-Rage was -0.5 (-1.75-0) and in ROARS was -1 (-2—0.25), reflecting overall improvement. On average, there was much improvement on the CGI-I.
CONCLUSIONS: This study met its recruitment goal and had good retention and excellent engagement. Preliminary data suggest improvement in rage severity. Given that rage attacks can be very challenging to treat in Tourette syndrome, this non-pharmacologic intervention may be a helpful tool in managing bothersome symptoms without medications.
KEYWORDS: Movement Disorders, Experimental Therapeutics

151. The Demographic, Clinical and Molecular Spectrum of Childhood-onset Movement Disorders Evaluated at an Academic Tertiary Care Movement Disorders Program

Srouji R (Cambridge, MA), Quiroz V, Yang K, Zubair U, Zaman Z, Schierbaum L, Ebrahimi-Fakhari D

OBJECTIVE: To describe the demographics, referral patterns, predominant phenomenology, etiology, and concurrent medical conditions in patients evaluated at an academic tertiary care movement disorders program during its establishment.
METHODS: A retrospective chart review was conducted for all patients referred to our movement disorders program between July 2022 and March 2024.
RESULTS: A total of 321 unique patients were included, with a total of 579 visits. Patients were referred regionally, nationally, and internationally. 92.5% had been previously evaluated by a neurologist, and 71.3% were referred to establish care. The majority of patients (51.4%) had an onset of symptoms before the age of 2. The predominant clinical phenomenology was dystonia (26.8%), followed by spasticity (22.4%), ataxia (8.4%) and stereotypies (8.1%). Approximately half of the patients (47.9%) had a mixed movement disorder with more than one phenomenology. A genetic or presumed genetic etiology was identified in 68.9% of cases. Among acquired movement disorders, 45.1% were attributed to vascular/ischemic causes. Common comorbidities included neurobehavioral symptoms (65.3%), seizures (28.7%), and psychiatric comorbidities (18.9%, mainly anxiety and depression). Eight patients underwent deep brain stimulation. 34.9% were enrolled in research studies.
CONCLUSIONS: Establishing a dedicated tertiary care movement disorders program is essential for improving care, fostering subspeciality training and advancing scientific progress in the field of pediatric movement disorders.

KEYWORDS: Movement Disorders, Neurogenetics, Neurometabolic

152. Additional Diagnostic Yield of Short-Read Whole Genome Sequencing in Childhood-Onset Movement Disorders: A One-Year Follow-Up Study

Schierbaum L (Boston, MA), Tam A, Quiroz V, Zubair U, Sveden A, Srouji R, Yang K, Chopra M, Ebrahimi-Fakhari D

OBJECTIVE: Hereditary movement disorders comprise a broad clinical spectrum, with over 500 disease-causing genes. Standard clinical genetic testing has limitations. Here, we assess the additional diagnostic yield of short-read whole genome sequencing (srWGS) in children with early-onset movement disorders.

METHODS: This study included 43 children with movement disorders of unclear etiology evaluated at an academic tertiary care movement disorders program, between March 2023-2024. SrWGS was conducted using the Illumina NovaSeq platform. Data was processed through DRAGEN. Variants were prioritized according to frequency, deleteriousness, associated phenotypes and reviewed by an interdisciplinary team.

RESULTS: SrWGS data from 43 patients (and parents when available) were analyzed. Spasticity was the predominant phenotype in 72.1% (31/43) followed by ataxia (25/43, 58.1%) and dystonia (24/43, 55.8%). A genetic diagnosis could be established in 37.2% (16/43) and candidate genes were identified in 34.9% (15/43). 86.1% (37/43) had previously undergone clinical genetic testing, with five solved cases showing variants already identified upon prior testing (5/16, 31.3%). Among solved cases, analysis on the genomic level revealed a diagnosis in 3 patients (3/43, 7.0%) through identification of a repeat expansion in HTT, a duplication in MECP2 and an ALU-insertion in ATM. In 4.7% (2/43) candidate copy number variations were identified at the genome level. SrWGS provided additional diagnostic yield in 11.6% (5/43).

CONCLUSIONS: The additional diagnostic yield of srWGS in a cohort of childhood-onset movement disorders is limited with most cases solved at the exome level. To leverage the additional potential of srWGS further development of analysis pipelines is warranted.

KEYWORDS: Movement Disorders, Neurogenetics

153. Dystonia, ataxia, and episodic weakness are common early symptoms in TANGO2 Deficiency Disorder and may respond to B-vitamin supplementation

Myers S (Rochester, NY), Sandkuhler S E, Hewitt A L, Vermilion J, Hull M, Mink J W, Mackenzie SJ

OBJECTIVE: To characterize the wide array of abnormal movements in TANGO2 Deficiency Disorder (TDD), and examine the impact of B-vitamin supplementation on these symptoms.

METHODS: Subjects with TDD were recruited from the TDD Natural History Study. Subjects' caregivers provided videos demonstrating subjects' abnormal movements. All submitted videos were reviewed by 3-4 pediatric movement specialists and a physician with expertise in TDD. Reviewers met to achieve consensus on the movement disorder phenomenologies present in each video. Caregivers participated in semi-structured interviews to collect additional information including movement disorder qualities, timing, and treatments trialed.

RESULTS: Videos for 24 subjects were reviewed, with interviews completed for 17/24 subjects at time of submission. 16/17 (94%) subjects had movement disorders or episodic weakness (13 dystonia, 6 ataxia, 9 episodic weakness) with multiple abnormal movements in 10/17 (59%). 9/17 (53%) reported abnormal movements as the first presenting symptom of TDD. 14/17 (82%) caregivers reported these symptoms had a moderate-severe impact on quality of life. 14/17 (82%) subjects initiated B-vitamin supplementation including B5, and 8/14 (57%) reported complete resolution of movement disorders and episodic weakness afterwards. The one subject without movement disorders or episodic weakness received early B-vitamin supplementation and has no symptoms of TDD at age 8 years.

CONCLUSIONS: Movement disorders and episodic weakness are a common and highly impairing symptoms in TDD. Presentation of these symptoms in early childhood represent an important opportunity for early diagnosis and treatment. Further studies are needed to elucidate the role and optimal dosing regimen of B-vitamins.

KEYWORDS: Movement Disorders

154. Quantitative natural history modeling of the HPDL-related neurodegenerative disease reveals genotype-phenotype correlations

Alecu J E (Boston, MA), Tam A, Saffari A, Ebrahimi-Fakhari D

OBJECTIVE: To delineate the genotypic and phenotypic spectra of patients with biallelic pathogenic HPDL variants, quantitatively model the disorder's natural history, and uncover genotype-phenotype correlations.

METHODS: A cross-sectional analysis of 90 published and one novel case was performed, employing a Human Phenotype Ontology-based systematic approach. Unsupervised phenotypic clustering (via multiple correspondence analysis, hierarchical clustering on principal components, and k-means consolidation) was used alongside in silico analyses and three-dimensional modeling of the HPDL-encoded enzyme to identify distinct patient subgroups and clinical trajectories.

RESULTS: The study quantitatively models the natural history of HPDL-related neurodegenerative disease in a global cohort, clarifying the disease's molecular and phenotypic spectrum and identifying three distinct patient subgroups characterized by significant differences in age at onset, clinical phenotype, developmental trajectories, and survival rates. It also establishes genotype-phenotype associations, finding that presence of a predicted moderately pathogenic missense variant in at least one allele typically leads to a milder, predominantly spastic paraplegic phenotype ($OR = 12.4$, $p < 0.0001$) with later disease onset (11 years [$IQR = 11$] vs. 6 months [$IQR = 11$], $p < 0.0001$), whereas biallelic, highly pathogenic missense or protein truncating variants are

associated with a more severe phenotype and reduced life expectancy (median survival = 11.0 years).
CONCLUSIONS: We delineate the phenotypic and molecular spectrum of the HPDL-related neurodegenerative disease and identify three distinct clinical trajectories. By quantitatively modeling the disorder's natural history and uncovering genotype-phenotype associations, we lay the groundwork for future prospective and longitudinal studies.
KEYWORDS: Movement Disorders, Neurogenetics, Neurodevelopmental Disorders

155. Treatment of status dystonicus in a child with SOX2-anophthalmia syndrome with deep brain stimulation

Morris A E (Saint Louis, MO), Viehoever A

OBJECTIVE: Deep brain stimulation (DBS) of the bilateral globus pallidus pars interna (GPi) has been used to treat medically refractory status dystonicus, however questions remain about which patients may benefit the most from DBS. Literature suggests that genetic forms of dystonia are more likely to benefit from DBS, but its use has not been reported for dystonia in SOXopathies. We describe the use of DBS for treatment of medically refractory status dystonicus in SOX2-anophthalmia syndrome.
METHODS: We measured dystonia severity with the Dystonia Severity Grading Scale before and after DBS. Our patient is a 9-year-old female with SOX2-anophthalmia syndrome with generalized dystonia. She presented with status dystonicus requiring intubation, deep sedation, and paralytics. She did not tolerate attempts to wean sedation and we thus recommended bilateral GPi DBS implantation which she underwent 1 month into her hospitalization. We selected stimulation contact locations demonstrating excessive synchronization on local field potential recordings.
RESULTS: After bilateral GPi stimulation, she initially improved and tolerated extubation and dexmedetomidine weans. Around 1-month post-op, dystonia worsened again. We turned DBS OFF due to concern it caused worsening, but we later identified an occult infection as the trigger. We turned DBS ON again and she improved gradually and with each increase in stimulation settings over 4 months at which time she discharged home. Dystonia severity improved from grade 5 to grade 1 from admission to discharge.
CONCLUSIONS: This case report illustrates the potential therapeutic benefit of GPi DBS to treat status dystonicus in SOX2-related disorders. Benefit may develop over months.
KEYWORDS: Movement Disorders, Experimental Therapeutics

156. Position-Dependent High Amplitude Horizontal Head Shaking in an Infant with NPHP1-related Joubert Syndrome

Lee F (Philadelphia, PA), White B

OBJECTIVE: Several types of atypical head movements have been reported in infants with benign, self-limited conditions, as well as in association with various intracranial malformations. Joubert syndrome is a genetic condition with locus heterogeneity that classically results in cerebellar vermis hypoplasia but has variable neurologic and systemic involvement dependent upon the underlying genetic etiology. Episodic head titubation described as 3 Hz, small amplitude horizontal shaking, more prominent during fatigue or agitation, has been noted in patients with Joubert syndrome. We report a case of a 3-week-old male born at term with position-dependent, abnormal head movements present since birth. Family history was unremarkable without report of consanguinity. Examination revealed axial hypotonia and 5 Hz high amplitude horizontal head shaking that was not present during lateral head turn in either direction. The movement exhibited a crescendo progression in frequency and amplitude as his head position approached midline. MRI brain identified isolated cerebellar vermis hypoplasia. Subsequent genetic testing confirmed a homozygous deletion of the NPHP1 gene, which has been associated with development of nephronophthisis later in childhood. Renal ultrasound was normal. Repeat evaluation at 3 months of age revealed resolution of the abnormal head movements. He remained hypotonic with truncal titubation and findings consistent with oculomotor apraxia, but no nystagmus. This case highlights a unique character of abnormal head movement in Joubert syndrome that, to our knowledge, has not been previously described. It also demonstrates the importance of genetic testing to ensure that patients are appropriately monitored for potential systemic abnormalities.
METHODS: N/A
RESULTS: N/A
CONCLUSIONS: N/A
KEYWORDS: Movement Disorders, Neurodevelopmental Disorders, Neurogenetics

157. Effect of Accelerated Intermittent Theta Burst Stimulation of the Pre-Supplementary Motor Area on Corticostriatal Connectivity in Tourette Syndrome

Larsh T R (Cincinnati, OH), Migneault K, Yuan W, Huddleston D, Gilbert D, Wu S

OBJECTIVE: Given its critical function in response inhibition and its primary connections with the striatum, the pre-supplementary motor area (pre-SMA) is a promising neuromodulatory target in Tourette Syndrome (TS). Therefore, we sought to investigate changes in corticostriatal structural connectivity induced by pre-SMA accelerated intermittent theta burst stimulation (iTBS).
METHODS: Yale Global Tic Severity Score and individualized Premonitory Urge for Tics Scale were collected. T1-weighted images were used for localization of the right pre-SMA. On separate, single study days (minimum 7 days apart), in a randomized, single-blinded crossover design, participants received either active or sham accelerated iTBS, consisting of two trains of iTBS separated by a mean of 36.6 minutes (range 27-50 minutes). Diffusion tensor imaging was obtained pre- and post-iTBS each study visit.
RESULTS: Seven right-handed children (mean age: 13.9 years, range: 11.3-17.4 years) with TS have completed

the study protocol. Accelerated active pre-SMA iTBS significantly increased right posterior corticostriatal tract fractional anisotropy (FA, p=0.01) and mean diffusivity (MD, p=0.03). Additionally, there were trends of increase in quantitative anisotropy (QA, p=0.099), and radial diffusivity (RD, p=0.07). Higher baseline QA and lower baseline MD and axial diffusivity (AD) were associated with more severe phonic tics (QA: r=0.6, p=0.02; MD: r=-0.5, p=0.05; RD: r=-0.5, p=0.06). Lower baseline MD was also associated with more intense urges (r=-0.45, p=0.1). '

CONCLUSIONS: These findings provide preliminary evidence that pre-SMA iTBS modulates corticostriatal connectivity in children with TS. Accelerated pre-SMA iTBS appears to be a promising neuromodulatory target in children with TS.

KEYWORDS: Movement Disorders, Early Stage Investigator, Neuroimaging

158. Deep Brain Stimulation Modulates Pallidal Aperiodic and Periodic Beta Activity during Rest and Motor Task in Children and Young Adults with Dystonia

Larsh T R (Cincinnati, OH), Pedapati E, Migneault K, Huddleston D, Gilbert D, Wu S

OBJECTIVE: To explore effects of deep brain stimulation (DBS) on globus pallidus pars interna (GPi) aperiodic (spectral exponent) and periodic (oscillatory) beta band activity in children and young adults with dystonia in order to quantify excitation-inhibition balance and pathologic oscillation.

METHODS: GPi local field potentials (LFP) were collected during two separate motor conditions: 1) 5-minute rest period and 2) externally cued motor task. Each condition was repeated with DBS off and on. Time resolved Fitting Oscillations & One Over F (FOOOF) models were used to parameterize neural power spectra within beta band (13-30Hz) into periodic and aperiodic components. Mixed effects modeling was used to assess the effects of DBS (on vs off), condition (rest vs motor task), and time (repeated measures) on aperiodic and periodic measures, accounting for within-subject effects.

RESULTS: Four subjects with GPi DBS have completed the protocol (mean age: 15.0, range: 9.2-21.4 years). Aperiodic activity (spectral exponent) increased with DBS, with significant interactions between DBS status, time, and motor condition observed (DBS*Condition: p=0.02; DBS*Time: p=0.08; DBS*Condition*Time: p=0.001). DBS reduced beta power in 3 of 4 patients; a significant rightward (increased frequency) shift in center frequency (DBS*Condition: p=0.006; DBS*Condition*Time: p=0.001) and flattening of beta peaks (DBS: p=0.06) were also observed.

CONCLUSIONS: Our findings provide preliminary evidence that GPi DBS modulates both aperiodic and periodic beta activity in time- and task-based fashions. Combining future LFP analysis with motion kinematics and/or surface muscle signals will deepen knowledge of DBS mechanism and may enhance precision in dystonia therapy.

KEYWORDS: Movement Disorders, Early Stage Investigator, Experimental Therapeutics

159. Congenital Hemifacial Spasm in a Neonate with a Pontine Mass: diagnostic and management challenges

Vara A S (Rochester, NY), Wiltrout K, Kaminsky H A, Brescia N, Sakonju A, Hughes I

OBJECTIVE: Congenital hemifacial spasm (HFS) is a rare condition with limited management guidance. HFS is described as episodes of painless involuntary contractions of muscles innervated by the facial nerve. This case was complicated by severe distress during episodes, breath holding spells, seizures and mass location.

METHODS: Case report.

RESULTS: A full-term, male neonate was noted to have recurrent left facial spasms soon after birth. Video-electroencephalography (vEEG) showed no epileptiform correlate. Initial neuroimaging was non-diagnostic. Multiple anti-seizure medications (ASM) were trialed for suspected myoclonic epilepsy with no improvement. CSF, metabolic and genetic work up were unrevealing. By one month, he experienced a generalized seizure after rapid clonazepam weaning. Ictal vEEG patterns ceased after restarting clonazepam. Various ASMs were trialed as escalating HFS episodes impaired his sleeping and feeding. By three months, prolonged episodes would lead to breath holding spells. Repeat neuroimaging identified a pontine hamartoma. Surgical excision was deferred based on location and age. No intralesional activity was suggested by functional neuroimaging (magnetoencephalography and positron emission tomography). Transcranial magnetic stimulation and left facial nerve block had minimal effect. Perioral Botox injections provided benefit, but the duration was unclear. He remains on multiple ASMs with functional improvement despite persisting episodes.

CONCLUSIONS: This case highlights how early high-resolution imaging helps guide congenital HFS diagnosis. There is little consensus on management, especially in painful HFS. In this case, topiramate and gabapentin have been most effective, perhaps due to their role in reducing pain. Multidisciplinary management, serial imaging, and cautious medication tapers are ongoing.

KEYWORDS: Movement Disorders, Epilepsy

160. Movement in SLC13A5: A Novel Approach Comparing Physician and Semi-automated Body Position Assessments

Teeyagura P (Tracy, CA), Goodspeed K, Liu J, Broderick J, Solidum R, Broderick J, Broderick J, Porter B

OBJECTIVE: SLC13A5 citrate transporter disorder (DEE25) is an ultra-rare genetic early infantile epileptic encephalopathy caused by absent citrate transport. DEE25 is characterized by seizures, developmental delays, and a poorly characterized movement disorder. Motor skill delays and movement disorders have been reported but have not been well characterized to date. Here we utilized physician and semi-automated OpenPose to better characterize movement in DEE25.

METHODS: Thirty-six subjects as part of a US-based and international natural history study funded by the TESS Research Foundation had video collected of a structured

motor skill assessment at up to 8 visits over 24 months. Fourteen patients underwent an additional semi-automated assessment of the same videos using OpenPose.

RESULTS: Physicians had good inter-rater reliability for motor skills but only fair for movement disorders. There was a stagnant or slow improvement in motor skills over the 2 years of study. Subjects were noted to have ataxia (60%), myoclonus (5%), dystonia (16%), and rarely chorea (3%). OpenPose was able to quantify the movement of 24 major body parts. OpenPose had inconsistent body part attribution with two-person videos, however additional processing allowed for accurate quantitative movements in most videos.

CONCLUSIONS: Our results indicate that patients with DEE25 have markedly impaired motor skills and a mixture of movement abnormalities with ataxia being the most common. OpenPose computes joint and body part trajectory measurements providing a fast, unbiased, and quantitative method to evaluate movement disorders.

KEYWORDS: Movement Disorders, Neurodevelopmental Disorders, Early Stage Investigator

161. Video-Based Quantification of Tic Variability Across Clinical Contexts

Wellen B (Minneapolis, MN), Bacon G, Pryor A, Wilton E, Brinker M, Breitenfeldt C, Khang I, Mungai T, Schneck D, Wang S, Conelea C

OBJECTIVE: The Yale-Global Tic Severity Scale (YGTSS) is a gold-standard tic severity measure. Ratings integrate clinician observation of tics, but the extent of variability in tic expression across clinical contexts is unclear. We compared video-coded tic frequency and type across clinical contexts to understand how possible variability may impact clinician impressions.

METHODS: Participants were N = 39 youth ages 12-21 years with chronic tics in a randomized trial (Conelea et al., 2023). Video recordings during three conditions were coded: 1) YGTSS interview (baseline and post-treatment), 2) MINI psychiatric diagnostic interview (baseline), and 3) Tic Suppression Task (TST, baseline and post-treatment). During the TST, the participant was alone and completed blocks of 3 min "Free to Tic" and "Suppression" conditions. All outcomes were non-normal, so nonparametric pairwise Wilcoxon signed rank-sum tests, adjusted using the Bonferroni correction procedure, were performed.

RESULTS: At baseline, there were significantly more tics per minute in TST-Free to Tic vs. MINI, TST-Suppression, and YGTSS. Significantly more types of tics were observed in TST-Free to Tic vs. MINI and TST-Suppression; no significant difference was observed between TST-Free to Tic and YGTSS. Average tics per minute significantly decreased from baseline to post in TST-Free to Tic (Mean Change = -7.1, p = .027), TST-Suppression (Mean Change = -1.2, p = .029), and YGTSS (Mean Change = -2.3, p = .005).

CONCLUSIONS: Tic expression can markedly differ across clinical contexts. Markers of tic severity were highest during the TST, suggesting that tics observed during clinician-patient interactions may not be representative of overall tic severity.

KEYWORDS: Movement Disorders, Neurodevelopmental Disorders

162. Disease Severity Correlates Inversely with Quality of Life for Children and Young Adults with SPAST-associated Hereditary Spastic Paraplegia (SPG4)

Tam A (Boston, MA), Schierbaum L M, Quiroz V, Battaglia N, Fong K, Srouji R, Yang K, Ebrahimi-Fakhari D

OBJECTIVE: SPAST-associated hereditary spastic paraplegia (HSP), also known as SPG4, is the most common subtype of HSP. Children with SPG4 have been observed to have greater occurrence of de novo variants. Patients with de novo SPG4 are more severely affected than patients with inherited SPG4, even when comparing amongst individuals sharing the same SPAST variant. Here, we systematically document disease severity and health-related quality of life (HrQoL) for children and young adults with SPG4.

METHODS: We evaluated HrQoL using the Caregiver Priorities and Child Health Index of Life with Disabilities (CPCHILD) and assessed disability using the Spastic Paraplegia Rating Scale (SPRS). Our cohort included 49 patients with de novo SPG4, 28 patients with inherited SPG4, and 12 patients with untested parents, recruited from the Registry and Natural History Study for Early Onset Hereditary Spastic Paraplegia (NCT04712812).

RESULTS: Patients with de novo SPG4 typically reported impaired HrQoL in all domains, and on average, reported greater impairment compared to patients with inherited SPG4 or untested parents. Mean CPCHILD scores for these groups were: de novo SPG4: 64±11 (SD, n=32); inherited SPG4: 88±9 (SD, n=11); SPG4 of unknown inheritance: 82±22 (SD, n=8). CPCHILD scores correlated inversely with SPRS scores (Pearson r=-0.749, p=2.64E-10), indicating that greater motor impairment correlated with lower HrQoL. Additionally, our survey highlighted areas important to caregivers, such as emotions, overall health, communication, and moving about indoors.

CONCLUSIONS: These results provide important insights into HrQoL in children and young adults with SPG4 and defined areas of unmet need for future interventional trials.

KEYWORDS: Movement Disorders, Neurodevelopmental Disorders, Neurogenetics

163. Movement Disorder Phenotypes in Leukodystrophies

Tochen L (Washington, DC), Rhee R, Shin M, Mahoney D, Harmon J, Fraser J

OBJECTIVE: Movement disorders and extrapyramidal dysfunction have not been well described in the leukodystrophy population. In this retrospective study, we sought to characterize frequency of hypokinetic and hyperkinetic extrapyramidal movement disorders within a cohort of selected conditions that affect myelination. The pathways of both the pyramidal and extrapyramidal systems rely heavily on myelinated fibers. Therefore, individuals with abnormalities of myelination are at risk for movement disorders in addition to pyramidal weakness.

METHODS: Subjects were recruited through clinical chart review from patients seen within our center between 2019-2024. Clinical evaluations and phenotyping occurred in-person by a pediatric movement disorders neurologist (LT.) A cohort including symptomatic patients with the following diagnoses were included in this study: Aicardi Goutierres Syndrome, Cockayne Syndrome, Pelizaeus-Merzbacher Disease, Vanishing White Matter Disease, Leukoencephalopathy with Calcifications and Cysts, TUBB4A-related leukodystrophy, Canavan Disease, and CSF1R-related Leukoencephalopathy.
RESULTS: Thirty out of forty patients had evidence of at least one extrapyramidal disorder. Thirteen patients had multiple movement phenotypes. Hyperkinetic phenotypes were more common than hypokinetic phenotypes. Dystonia and ataxia were the most common movement disorders observed.
CONCLUSIONS: Extrapyramidal movement disorders are common in leukodystrophies. Many patients have complex phenotypes. Phenotypes can vary within the same genetic disorder. Further characterization of motor phenotypes will improve our understanding of natural history of leukodystrophies. Better recognition of movement disorders can also improve targeted symptomatic management and improve function, comfort, and quality of life.
KEYWORDS: Movement Disorders, Neurogenetics

164. Safety, Tolerability, and Neural Change in the CBIT +TMS Trial for Youth with Tic Disorders

Hodapp S (Minneapolis, MN), Breitenfeldt C, Hendrickson T, Grenne D, Houlihan K, Mueller B, Fiecas M, Lim K, Jacob S, Conelea C

OBJECTIVE: Comprehensive Behavioral Intervention for Tics (CBIT) benefits are variable and may be related to hyperconnectivity of supplementary motor area (SMA)-directed neurocircuitry. The two-phase CBIT+TMS Trial is testing CBIT augmentation with inhibitory transcranial magnetic stimulation (TMS) to SMA. Phase 1 milestones focused on feasibility, safety, and neural target engagement.
METHODS: Participants were N = 50 youth (12-21 years) with chronic tics. Treatment consisted of 10 daily CBIT sessions plus randomized TMS regimens of 1 Hz, cTBS, or sham. Assessments occurred at pre- and post-treatment (clinical symptoms, MRI) and 1- and 3-month follow-ups (clinical symptoms). Adverse events (AEs) were evaluated at all visits.
RESULTS: Treatment completion was high (96%). There were no serious AEs, no severe treatment-related AEs, and no tolerability-related withdrawals. During acute treatment, AEs occurred in more 1 Hz sessions (27%) than sham (11.3%) and cTBS (14.7%), the most frequent being headache, muscle twitch, and sleep disturbance. During follow-up, AE rates were higher in sham (12.5%) vs. active (1Hz=11.7%, cTBS=3.3%). cTBS was associated with strong within-subject functional connectivity decreases between SMA-putamen ($\eta2=0.22$; 1Hz: $\eta2=0.001$, sham: $\eta2=0.02$) and putamen-M1 ($\eta2=0.26$; 1Hz: $\eta2=0.02$, sham: $\eta2=.15$). 1Hz was associated with a strong SMA-M1 within-subject functional connectivity decrease ($\eta2=0.26$; sham: $\eta2=0.00004$, cTBS: $\eta2=0.07$).
CONCLUSIONS: CBIT augmentation with TMS is feasible, safe, and may reduce tic-associated hyperactivity in SMA-directed neurocircuitry. AEs and neural effects may differ by TMS regimen.
KEYWORDS: Movement Disorders, Neurodevelopmental Disorders, Behavioral Neurology

165. Changes in Tic Severity and Impairment Following Daily CBIT and TMS Treatment

Mungai T (Minneapolis, MN), Hodapp S, Khang I, Breitenfeldt C, Houlihan K, Wilton E, Wellen B, Jacob S, Conelea C

OBJECTIVE: Tics are quick, non-rhythmic, and repetitive movements and/or vocalizations often associated with impairments in school performance, relationships, and self-esteem. Although Comprehensive Behavioral Intervention for Tics (CBIT) is the first line treatment for tic disorders, it is only effective in 50-60% of those who receive it. The CBIT +TMS Trial tested CBIT augmentation with transcranial magnetic stimulation (TMS) to the supplementary motor area (SMA). The current study examined changes in tic severity and impairment across treatment.
METHODS: 50 individuals with tic disorders (ages 12-21) were randomized into one of three TMS conditions: continuous theta burst stimulation (cTBS), 1Hz repetitive TMS (1Hz rTMS), and sham stimulation. All participants received 10 daily sessions consisting of TMS immediately followed by a CBIT session. Assessments pre- and post-treatment captured clinician-rated tic severity and impairment (Yale Global Tic Severity Scale; YGTSS) and self-reported tic-related impairment (Tourette Syndrome Impairment Scale; TSIS).
RESULTS: Preliminary analyses examined change across all participants (group-wise analyses will follow unmasking in May 2024). Results showed significant decreases in YGTSS motor tic ($t(45)=6.19$, $p<.001$), vocal tic severity ($t(45)=3.08$, $p=.004$), and impairment ratings ($t(45)=7.19$, $p<.001$) from pre- to post-treatment. Additionally, TSIS scores significantly decreased ($t(45)=2.11$, $p=.041$) from pre- to post-treatment.
CONCLUSIONS: CBIT delivered in an intensive 10 session format led to tic improvements. Future analysis will explore whether TMS conditions differentially impacted specific domains of impairment.
KEYWORDS: Movement Disorders

166. Case Report: Novel SCN2A Mutation Identified in a Patient with Paroxysmal Kinesigenic Dyskinesia (PKD)

Cheung C (Elk Grove, CA), Mackenzie K

OBJECTIVE: Paroxysmal kinesigenic dyskinesia (PKD) is characterized by sudden, brief, and recurrent episodes of dystonic or choreoathetotic movements provoked by a sudden movement. Familial PKD is predominantly linked to mutations in the gene PRRT2, in addition to other less common mutations. This case report highlights a new pathogenic mutation, SCN2A, in a patient with isolated PKD.
METHODS: We present a 16-year-old male diagnosed with paroxysmal kinesigenic dyskinesia and a pathogenic mutation in SCN2A.

RESULTS: Our patient first presented with symptoms of PKD at the age of 15 with no pertinent family history. His daily episodes responded well to the standard treatment of Carbamazepine, which was switched to an equally efficacious Oxcarbazepine due to provider preference. As expected, his brain MRI yielded normal results, and the comprehensive dystonia genetic panel, including PRRT2, was unremarkable. However, an SCN2A mutation at exon 25 (c.4503G>A p.-Met1501Ile) was discovered on subsequent whole-exome sequencing, a finding not documented in existing PKD literature, to our knowledge.
CONCLUSIONS: The exact pathogenesis of PKD is still unclear, but is suggested to involve disrupted ion channels, ion transporters, and synaptic transmission. The PRRT2 gene acts as a negative regulator for the voltage-gated sodium channel, Nav1.2, encoded by the SCN2A gene. Mutations in the SCN2A gene are associated with neuropsychiatric syndromes, including developmental and epileptic encephalopathy, ataxia, intellectual disability, and autism. We report a novel mutation, which can help advance our understanding of the molecular mechanisms and identification of genes associated with clinical symptoms of PKD.
KEYWORDS: Movement Disorders, Neurogenetics

NEUROCRITICAL CARE

167. ELECTROENCEPHALOGRAPHY PREDICTORS OF PEDIATRIC CEREBRAL PREFORMANCE CATEGORY SCALE SCORES AFTER CARDIAC ARREST

Smith J D (Washington, DC), Keenan J S, Staso K, Conley C, Harrar D, Sansevere A

OBJECTIVE: To assess EEG predictors of pediatric cerebral performance category scale (PCPC) scores after cardiac arrest (CA).
METHODS: This is a retrospective review of patients admitted to the PICU at Children's National Hospital from July 2021 to January 2023. We included patients with CA greater than 5 minutes, monitored with continuous EEG. EEG background was identified using standardized classification, other features included epileptiform discharges (ED), and electrographic seizures (ES). PCPC score was assessed at discharge. Statistical analysis was done via ANOVA and t-tests.
RESULTS: Seventy-one patients were included, age at CA was 9.9 years (SD=12.8): 37% female, 63% male. Four patients had a normal background (6%): 4 survived (100%), average PCPC score was 1.25(SD=0.4). Twenty-eight patients (39%) classified as slow/disorganized: 24 survived (86%), 4 died (14%), average PCPC score was 2.1(SD=1.3). Twenty-six patients had burst suppression (37%): 5 survived (19%), 21 died (81%), average PCPC score was 3(SD=1.3). Thirteen patients had attenuation (18%): 2 survived (15%), 11 died (86%), average PCPC score was 5(SD=0). One-way ANOVA was significant for difference in background ($p<0.01$), Bonferroni correction indicated PCPC scores for the attenuated group were higher than the slow ($p<0.01$) and normal groups ($p<0.01$). Ten patients had ES (14%): 5 survived (50%), 5 died (50%), average PCPC score was 3.6 (SD=1.0). Patients with ES had higher PCPC scores ($p=0.03$). Twenty-four patients had ED (34%): 9 survived (38%), 15 died (63%), average PCPC score was 3.4 (SD=1.4). Patients with ED had higher average PCPC scores ($p<0.01$).
CONCLUSIONS: EEG features impart significant prognostic value when estimating long term functional outcome.
KEYWORDS: Neurocritical Care, Epilepsy

168. Abusive Head Trauma: Can we predict who will develop Infantile Spasms?

Bartscherer A (Cincinnati, OH), Horn P, Vawter-Lee M, Care M, Broomall E

OBJECTIVE: Infantile spasms (IS) is a catastrophic form of epilepsy that occurs most often during the first year of life. In our institutional experience, a proportion of children with abusive head trauma (AHT) develop IS, however this correlation has not been previously studied and/or reported in larger numbers. The purpose of our study is to evaluate risk factors for AHT infants who develop IS.
METHODS: We conducted a retrospective chart review of children less than 2 years old with AHT admitted at our institution between January 1, 2010 to January 1, 2023. This review included both in-hospital and outpatient follow up data with a focus on histories, EEG data, and brain imaging.
RESULTS: Of 165 infants with abusive head trauma, 10 developed IS which is significantly higher than the national prevalence of IS (0.061 vs 0.0045, $p=0.0001$). Patients who later developed IS were more likely to have status epilepticus ($n=7$, $p=0.0007$), subclinical seizures ($n=10$, $p=0.0001$), slowing on EEG ($n=8$, $p=0.0221$), and venous injury on initial CT-imaging ($n=3$, $p=0.0335$) during initial admission for AHT. Patients who later developed IS were more likely to have abnormal sleep architecture ($n=4$, $p=0.0258$) on outpatient EEG.
CONCLUSIONS: Our study shows that there are several unique findings on initial EEG and CT that allow neurology providers to stratify risk of a child with AHT later developing IS. This information will allow neurology providers to proactively counsel at-risk families and consider screening EEG's at follow up leading to more timely treatment and improved long-term outcomes.
KEYWORDS: Neurocritical Care, Epilepsy, Traumatic Brain Injury

169. Electroencephalography in critically ill children with cancer

Pickup E (Washington, DC), Keenan J S, Packer R J, Wells E, Conley C, Staso K, Harrar D, Sansevere A

OBJECTIVE: Electrographic seizures are common in critically ill children. Continuous EEG (cEEG) is frequently obtained in children with both systemic and neurologic cancer, although little is known about the incidence of electrographic seizures (ES) or EEG background features in

this population. Further, little is known about EEG differences between these two groups.
METHODS: This is a prospective single center study of critically ill children with oncologic diagnoses admitted to the pediatric intensive care unit (PICU) from July 2021 to July 2023. Patients with new or known oncologic diagnoses and cEEG completed during their admission were included. Clinical variables included age, sex, oncologic diagnosis, indication for EEG, EEG features, and changes in management.
RESULTS: Fifty-seven patients were identified meeting inclusion criteria, with a total of 62 PICU admissions and 86 EEGs in this cohort. Thirty-two patients had a primary brain tumor and 25 patients had a systemic cancer. The most common indication for cEEG in both groups was acute encephalopathy (41%). Periodic or rhythmic patterns (21%) and ictal-interictal continuum (14%) were common in both groups. ES were frequently identified in both groups (15%), although status epilepticus was more common in patients with brain tumors (relative risk 6.6, p=0.03). EEG led to a change in management in 22%. Prior seizure history or cEEG indication were not correlated with ES.
CONCLUSIONS: Electrographic seizures are common in children with either systemic or neurologic cancers and would be missed without cEEG. cEEG is a vital tool in the evaluation of this population and frequently leads to a management change.
KEYWORDS: Neurocritical Care, Neuro-oncology, Early Stage Investigator

170. Management of Spontaneous Epidural Hematoma in the setting of Vaso-occlusive Crisis among Pediatric Patients with Sickle Cell Disease: A Case Series and Scoping Literature Review

Patel R (Bronx, NY), Reisert H, Keymakh M, Drakou E, Briggs J, Strumph K, Kobets A, Lax D

OBJECTIVE: Spontaneous, non-traumatic epidural hematoma (EDH) is an exceedingly rare complication of vaso-occlusive crisis (VOC) in sickle cell disease. Early diagnosis and management are vital to decrease mortality.
METHODS: We report two SCD patients with multifocal spontaneous EDH and one with subgaleal hematomas and conduct a scoping literature review (PubMed & Embase).
RESULTS: A 15-year-old female with SCD presented with VOC, altered mentation, and mild right-sided weakness was found to have bilateral EDH. She underwent urgent bilateral craniotomy, exchange transfusion, and made a full recovery.
A 14-year-old male with SCD presented for VOC and developed visual hallucinations before becoming unresponsive. CT demonstrated multifocal EDH and a calvarial infarct. He underwent conservative management with an exchange transfusion in addition to adequate pain management. Despite suffering disseminated intravascular coagulation, he recovered well without neurologic deficits.
An 18-year-old male with SCD presented for a VOC and developed severe headache and visual disturbances. Neuroimaging confirmed numerous subgaleal hematomas. Conservative management was pursued.
Scoping review identified 71 additional SCD patients with spontaneous EDH from 1970-2024. Cases were 82% male, median 16.5-years-old, presenting with VOC (59%) and/or headache (54%). Half (52%) underwent neurosurgery. Of the 73% survivors, 21% had neurologic deficits.
CONCLUSIONS: Spontaneous EDH is a life-threatening complication of SCD that can be managed neurosurgically or conservatively but can be as fatal as their traumatic counterparts. Early diagnosis and management are crucial. In conjunction with our literature review, this report further delineates features of spontaneous EDH in SCD and clarifies optimal management strategies for these rare patients.
KEYWORDS: Neurocritical Care

171. Machine learning predicts cerebral injury in the Pediatric Intensive Care Unit

Sansevere A (Washington, DC), Anwar S M, Keenan J, Conley C, Staso K, Harrar D

OBJECTIVE: To apply machine learning techniques using clinical and EEG background features, to predict cerebral injury in the PICU.
METHODS: Prospective study of patients admitted to the PICU from July 2021 to January 2023. We excluded patients with pre-existing cerebral injury. Clinical variables collected included age, sex, reason for admission, EEG background, epileptiform discharges (ED), electrographic seizures (ES), and neuroimaging findings. Machine learning techniques to predict cerebral injury included K-nearest neighbor, logistic regression, support vector machines (SVM), random forest, gradient boosting, and Adaboost classifiers. For SVM, we used the linear and radial basis function kernels (RBF) . We designed a binary classification for predicting brain injury (class 1) and no brain injury (class 2) and a multiclass classification to better identify details of the brain injury: no injury (class 1), focal injury (class 2), and bilateral injury (class 3). The performance was evaluated in terms of precision, recall, and area under the receiver operating characteristic (AUROC) curve.
RESULTS: Of 197 patients, 42% were female, and the median age was 3.5 years. The most common EEG background was slow/disorganized (73%). Twenty-five percent of patients had EDs and 13% of patients had ES. Cerebral injury was detected in 51%. For the binary classification, SVM with RBF was most accurate with area under the AUROC of 0.95 and test accuracy of 0.90% for predicting cerebral injury. For the multiclass classification logistic regression had the highest accuracy with 0.77%.
CONCLUSIONS: Machine learning can be employed using appropriate clinical and EEG features to accurately predict cerebral injury.
KEYWORDS: Neurocritical Care, Neuroimaging

172. CARES: A Holistic Approach to Pediatric Brain Death Determination

Wiest H (Albany, NY), Quinlan M, Harwayne-Gidansky I, Pugh J A

OBJECTIVE: Pediatric brain death (BD) determination has been controversial since concept inception in 1987. Given

the gravity of making a pediatric BD determination, methodical adherence to the AAN Brain Death/Death by Neurologic Criteria (BD/DNC) practice guideline is paramount. Just as checklists are used for the clinical portions of BD determination, we propose a checklist be used as an ethical framework to guide clinicians in considering emotional, cultural and social aspects of the patient's care.
METHODS: We developed an acronym to guide pediatric BD determination based on a literature review of ethical and philosophical dilemmas surrounding pediatric BD/DNC, the 2023 AAN guidelines, and expert consensus.
RESULTS: We propose the CARES acronym: Communication, Accommodation, Resource sharing, Examination, and Support to further guide clinicians in declaring brain death in pediatric populations. Communication will shift from notification of beginning BD/DNC determination to an invitation for family participation, with explanation of the process at every step. Accommodation encompasses providing space for addressing religious or cultural beliefs, whether with the care team, a chaplain, or a social worker. Resource sharing via consultation from the ethics or palliative care teams can aid clinicians in effectively counseling families. Examination for BD/DNC determination should adhere to the 2023 AAN guidelines. Finally, support should be offered throughout the process with a focus on helping families cope, grieve, and process.
CONCLUSIONS: Creating a stepwise, family-centered approach to pediatric BD is an important step in guiding caregivers and families through the often difficult process of pediatric BD declaration.
KEYWORDS: Neurocritical Care, Practice Parameters

173. Application of consensus recommendations for new onset refractory status epilepticus (NORSE) and febrile infection-related epilepsy syndrome (FIRES): a single-institution perspective.

Xie V X (Washington, DC), Har C, Roper H, Kahn I, Sepeta L, Harrar D, Wells E, Kornbluh A

OBJECTIVE: Multidisciplinary case conferences improve outcomes and encourage practice uniformity in rare diseases. We aimed to survey an academic neurology department on knowledge and application of international consensus recommendations for diagnosis and acute phase management of NORSE/FIRES (Wickstrom et al. 2022).
METHODS: A 17-question survey was sent to 81 neurology faculty and trainees. The questions assessed knowledge and practice of diagnostic and management recommendations.
RESULTS: 27/81 (33%) of surveys were completed. 21/27 (78%) participants were neurology faculty and 6/27 (22%) were child neurology residents. The majority of respondents practiced recommendations regarding EEG monitoring (25/27, 93%) and initial treatment of seizures (26/27, 96%). Only 5/27 (18%) were aware of and practiced the recommendation for brain biopsy when there is a targetable lesion in cryptogenic NORSE/FIRES. Among faculty who regularly care for ICU patients (n=6), 67 - 100% respondents practiced recommendations included in the survey, compared to 40 - 93% of non-ICU faculty (n=15). The most common feedback for all participants was perceived rapidity of the recommended timelines for initiating the ketogenic diet or second line immunotherapy.
CONCLUSIONS: This survey identifies variability in knowledge and application of NORSE/FIRES consensus recommendations at an academic institution. This survey was administered prior to release of an updated FIRES/NORSE clinical protocol at our hospital. Given NORSE/FIRES patients require highly collaborative care, this data supports the need for regular multidisciplinary case conferences to increase familiarity with consensus recommendations and ensure timely application of treatments. Future directions include establishing a national case conference series to reinforce guidelines on an institutional level.
KEYWORDS: Neurocritical Care, Neuroimmunology, Epilepsy

174. Post-hypoxic myoclonus in pediatric cardiac arrest - incidence and treatment

Keenan J S (Washington, DC), Harrar B, Conley C R, Staso K, Sansevere A

OBJECTIVE: To describe the incidence, electroencephalogram (EEG) features, treatment approach and outcomes of pediatric patients with post-hypoxic myoclonus (PHM) after cardiac arrest (CA).
METHODS: Retrospective review of pediatric patients with CA that developed PHM from June 2021-April 2024. Clinical variables included demographics, CA details, treatment approach and mortality. EEG features included EEG background, presence of epileptiform discharges, rhythmic and periodic patterns and EEG correlate of PHM.
RESULTS: We reviewed 129 patients with CA, and 8% (N=10) had PHM. Of the 10 patients, the median age was 2.44 years [IQR 1.78-10.69], and 80% were male. Out of hospital arrest was most common (70%) and the median duration of CPR was 40 minutes (IQR 25-45). All patients had hypoxic brain injury. Seventy percent had EEG correlate (four patents had generalized periodic discharges, two patients had clinical correlate with independent bursts, and one patient had 2 to 3 Hz generalized spike wave. Three had no EEG correlate and in those cases, the EEG background was attenuated. The most common semiology was full body myoclonus, two patients had facial and upper extremity myoclonus with eye opening and one had eye opening alone. Three patients had stimulus-induced PHM. Intravenous loading dose of anti-seizure medications (ASM) was administered in 90%, one patient did not receive a loading dose but was started on standing ASM, and 20% needed continuous infusion. Eighty percent of patients died with 30% meeting criteria for brain death.
CONCLUSIONS: PHM is common after pediatric CA. Despite treatment, the prognosis remained poor.
KEYWORDS: Neurocritical Care

175. Burdened by trauma: beyond the initial PICU admission

Plaud Gonzalez J (Houston, TX), Aras S, Faber E, Schultz R, Ramirez B, Risen S

OBJECTIVE: To assess symptoms of post-traumatic stress disorder (PTSD) in parents of children admitted to the neurocritical care unit and followed in a post-pediatric intensive care unit (PICU) clinic.
METHODS: A retrospective chart review was conducted among 135 children admitted with neurocritical illness to a tertiary children's hospital, followed later at the post-PICU clinic. Data recovered included: demographics, etiology (e.g., trauma, vascular, seizures, inflammatory, etc) age of admission and Functional Status Scale scores (FSSs) at first clinic visit. To assess PTSD in parents, we used the Impact of Event-Revised scale score (IoERss) obtained during the initial follow-up visit.
RESULTS: Over 52% of parents reported moderate to severe stress at initial clinic follow up. No association was identified between parental IoERss and type of brain injury, illness severity, length of stay or FSSs. The only factor associated with higher levels of parental stress that was statistically significant ($p=0.049$) was age of child at admission.
CONCLUSIONS: This study identifies significant degree of stress in parents of children admitted to the neurocritical care unit with an acute life-threatening illness regardless of etiology and level of functioning. Age of presentation may play a significant role in how parents are able to respond and cope with the stress of a PICU hospitalization. Identifying factors that contribute to parental stress may lead to the development of strategies that mitigate triggers and target psychological health.
KEYWORDS: Neurocritical Care

NEURO-CUTANEOUS DISORDERS

176. Absent deep and basal veins in Sturge-Weber syndrome: Radiological and clinical correlates

Albazron F M (Detroit, MI), Haacke EM, Xuan Y, Jeong J-W, Luat A, Gjolaj N, Behen M, Juhasz C

OBJECTIVE: Sturge-Weber syndrome (SWS) is a rare sporadic neurocutaneous disorder, whose neurological complications include early-onset epilepsy, motor impairment, and learning difficulties. Intracranial vascular abnormalities in SWS include leptomeningeal venous malformation (LVM) and enlarged medullary veins (EMVs). Small studies have reported absent deep veins in some patients with SWS, but their prevalence and clinical impact remain unknown.
METHODS: In this prospective study, 30 young patients with unilateral SWS and 20 healthy controls (mean age: 12.3 ± 7.0 and 13.8 ± 7.8 years, respectively) underwent 3T brain MRI including susceptibility-weighted imaging (SWI), an MRI sequence uniquely sensitive to detecting small veins. The presence or absence of three major deep cerebral veins and the basal vein of Rosenthal (BVR) were evaluated in all 50 subjects and correlated with other brain vascular and parenchymal abnormalities and clinical symptoms in the SWS group.
RESULTS: While deep cerebral veins and the BVR were identified bilaterally by SWI in all 20 controls, absence of cerebral veins was commonly observed in the SWS-affected hemispheres: absent internal cerebral vein in 15 (50%; including 5 with bilateral absence), thalamostriate vein in 10 (33%), septal vein in 7 (23%), and BVR in 9 (30%) patients. Absent internal cerebral vein and BVR were associated with more extensive EMVs ($p<0.05$); absent BVR was also associated with extensive LVM and brain atrophy, as well as worse motor functions ($p<0.01$ in all).
CONCLUSIONS: In SWS, absent deep and basal veins are commonly detected on SWI and are associated with more severe cerebral vascular and parenchymal abnormalities, with a potential impact on clinical symptoms.
KEYWORDS: Neuro-Cutaneous Disorders, Neuroimaging, Neurodevelopmental Disorders

177. Survey of an Urban NF Clinic Hispanic Population to Improve NF Education and Outreach

Rosser T (Los Angeles, CA), Powers K, Wanninger K

OBJECTIVE: Patients have a more positive experience within the medical system when information is provided in their native language. The goals of this study were to better understand how to provide our Hispanic NF population with education and opportunities to participate within the NF community.
METHODS: A survey with 23 questions was used to query our Hispanic population's home language fluency, internet access, preferred means of receiving educational materials and community engagement.
RESULTS: Twenty families (9 females, 11 males) were recruited with ages ranging from 1-27.9 years (mean 12.7 years). 31.6% of households speak only Spanish with the majority being bilingual. 77.8% prefer office visits to be conducted in Spanish. 94.4% agree that they receive adequate interpreting services in our clinic. All families have internet access. Two parents have no email address. 68.4% prefer to receive brochures in Spanish but 26% would like to receive information by internet link. 89.5% have received information in Spanish from our clinic. 83.3% have interest in attending an educational symposium in Spanish either in person or virtually. 94.7% of families would be interested in watching educational videos in Spanish. 72% have a good understanding of their child's NF diagnosis and 77.8% have done research online.
CONCLUSIONS: The majority of our Hispanic NF clinic population come from bilingual households. There is appreciation for receiving information in clinic through a live Spanish interpreter and with written brochures in Spanish. There are many opportunities to increase our Hispanic population's NF educational experiences and engagement with the NF community.
KEYWORDS: Neuro-Cutaneous Disorders, Diversity, Equity, Inclusion

178. Neuropsychological Profile for Lesions of the Corpus Callosum in Children with Neurofibromatosis Type I

Jandhyala N R (New York, NY), Garcia M R, Powell S, Yohay K, Segal D

OBJECTIVE: To describe the neuropsychological profiles of a cohort of children with NF1 and unidentified bright objects (UBOs) and/or gliomas present in the corpus callosum (CC).
METHODS: We performed a retrospective chart review of 63 patients with NF1 with UBOs and/or gliomas of the corpus callosum on MRI. For patients with neuropsychological evaluation, we collected the results of testing across multiple cognitive domains including: FSIQ, attention, language, and executive functioning.
RESULTS: There were 9 patients (median age of 10 years) with detailed neuropsychological reports for review - 5 had UBOs and 4 had gliomas. The median FSIQ was 85 (16th percentile). There was no significant difference in score between those with UBOs and gliomas. When analyzed by subdomain, median scores were: 85 in verbal comprehension (17th percentile), 92 in perceptual reasoning (30th percentile), 83 in working memory (13th percentile), and 78 in processing speed (12th percentile). Median academic performance testing was in the 34th and 20th percentile for reading comprehension and math computation, respectively. Among patients who completed the grooved pegboard test for fine motor skills and CELF-5 test for language, scores were within the impaired to low average range for all children.
CONCLUSIONS: In this study, we provide neuropsychological profiles for a cohort of children with NF1 and lesions localized to the corpus callosum. Difficulty emerged with processing speed, working memory, fine motor skills, and language. Better elucidation of the cognitive effects of corpus callosal lesions is necessary to provide appropriate support to this patient subgroup.
KEYWORDS: Neuro-Cutaneous Disorders, Neurodevelopmental Disorders, Behavioral Neurology

179. Halo effect of Cafe au lait macules in congenital dermal melanocytosis

Hendricks M (Louisville, KY), Mustafa M, Kinney M, Lakhotia A

OBJECTIVE: Discuss an unusual presentation of cafe au lait macules (CALMs) superimposed on congenital dermal melanocytosis (CDM) in a patient with darker skin complexion, by highlighting a case of phacomatosis pigmento-halo-pigmentalis
METHODS: Chart Review
RESULTS: A 13-month-old, neurodevelopmentally normal, male presented to child neurology clinic for evaluation of multiple (>6) cutaneous hyperpigmented macules, which were clinically concerning for CALMs. Skin exam showed typical CALMs, but also showed several atypical skin lesions on the back when CALMs were superimposed on CDM. There was clearing of the CDM, to create an annular "halo effect" with CALM at the center. Genetic testing for neurofibromatosis 1 (NF1) was positive.
CONCLUSIONS: This case aims to draw attention to an atypical presentation of CALMs, which are the most common diagnostic feature of NF1. The presentation of CALMs was unusual due to their interaction with CDM, which is a common cutaneous finding in patients with darker skin. There is unfortunately often limited exposure to the appearance of certain dermatological manifestations in dark skinned individuals. Education of atypical presentations of a common finding can be even less. This report adds to the scant literature surrounding the uncommon phenomenon of phacomatosis pigmento-halo-pigmentalis, which can sometimes be seen due to an interaction of two common skin findings.
KEYWORDS: Neuro-Cutaneous Disorders, Diversity, Equity, Inclusion, Early Stage Investigator

NEURODEVELOPMENTAL DISORDERS

180. Differentiating Early Motor Phenotypes Between Toddlers at Genetic Risk for Autism

Kottakota H (Los Angeles, CA), McDonald N, Hyde C, Jeste S, Wilson R

OBJECTIVE: Motor dysfunction is common but understudied in autism. We studied motor skills in toddlers at greater genetic risk for autism, either due to a diagnosis of tuberous sclerosis complex ("TSC") or due to a family history of autism ("Fhx").
METHODS: At three timepoints, we compared toddlers with: typical development (TD, n=39); TSC with no autism concerns (TSC+NC, n=15); TSC with autism concerns (TSC+AC, n=35); and Fhx with autism concerns (Fhx +AC, n=23). Gross motor (GM) and fine motor (FM) skills were measured using Vineland Adaptive Behavior Scales and Mullen Scales of Early Learning. Inter-group mean differences ("md") were assessed using analysis of variance testing.
RESULTS: At 1 year, Vineland found TSC+AC scored lower on GM (md=5.8) and FM (md=4.5) than TD ($p<0.001$). TSC+AC had lower GM (md=5.4) and FM (md=3.8) than Fhx+AC ($p<0.001$). On Mullen, TSC+AC had lower FM ($p<0.001$) compared to TD (md=28.3) and Fhx+AC (md=21.1).
At 2 years, Vineland found TSC+AC scored lower on GM (md=5.5) and FM (md=3.9) than TD ($p<0.001$). TSC +AC had lower GM (md=4.1) and FM (md=2.5) than Fhx +AC ($p<0.05$). On Mullen, TSC+AC had lower GM (md=15.7) and FM (md=23.2) compared to Fhx+AC ($p<0.001$).
At 3 years, Vineland found TSC+AC scored lower on GM (md=4.4) and FM (md=5.1) than TD ($p<0.001$). TSC +AC had lower GM (md=2.8) and FM (md=2.6) compared to Fhx+AC ($p<0.05$). On Mullen, TSC+AC had lower FM ($p<0.001$) compared to TD (md=33.2) and Fhx +AC (md=18.6).
CONCLUSIONS: Motor development may serve as a measurable endophenotype that could facilitate early characterization of specific subgroups with genetic susceptibilities to autism.
KEYWORDS: Neurodevelopmental Disorders, Neurogenetics

181. DNA Methylation Signatures of Prenatal Socioeconomic Position and 36-month Neurodevelopmental Outcomes

Rajaprakash M (Baltimore, MD), Palmore M, Bakulski K, Lyall K, Schmidt R, Newschaffer C, Croen L, Herz-Picciotto I, Volk H, Ladd-Acosta C, Fallin M

OBJECTIVE: To determine whether DNA methylation signatures of prenatal socioeconomic position (SEP), measured in birth samples, are associated with neurodevelopmental outcomes at 36 months.

METHODS: Prenatal interviews were administered to pregnant women recruited from four Early Autism Risk Longitudinal Investigation (EARLI) sites (Philadelphia, Baltimore, San Francisco, Sacramento). A variable reflecting low SEP was created with coding=1 if any of three indicators were endorsed: maternal education= no degree, marital status=single, and insurance status=public, and 0 for none. We measured DNA methylation at 485,512 loci using the Illumina Infinium HumanMethylation450 BeadChip (Illumina, San Diego, CA) in 97 placenta and 127 cord blood biospecimens. Methylation signature scores were computed from CpG sites based on external association studies with SEP, with higher scores reflecting lower SEP. Participants completed the Mullen Scales of Early Learning (MSEL) and Vineland Adaptive Behavior Scales (VABS) at 36 months of age. Generalized regression analyses, adjusting for maternal age and race, were performed to test the association between SEP methylation score, for each birth biospecimen type, and MSEL and VABS scores.

RESULTS: Significant associations were observed between placenta SEP methylation score and MSEL Expressive Language outcomes (beta = -2.7, $p = 0.046$) and Receptive Language outcomes (beta = -2.5, $p = 0.037$). In cord blood, methylation-SEP scores were significantly associated with Receptive Language outcomes (beta = -2.0, $p = 0.037$).

CONCLUSIONS: Our preliminary results suggest that DNA methylation signature scores reflecting prenatal SEP in placental tissue and cord blood are associated with language outcomes at 36 months of age.

KEYWORDS: Neurodevelopmental Disorders, Neonatal Neurology

182. Comprehensive Assessment of Body Composition, Physical Activity, and Health Markers in Pediatric Prader-Willi Syndrome

Cassidy J W (Houston, TX), Stockton B, Ravindranathan G, Thomey D

OBJECTIVE: The objective of this study is to evaluate the efficacy of a comprehensive inpatient program for pediatric Prader-Willi syndrome (PWS) at Nexus Children's Hospital, Texas, utilizing standardized fitness trackers to monitor treatment progress.

METHODS: Patients with PWS were consented and enrolled with IRB exemption. Fitbit Inspire 3 watches and an InBody 570 scanner were used to analyze health parameters during admission. Fitbit monitored daily heart rate, sleep patterns, and activity levels, while the InBody 570 scanner assessed changes in weight, BMI, and body composition weekly. Monthly assessments by occupational and physical therapy staff evaluated endurance, strength, and coordination.

RESULTS: Ten pediatric PWS patients (3 male, 7 female) participated in the study, with an average length of stay of 125 days. Significant improvements were observed, including a 9.64% decrease in weight, a 9.61% reduction in BMI, and a 7.15% decrease in body fat percentage ($p < 0.05$). Endurance, cardiovascular health, and mobility showed significant enhancements as evidenced by changes in the 6 Minute Walk Test and WeeFIM II scale ($p < 0.05$). Activity levels increased by 36.16% ($p < 0.05$), and sleep quality, particularly REM sleep, significantly improved ($p < 0.05$). Nine out of ten patients were discharged home with improved quality of life and tools for continued fitness maintenance.

CONCLUSIONS: The findings highlight the effectiveness of the comprehensive management program in improving various health metrics among pediatric PWS patients. The utilization of fitness trackers proved valuable in quantifying treatment efficacy and managing PWS effectively.

KEYWORDS: Neurodevelopmental Disorders, Behavioral Neurology

183. A SEVERE CLINICAL PRESENTATION ASSOCIATED WITH AUTS2: FURTHER DELINEATION OF THE HX REPEAT DOMAIN-RELATED PHENOTYPE

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OBJECTIVE: Haploinsufficiency of AUTS2 is associated with a neurodevelopmental disorder characterized by intellectual disability, autistic features, and spasticity. AUTS2 protein interacts with p300, encoded by EP300, through the HX repeat domain of AUTS2, thereby activating transcription. We previously reported two individuals with distinct heterozygous de novo variants in the HX repeat domain of AUTS2. These variants disrupt the AUTS2-P300 interaction, resulting in a phenotype resembling Rubinstein-Taybi Syndrome (RSTS) associated with variants in EP300/CREBBP. Here, we expand beyond the initial clinical description to delineate the HX domain-associated phenotype.

METHODS: Clinical data, photographs, and neuroimaging studies were reviewed to examine genotype-phenotype relationships among seven individuals with heterozygous de novo variants in the HX domain, with two recurrent variants (p.Thr534Pro, p.His535_Thr542del) and one single variant (p.His533Tyr).

RESULTS: The clinical features for these individuals includes severe intellectual disability, distinct craniofacial and skeletal dysmorphic features, and consistent neuroimaging findings. Facial dysmorphisms included wide (6/7) and prominent (5/7) nasal bridges with complex nasal shapes and dysmorphic eyebrows (7/7). Five individuals had broad thumbs/halluces, two had low-hanging columella, and one had involuntary grimacing as RSTS-overlapping features. Dysmorphisms included digit anomalies: symphalangism and

hypoplasia of distal phalanges, exclusive to the HX domain variant group. All seven individuals within this group had varying degrees of cerebellar hypoplasia, and five had hypoplasia of the corpus callosum.
CONCLUSIONS: Our report delineates a distinct and severe clinical phenotype associated with variants in the AUTS2 HX domain, including an in-depth comparison with the AUTS2 haploinsufficiency phenotype features.
KEYWORDS: Neurodevelopmental Disorders, Neurogenetics

184. Efficacy and Safety of Once-Daily Extended-Release Centanafadine for the Treatment of ADHD in Children Aged 6–12 Years

Ward C L (Princeton, NJ), Jin N, Turkoglu O, Skubiak T, Childress A, Mattingly G, van Stralen J

OBJECTIVE: ADHD is one of the most common pediatric neurodevelopmental disorders, characterized by symptoms of hyperactivity, impulsivity, and inattention. This phase 3 trial (NCT05428033) evaluated the efficacy and safety of once-daily, extended-release centanafadine (CTN)—a norepinephrine, dopamine, serotonin reuptake inhibitor—for treatment of ADHD in children aged 6–12 years.
METHODS: Eligible patients with a primary ADHD diagnosis were randomized to weight-based high- or low-dose CTN or placebo. Primary and key secondary efficacy endpoints included changes from baseline in ADHD-RS-5 symptoms total raw score, CGI-S-ADHD, and Conners 3-Parent Short (PS) content scale T-scores at Week 6 and were analyzed using a mixed-effect model for repeated measures. Safety and tolerability were assessed.
RESULTS: Overall, 367/480 (76.5%) randomized patients completed the study (mean age 9.2 years; 58% male). Change from baseline in ADHD-RS-5 symptoms total raw score at Week 6 was –16.3 for CTN high dose versus –10.8 for placebo (P=0.0008), with improvement seen from Week 1 (P=0.0009). Low-dose CTN did not meet the primary endpoint. Numerical improvements in ADHD severity per the CGI-S-ADHD at Week 6 were observed as well as nominally significant improvements in ADHD symptoms of Hyperactivity/Impulsivity and Inattention for high-dose CTN versus placebo on the Conners 3-PS content scale T-scores. Treatment-emergent adverse events were reported in 38.9% of patients treated with high dose, 35.4% with low dose, and 25.5% with placebo; most were mild to moderate.
CONCLUSIONS: The high dose of CTN was efficacious, and safe and well tolerated in the treatment of ADHD in children.
KEYWORDS: Neurodevelopmental Disorders

185. Case of CYFIP2-Associated Epileptic Encephalopathy – A Window of Hope

Squire M (Chapel Hill, NC), Lea J, Trau S P, Fan Z, Hunter S

OBJECTIVE: Pathogenic CYFIP2 variants cause developmental and epileptic encephalopathy type 65 (DEE-65), characterized by early-onset intractable epilepsy and psychomotor developmental delay. There are no known targeted therapies. Position Arg87 of CYFIP2 is a hot spot causing de-novo gain-of-function variants, typically reported with a profound phenotype. We describe an infant with CYFIP2-associated DEE to inform future treatments.
METHODS: To present a case of CYFIP2-associated epileptic encephalopathy with the development of infantile spasms and hyperkinetic choreiform movement disorder.
RESULTS: A 2-month-old with developmental delay presented with seizures confirmed on EEG. A multi-gene panel identified a de novo pathogenic CYFIP2 c.259C>T (p.-Arg87Cys) variant. Following transition to lacosamide monotherapy, seizures were controlled, EEG normalized, and he met age-appropriate developmental milestones. At 6 months, he developed epileptic spasms and mild regression in language/communication. He was treated successfully with ACTH followed by vigabatrin. At 7 months he developed a hyperkinetic choreoathetoid movement disorder, improved with clonazepam initiation. A second course of ACTH was started for EEG findings of modified hypsarrhythmia, with EEG improvement and resolution of hyperkinetic movements. At 9 months, he remained seizure-free with moderate global developmental delay.
CONCLUSIONS: In other genetic disorders, gene-modifying therapies demonstrated positive outcomes when initiated at pre- or early symptomatic ages. This presentation, including a period of seizure freedom and reassuring development following initial diagnoses, suggests that individuals with CYFIP2-associated DEE may have a therapeutic window in which disease-modifying therapies could be administered. Studies are needed regarding targeted therapies for CYFIP2 variants that may prevent epileptic spasms and development delay, and improve outcomes.
KEYWORDS: Neurodevelopmental Disorders, Epilepsy, Movement Disorders

186. Longitudinal Adaptive Behavioral Outcomes in Ogden Syndrome by Seizure Status and Therapeutic Intervention

Lyon G J (New York, NY), Makwana R, Christ C, Marchi E, Harpell R

OBJECTIVE: To conduct a natural history study in parallel with gene therapy development for an ultra-rare severe human neurodevelopmental disorder, Ogden syndrome (OS), involving pathogenic variants in NAA10, which encodes the N-terminal acetyltransferase A complex (in association with NAA15 and HYPK).
METHODS: The study included 58 distinct participants, with 43 caregivers interviewed using the Vineland-3 and a self-administered survey regarding therapy, along with 10 who completed the Vineland-3 only and 5 who only answered the survey. The average age at time of most recent assessment was 12.4 years old, but ranging in age from 11 months to 40.2 years old.
RESULTS: Using Vineland-3 scores, we show decline in cognitive function over time in individuals with OS (n=53). Sub-domain analysis found the decline to be present across all modalities. Additionally, we describe the nature of seizures

in this condition in greater detail, as well as investigate how already-available non-pharmaceutical therapies impact individuals with OS. Additional investigation between seizure and non-seizure groups showed no significant difference in adaptive behavior outcomes. Therapy investigation showed speech therapy to be the most commonly used therapy by individuals with OS, with more severely affected individuals receiving more types of therapy than their less-severe counterparts. Early intervention analysis was only significantly effective for speech therapy.

CONCLUSIONS: Our study portrays the decline in cognitive function over time of individuals within our cohort, independent of seizure status and therapies being received, and highlights the urgent need for the development of effective treatments for OS, including an ongoing gene therapy development program.

KEYWORDS: Neurodevelopmental Disorders, Lifespan Manifestations of Childhood Onset Conditions, Neurogenetics

187. Disrupted Neurogenesis in the Developmental Gene DDX3X

Yang C (San Francisco, CA), Li J, Sherr E H

OBJECTIVE: DDX3X encodes an RNA helicase of the DEAD-box helicase family and plays an important role in neurogenesis. Patients carrying pathogenic DDX3X variants exhibit a range of brain abnormalities indicative of disrupted neurodevelopment. The objective of this study is to examine how different DDX3X variants disrupt the balance in the number of neural progenitor subtypes during early neurogenesis.

METHODS: PBMCs from patients with DDX3X variants T532M, R376C, and I415M and PBMCs from their healthy mothers (as controls) are used to generate pluripotent stem cells (PSCs). With the neuronal morphogens dorsomorphin and SB431542, PSCs are differentiated into dorsal neural progenitor cells. The number of radial glial cells (RGCs) and intermediate progenitors (IPs) are measured with the marker gene sets PAX6+/SOX2+/KI67+ and TBR2+/KI67+/TUJ1- respectively with ICC-IF and qPCR from differentiation day 0 to 40.

RESULTS: We find that variants T532M and I415M cause an increase in the number of IPs while variant R376C causes a decrease in the number of IPs. Consistent with this finding, BRN2, a transcriptional regulator of TBR2 that suppresses its expression, is decreased in neural progenitor cells with the T532M variant. There was no significant change in the number of RGCs by DDX3X mutations.

CONCLUSIONS: DDX3X disrupts early neurogenesis through the overproduction of IPs in the variants T532M and I415M and the underproduction of IPs in R376C. Of note, variants T532M and I415M were previously found to cause severe loss of the DDX3X protein helicase activity, while R376C was found to cause moderate loss of helicase activity.

KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Neonatal Neurology

188. An open-label study of eladocagene exuparvovec administered using the SmartFlow magnetic resonance-compatible ventricular cannula in paediatric participants: 48-week interim analysis

Warn L (South Plainfield, NJ), Gilbert D L, Ben-Zeev B, Curry D, Stone S, Vestal M, Werner C, Krolick A, Wuh-Liang Hwu P, Penematsa V, Wang A, Golden L, Pearl P

OBJECTIVE: To assess the pharmacodynamics of eladocagene exuparvovec gene therapy in pediatric participants with aromatic L-amino acid decarboxylase deficiency (AADCd). Safety of the SmartFlow magnetic resonance (MR)-compatible ventricular cannula used for the bilateral intraputaminal infusion of eladocagene exuparvovec was also assessed.

METHODS: This was a phase 2, multicentre, open-label trial in Israel, Taiwan and the USA. Overall, 13 children (aged 16–129 months) with AADC deficiency received eladocagene exuparvovec. Cerebrospinal fluid (CSF) homovanillic acid (HVA) levels, intraputaminal uptake of [18F] fluorodopa (F-DOPA) and acquisition of motor milestones were assessed.

RESULTS: At baseline, the mean (SD) age of the 13 participants with severe motor developmental delay was 45.2 (29.5) months. Only one participant had partial head control. Significantly increased mean (SD) CSF HVA levels and F-DOPA uptake from baseline observed 8 weeks after gene therapy (29.5 [12.9] nmol/L and 0.243 [0.085], respectively; both $p<0.0001$; $n=12$) were sustained at the interim analysis 48 weeks post-gene therapy (CSF HVA levels, 22.0 [6.6] nmol/L; $p=0.0005$; $n=6$) (F-DOPA uptake, 0.284 [0.102]; $p=0.0003$; $n=7$). At week 48, 8/9 participants achieved full head control, 6/9 achieved sitting with assistance and 1/9 could walk independently. TEAEs recorded in >50% of participants in the 48 weeks post-gene therapy were dyskinesia, pyrexia and diarrhoea. No TEAEs were deemed to be related to the SmartFlow MR-compatible ventricular cannula.

CONCLUSIONS: Significantly increased CSF HVA levels and F-DOPA uptake from baseline were sustained up to 48 weeks following treatment with eladocagene exuparvovec in participants with AADC deficiency and coincided with increased acquisition of motor milestones.

KEYWORDS: Neurodevelopmental Disorders

189. From bed to bench and back again: circadian dysfunction in a patient-derived allele of DLG4 synaptopathy

Tamir S (Cincinnati, OH), Paulose J, Witt R M, Hogenesch J

OBJECTIVE: SHINE syndrome is a rare neurodevelopmental disorder resulting from autosomal dominant mutations in the DLG4 gene, in which sleep disturbances are a key symptom. DLG4 encodes the protein PSD-95, which plays a role in scaffolding and clustering of receptors at the postsynaptic membrane. We aim to elucidate the mechanism of sleep disturbances in SHINE syndrome by studying its role in cellular circadian rhythms and investigating sleep and locomotor behavior in DLG4 mutant mice.

METHODS: We recorded real-time circadian rhythms in U2 OS cells expressing BMAL1 promoter-driven luciferase in the presence or absence of DLG4 siRNAs. For behavioral assessment, we generated mice expressing the Val692-Trpfs*12 mutation that was identified in a patient with a severe case of SHINE syndrome. Locomotor behavior was assessed via wheel running, and sleep behavior was studied using PiezoSleep Behavioral Tracking System.
RESULTS: DLG4 siRNA knockdown in cells resulted in period shortening of BMAL1 oscillations. Mutant DLG4 mice had lower cerebellar PSD-95 expression by Western blot, less total activity in wheel running, and increased average sleep bout length during the inactive phase compared to wild-type mice. Periodograms for the patient and mice with Val692Trpfs*12 mutations were normal.
CONCLUSIONS: This study represents one of the first comprehensive circadian models of a patient-derived deleterious allele in mice. These findings further support that DLG4 is involved in regulation of sleep and circadian rhythms. Future experiments will seek to evaluate whether DLG4 loss impacts neural network connectivity crucial for sleep and circadian rhythms.
KEYWORDS: Neurodevelopmental Disorders, Sleep, Neurogenetics

190. Detailed motor assessment in infants 3-12 months of age with and without a family history of autism

Wong S (Los Angeles, CA), Abdullahi S, Ly R, Wilson R

OBJECTIVE: Motor impairments may be the earliest presentation of autism spectrum disorder, but more is needed to understand what these motor impairments are, when they emerge, and how they are related to autism outcomes. We studied motor skills in the first year of life in infants at risk for autism due to a family history of autism (FHx) and infants with no family history of autism (nFHx).
METHODS: At 3, 6, 9, and 12 months of age, we compared 83 infants with: (1) FHx of ASD (n=60); (2) nFHx of ASD (n=23) and stratified by ASD outcome determined at 3 years of age (ASD: n=12; noASD: n=36). Motor skills were measured by the Alberta Infant Motor Scale [AIMS] (prone, supine, sit, stand subscales, and total score). Age of walking onset was obtained from caregivers. Between group differences were assessed using t-tests.
RESULTS: All reported results have $p<0.05$. At 6 months, FHx infants scored lower on AIMS prone and supine subscales and total score (M=22.8;SD=6.5) than nFHx (M=26.9;SD=4.5). At 3 and 6 months, ASD group scored lower on the prone subscale, with a lower total score at 6 months (M=20.0;SD=8.1) than noASD (M=24.9; SD=5.5). At 9 months, ASD group scored lower on the supine scale. There was no difference in walking onset between groups.
CONCLUSIONS: Motor impairments may present as early as 3 months of age and may aid in autism diagnosis. These differences may not persist through 12 months when locomotion is achieved. Additional investigation may reveal if differences in motor quality persist.
KEYWORDS: Neurodevelopmental Disorders

191. Multi-Echo Resting-State fMRI Analysis of Neurocognitive and Motor Dysfunction in a Pediatric Sample of Neurofibromatosis Type 1

Batschelett M A (Cincinnati, OH), DiFrancesco M W, Cecil K M, Migneault K, Aschbacher-Smith L, Huddleston D, Gilbert D

OBJECTIVE: Neurofibromatosis Type 1 (NF1) is an autosomal dominant genetic disorder caused by a loss-of-function mutation in the NF1 gene, affecting ~1: 2500 individuals. Although the genetic mechanisms of NF1 are understood, less is known about the pathophysiology underlying highly prevalent cognitive and motor impairments. This project investigated associations between resting-state functional connectivity and quantitative measures of cognitive and motor function in youth with NF1.
METHODS: Sixteen youth with NF1 aged 8-16 years (mean(SD) = 12.25(3.17), 9 female) participated. Multi-echo resting-state functional MRI, the Attention Deficit/Hyperactivity Disorder Rating Scale (ADHD-RS), the computer-based Test of Variable Attention (TOVA), and the Physical and Neurological Examination of Subtle Signs (PANESS) motor development assessment were collected. Multivariate regressions, with Family Wise Error (FWE) correction and controlling for age and sex, explored associations between the behavioral/motor measures and seed-to-voxel functional connectivity in previously defined networks of motor and executive function.
RESULTS: Our analyses revealed that increased connectivity between sensorimotor regions (postcentral gyrus and supplementary motor area) and occipital and sensory-related cortical areas significantly predicted (FWE-corrected p-values < .001) enhanced motor performance. Furthermore, more severe behavioral scores were associated with greater connectivity between the dorsal attention (frontal eye field) and default mode (medial prefrontal cortex) networks and inferior frontal and occipital cortical areas (FWE-corrected p-values < .05).
CONCLUSIONS: Connectivity patterns in networks subserving sensorimotor, attention, and executive function may underly the NF1-associated dysfunction within these domains. These results both replicate and expand upon prior findings, providing potential brain-based biomarkers for prognostication and clinical trial response measurements.
KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Neuroimaging

192. Abnormal electroencephalogram findings and its correlation with clinical features from pediatric patients in psychiatric clinic

Ko Y J (Gwangmyeong-si, Republic of Korea), Cho A, Kim H

OBJECTIVE: We aimed to evaluate the occurrence of electroencephalogram (EEG) abnormalities in pediatric patients attending an outpatient psychiatry clinic at a tertiary center. We examined the rates of abnormalities and specific findings based on demographics, specific diagnoses, and clinical severity.
METHODS: This study included pediatric patients who underwent EEG at the outpatient psychiatry clinic. Patient demographics, psychiatric diagnosis, intellectual disability,

intelligent quotient (IQ) score, family history of psychiatric disorders, and Clinical Global Impression-Severity (CGI-S) score were obtained through retrospective electronic health record analysis. The rate of EEG abnormalities was calculated, and specific abnormal findings were reviewed. Relationships between the rate of EEG abnormalities and diagnosis, severity, IQ, and age at EEG examination were analyzed.
RESULTS: Of 319 patients who underwent EEG, 21.3% (68 patients) of patients exhibited abnormalities, including background abnormalities (14.7%, 47 patients), interictal epileptiform discharges (IEDs) (10.3%, 33 patients), and a slow posterior dominant rhythm (3.8%, 10 patients). The frontal region was the most commonly affected area. Neurodevelopmental disorders (NDDs) had the most frequent abnormalities (29.8%), followed by anxiety (16.7%), sleep (14.3%), mood (11.7%), psychotic (5%), and conduct disorders (0%). Disease severity did not correlate with the rate of EEG abnormalities. Adjusted for age, sex, severity, and family history, patients with EEG abnormalities exhibited lower IQ scores.
CONCLUSIONS: EEG abnormalities were common in pediatric patients with psychiatric disorders, with background abnormalities detected as frequently as IEDs. Disease severity was not associated with EEG abnormality, while IQ scores showed a negative correlation.
KEYWORDS: Neurodevelopmental Disorders

193. Efficacy and Safety of Once-Daily Extended-Release Centanafadine for the Treatment of ADHD in Adolescents Aged 13–17 Years

Ward C L (Princeton, NJ), Jin N, Turkoglu O, Skubiak T, Childress A, Mattingly G, van Stralen J

OBJECTIVE: ADHD is one of the most common pediatric neurodevelopmental disorders, characterized by symptoms of hyperactivity, impulsivity, and inattention. This phase 3 trial (NCT05257265) evaluated the efficacy and safety of once-daily, extended-release centanafadine (CTN)—a norepinephrine, dopamine, serotonin reuptake inhibitor—for the treatment of ADHD in adolescents aged 13–17 years.
METHODS: Eligible patients with a primary ADHD diagnosis were randomized to CTN 328.8mg, 164.4mg, or placebo. Primary and key secondary efficacy endpoints included changes from baseline in ADHD-RS-5 symptoms total raw score, CGI-S-ADHD, and Conners 3-Parent Short (PS) content scale T-scores at Week 6 and were analyzed using a mixed-effect model for repeated measures. Safety and tolerability were also assessed.
RESULTS: Overall, 371/459 (80.8%) randomized patients completed the study (mean age 14.7 years; 59% male). The change from baseline in ADHD-RS-5 symptoms total raw score at Week 6 was –18.5 for CTN 328.8mg versus –14.2 for placebo (P=0.0006), with benefit seen from Week 1 (P=0.001). CTN 164.4mg did not meet the primary endpoint. At Week 6, CTN 328.8mg achieved nominally significant reductions in ADHD severity per CGI-S-ADHD versus placebo (–1.4 vs –1.1 [P=0.0038]). Similarly, nominally significant improvements in Conners 3-PS content scale T-scores for Hyperactivity/Impulsivity and Inattention were observed for CTN 328.8mg versus placebo. Treatment-emergent adverse events were reported in 50.3% of patients treated with CTN 328.8mg, 31.4% with CTN 164.4mg, and 23.8% with placebo; most were mild to moderate.
CONCLUSIONS: CTN 328.8mg was efficacious, and safe and well tolerated in the treatment of adolescent ADHD.
KEYWORDS: Neurodevelopmental Disorders

194. Disease Course of MECP2 Duplication Syndrome: Insights from a Retrospective Natural History Study

Malik P R (Carlsbad, CA), Lyu F, Brimble E, Coquery C

OBJECTIVE: MECP2 duplication syndrome (MDS) is a rare X-linked neurodevelopmental disorder characterized by infantile hypotonia, progressive spasticity, and global developmental delay ultimately resulting in severe to profound intellectual disability, with a pattern of neurological symptoms that can present heterogeneously. The natural history of MDS and clinical domains that are sensitive to change over time have not been determined. This study aims to characterize the disease course and investigate clinical phenotypes.
METHODS: This study uses secondary data from Ciitizen, a patient-facing platform that extracts key data fields from predominantly U.S. medical records into a standardized longitudinal dataset from first medical contact through to the data cut. Data from up to 50 individuals with MDS will be analyzed including demographic information, clinical diagnoses, genetic information, seizure history, and developmental and disease progression milestones.
RESULTS: Initial data on 16 patients (1 to 22 years old) are consistent with previous reports. Most patients present with developmental delay, intellectual disability, and hypotonia. Neurological symptoms including stereotypy, autistic features, and seizures are common. There are significant delays in achieving motor milestones (ability to crawl, ability to pull to stand, ability to walk). Developmental regression is observed in some individuals. Respiratory infections and gastrointestinal problems contribute to disease burden. The presentation will include descriptive statistics of up to 50 individuals plus longitudinal analyses.
CONCLUSIONS: Preliminary results support the potential utility of real-world data to delineate features of MDS, understand patterns of progression and inform on clinical domains that may be sensitive to change in prospective studies.
KEYWORDS: Neurodevelopmental Disorders, Lifespan Manifestations of Childhood Onset Conditions

195. Cell type-specific gene expression and chromatin accessibility in dup15q syndrome

Mo A (Boston, MA), Dias C, Cai C, Sun L Cabral K, Brownstein C, Rockowitz S, Walsh C

OBJECTIVE: Duplication of 15q11.2-13.1 (dup15q syndrome) is a neurodevelopmental disorder that is strongly associated with autism spectrum disorder (ASD), intellectual disability, and epilepsy. However, the effect of this duplication on specific cell types in the human brain is unknown. Here, we examined cell type-specific effects of dup15q on

gene expression and chromatin accessibility in the human brain.
METHODS: We performed single cell RNA and multiomic (combined RNA and ATAC, an assay for chromatin accessibility) sequencing on postmortem human brains with dup15q (n=6), non-dup15q ASD (n=7), and neurotypical controls (n=7), followed by computational analysis.
RESULTS: Compared to non-dup15q ASD versus control brains and dup15q versus non-dup15q ASD brains, dup15q versus control comparisons showed the largest number of differentially expressed genes in both neurons and glia. As expected, gene expression within the duplicated region was increased in dup15q brains, but the degree of the upregulation was mediated by cellular identity and gene expression level. Neuronal cell types showed greater upregulation of gene expression in the dup15q region compared to astrocytes, microglia, and oligodendrocytes. We further identified peaks of chromatin accessibility in dup15q, non-dup15q ASD, and control brains. Thousands of peak regions showed different levels of chromatin accessibility in each condition and revealed unique patterns of gene regulation in dup15q compared to non-dup15q ASD.
CONCLUSIONS: We find evidence for marked cell type-specific effects of dup15q in the human brain and unique biological changes in dup15q syndrome compared to non-dup15q ASD. This study deepens our understanding of dup15q disorder and has implications for therapeutic development.
KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Behavioral Neurology

196. Retrospective case series of co-occurring functional neurological disorder (FND) and autism spectrum disorder (ASD)

Tao S Y (Austin, TX), Hartzell A, Elliott L, Freedman D Brumback A

OBJECTIVE: To analyze characteristics of patients with functional neurological disorder (FND) with co-occurring autism spectrum disorder (ASD) to understand if there is a link between diagnoses and outcomes.
METHODS: This is an IRB-approved retrospective case series of electronic health records from an FND clinic at an academic medical center. Data from 2020 to 2024 were utilized. Cases of FND with co-occurring ASD were selected based on referrals to the FND clinic.
RESULTS: We identified 15 patients diagnosed with FND who had co-occurring ASD. Ten had psychogenic nonepileptic events (PNEE), a subtype of FND, and 5 had functional movement disorders. Most patients were female (11) and white (11). The median age of diagnosis of ASD was 12 and FND 15 years old. Difference in median age from onset of FND symptoms to FND diagnosis was 2 years. Nine patients had been hospitalized for FND. The most common comorbid conditions were anxiety, depression, and ADHD. The most commonly prescribed class of medication was selective serotonin reuptake inhibitors (SSRIs). Fourteen patients reported history of life stressors, and 11 patients had a 504 plan or an Individualized Education Program at school.
CONCLUSIONS: This small, single-institution retrospective case series suggests that patients diagnosed with FND and ASD are commonly female and white with frequently reported life stressors and comorbid psychiatric conditions. Understanding co-occurring FND and ASD may lead to a deeper understanding of the neurobiology of these conditions and suggest treatments that could benefit this population.
KEYWORDS: Neurodevelopmental Disorders, Behavioral Neurology, Lifespan Manifestations of Childhood Onset Conditions

197. Predicting Neurodevelopmental Outcomes: Unveiling the Potential of Biomarkers in Infants Born to Mothers with Hypertensive Disorders of Pregnancy

Vythinathan C (Brooklyn, NY), Mantilla-Garcia M, Ghosh S, Hand I

OBJECTIVE: Hypertensive disorders of pregnancy (HDP) places newborns at risk for neurodevelopmental impairment (NDI) due to the potential impact of these disorders on fetal brain development. We sought to identify fetal and newborn biomarkers for the early prediction and detection of neurological impairments in infants born to mothers with hypertension.
METHODS: A systematic review was conducted using PubMed and EMBASE databases which were queried for scientific papers published after the year 1990. Methodology from Preferred Reporting Items for Systematic Reviews and Meta Analysis (PRISMA) was employed.
RESULTS: 855 articles were screened, of which four met inclusion criteria. Beuker et al., investigated the pulsatility index of the UA and middle cerebral artery ratio and found no difference in neurocognitive, behavioral problems or executive function. Delorme et al., linked absent or reversed end-diastolic flow on UA doppler with moderate to severe neuromotor and/or sensory disability. Kirsten et al., found no difference in motor and cognitive outcomes in infants who had absent end-diastolic UA doppler compared to normal dopplers at 24 and 48 months of age by. Bharadwaj et al., determined that cord blood protein carbonyl as oxidative marker levels were inversely related to motor developmental quotient.
CONCLUSIONS: The paucity of available literature highlights the need for evaluating potential biomarkers to enhance assessment of NDI that can offer additional prognostic information and identification of infants at elevated risk of long-term neurological morbidity. This would facilitate timely interventions to mitigate the impact of NDIs on their developmental trajectories.
KEYWORDS: Neurodevelopmental Disorders, Neonatal Neurology

198. Design and Rationale of the ATTUNE Study in Patients with MECP2 Duplication Syndrome

Coquery C M (Carlsbad, CA), Watanabe T, Norris D, Pehlivan D, Neul J, Marsh E, Chen C, Lewis S, Yarborough M, Mathews J, Yarlas A, Stanton S

OBJECTIVE: MECP2 Duplication Syndrome (MDS) is a rare X-linked disorder caused by overexpression of the

MECP2 gene. Cardinal symptoms include infantile hypotonia, progressive spasticity, developmental delay in childhood resulting in severe to profound intellectual disability, minimal or absent speech, recurrent respiratory infections, gastrointestinal symptoms, development of refractory seizures, and shortened lifespan. ION440 is a modified antisense drug that selectively targets MeCP2 pre-mRNA. In preclinical MDS models, lowering MeCP2 resulted in a reduction in seizures, improvement in motor and social skills, and normalization of an aberrant gene expression profile. This study aims to evaluate safety, tolerability, and pharmacokinetics of ION440 in MDS patients.

METHODS: ATTUNE is a Phase 1-2 study of ION440 in children and adults with MDS. ATTUNE comprises 2 parts. Part 1 is a 36-week sham-controlled (3: 1 [active/sham] randomization), double-blind multiple ascending dose evaluation of ION440. In Part 2, participants will receive open-label ION440 for up to 156 weeks. Multiple dose levels will be evaluated in two subcohorts, starting with older children, adolescents, and adults, followed by a cohort of younger children. An independent safety monitoring committee will provide recommendations for dose escalation and subcohort initiation. This design will allow for thorough evaluation of safety, tolerability, and pharmacokinetics. Exploratory measures of efficacy have also been included.

RESULTS: Study enrollment is anticipated to start in 2024.

CONCLUSIONS: The ATTUNE study will investigate safety and tolerability of ION440 in patients who have MDS, a disease for which there are currently no treatment options beyond symptom management.

KEYWORDS: Neurodevelopmental Disorders, Experimental Therapeutics, Epilepsy

199. Meeting the Challenge: Implementation of a Transition Clinic for Neurodevelopmental Disabilities

Elias R (Boston, MA), Chiujdea M, Frueh J S, Pillai R, Press D, Sanders J, Urion D

OBJECTIVE: Neurodevelopmental disabilities (NDDs) are associated with a variety of health issues throughout the lifespan, with a higher risk of poor health outcomes and premature mortality. Many neurologists feel that they did not receive enough training in caring for adults with NDDs. We aim to describe our process in building a resident teaching clinic geared specifically towards adults with NDDs.

METHODS: The adult NDD clinic was created within an adult neurology department at a tertiary academic center in 2018. The clinic was staffed by residents and attendings from pediatric and adult neurology. Starting in 2022, the clinic was included into the training curriculum as a required rotation for child and adult neurology residents. We retrospectively reviewed the charts of patients who were referred to the NDD clinic between 8/2018 and 4/2024.

RESULTS: A total of 95 people have been referred since the inception of the clinic. Since becoming part of the residency curriculum, 35 patients have been actively followed with a mean age of 30 years (range 20-61 years). 15 patients are waitlisted. The clinic is staffed by a pool of 10 child neurology residents being supervised by one adult cognitive neurology attending, and a pool of 8 adult neurology residents with one supervising child neurology attending.

CONCLUSIONS: Incorporating a residency rotation requirement for specialized clinics may offer a sustainable treatment option to adults with NDDs while increasing trainee exposure to this underserved population.

KEYWORDS: Neurodevelopmental Disorders, Education, Diversity, Equity, Inclusion

200. Impact of Social Determinants of Health on Development of Children with Down Syndrome

Totoiu M O (Orange, CA), Hom C, Allhusen V, Mapstone M, Do L, McIntyre C

OBJECTIVE: Assess the relation between residential location-based child opportunity, as measured by the Child Opportunity Index (COI), and verbal intelligence (KBIT-2 VIQ), cognitive function (RADD-2), and head circumference in children with Down Syndrome (DS).

METHODS: This prospective cohort study analyzed the relation between head circumference, cognitive development, and COI, adjusting for age and sex, in 50 children 6-17 years with DS, evaluated at a hospital between May 2022 - October 2023.

RESULTS: The median COI value was 71 distributed across categories (8% low, 28% moderate, 32% high, 32% very high). In 42 patients completing KBIT-2 testing, raw verbal IQ scores varied with COI and age, showing significant association starting at age 10 ($p=.004$). Scores were lower in lower COI neighborhoods (10.9 ± 4.1) compared to high (20.1 ± 4.9) and very high neighborhoods (22.9 ± 4.4). In 33 children able to complete the RADD-2, average total scores were significantly higher in high and very high COI neighborhoods across all ages. Non-verbal KBIT-2 and RADD-2 scores did not vary by COI. Head circumference varied with COI in females, where high COI areas correlated with larger circumference than lower and very high areas ($p<0.05$).

CONCLUSIONS: Even in a cohort with a known genetic cause for their intellectual disability, social determinants of health (SDH) are significantly related to development of verbal intelligence in DS. Consistent with literature, development of language skills and crystallized intelligence appear to be associated with home environment or quality of education. Based upon the relationship between COI and head circumference, females may be more affected by SDH than males.

KEYWORDS: Neurodevelopmental Disorders, Lifespan Manifestations of Childhood Onset Conditions, Diversity, Equity, Inclusion

201. The Natural History of NGLY1 Deficiency, a Rare Neurodevelopmental Disorder

Suter B (Houston, TX), Thompson J, Deck R, Dwight S, Landy H

OBJECTIVE: N-glycanase 1 (NGLY1) is a key enzyme in the degradation of misfolded glycosylated cytosolic proteins. Variants in the NGLY1 gene cause a rare neurodevelopmental

disorder with a core phenotype comprising severe global developmental delay/intellectual disability, hyperkinetic movement disorder, transient transaminase elevation, (hypo)alacrima and progressive sensorimotor polyneuropathy. Shortened life span has also been described. In the absence of functional NGLY1, there is an accumulation of aspartylglucosamine (GlcNAc-Asn, or GNA). As only 130 patients have been identified worldwide, natural history data are sparse. We present data on an observational study conducted in parallel with a recently initiated gene therapy study for NGLY1 deficiency (NCT0619953) to determine optimal clinical outcomes and biomarkers.

METHODS: This is a longitudinal observational study in NGLY1-deficient patients with assessments at Baseline and Months 6, 12 and 24. Each visit includes neurological and physical examination, ophthalmological assessment (including Schirmer test), plasma GNA levels and developmental assessments (BSID-4, Vineland-3, and WPPSI); additional assessments include GMFCS, GMFM-88, EEG, and nerve conduction studies.

RESULTS: Fifteen patients (9 females) aged 4-13 years from the USA, Canada, Mexico, England, and Brazil are enrolled. Data for all patients through Month 12 will be presented.

CONCLUSIONS: Natural history studies of rare genetic disorders provide information that assists with disease diagnosis, understanding of disease course and phenotypic spectrum, and planning of interventional studies. With this endeavor, we hope to gain a thorough understanding of NGLY1 deficiency to further inform the design of our ongoing and future gene therapy trials.

KEYWORDS: Neurodevelopmental Disorders, Neurogenetics

202. Improving Outcome Measures for Trials in Phelan-McDermid Syndrome (PMS): Development of PMS-Specific Clinician and Caregiver Impression-of-Change Measures

Berry-Kravis E (Chicago, IL), Valluripalli Soorya L, Kolevzon A, Thurm A, Glass L, Squires L, Jones N

OBJECTIVE: Phelan-McDermid syndrome (PMS) is a rare genetic condition associated with neurodevelopmental delay. Currently, no medications are approved to treat PMS, and no syndrome-specific outcome measures are available. We developed the PMS-specific Clinical Global Impression (PMS-CGI) of severity (PMS-CGI-S) and improvement (PMS-CGI-I) with anchors focused on characteristic PMS symptoms (expressive communication, receptive communication, gross motor skills, fine motor skills, social interaction, self-care, and cognition/learning) and a caregiver impression scale, the PMS Caregiver Impression of Change (PMS-CIC).

METHODS: The PMS-CGI and PMS-CIC were evaluated as clinical outcome assessments in an open-label trial of NNZ-2591 (an analog of an IGF-1 metabolite) in 18 children (aged 4–13 years) with PMS who were titrated to 12 mg/kg twice daily for up to 13 weeks.

RESULTS: Pre-treatment PMS symptom severity was moderately to markedly impaired (PMS-CGI-S mean and median 4.5; SD=0.99; range 3,6), with 100% consistency between PMS-CGI-S evaluations at Screening and Baseline. The PMS-CGI and the PMS-CIC were sensitive to treatment effects. There was statistically significant improvement (Wilcoxon Signed Rank test) on the PMS-CGI-I ($p<0.0001$; median 2.0; range 1,4; mean 2.4; SD 0.86) and the PMS-CIC ($p=0.0003$; median 3.0; range 1,5; mean 2.7; SD 1.02). There was also statistically significant improvement in overall symptom severity on the PMS-CGI-S ($p=0.0156$); 7 of 18 participants had a one-point improvement on the measure. Improvements in symptom areas were consistent across clinician and caregiver measures.

CONCLUSIONS: Both the PMS-CGI and PMS-CIC assessments show potential as useful measures of treatment effects on PMS-related symptoms, including those prioritized by caregivers, in intervention studies.

KEYWORDS: Neurodevelopmental Disorders, Experimental Therapeutics

203. A Whole Child Scorecard Approach to Comprehensive Autism Care

Gonzalez N J (San Diego, CA), Troxell R M, Hattangadi N, Aitken A, Newton E, Klusky J, Alosi S, Howe Y

OBJECTIVE: To develop and implement a clinical tool that tracks progress and measures outcomes in autistic children over course of treatment across 10 medical, developmental, behavioral, and family wellness domains.

METHODS: The Whole Child Scorecard (WCSC) is a novel scoring tool designed to track patient progress in 10 wellness domains: Genetic/Metabolic Etiology, Seizure, Sleep Disturbance, Gastrointestinal Symptoms, Mental Health, Medication management, Communication/Socialization, Behavior, Sensory/Motor, and Child and Family Wellness. Each domain is scored 4 through 0, for a total of 40, with decreasing scores indicating positive progress. The WCSC utilizes standardized assessment tools, quantifies goal treatment progress, and involves detailed record review. For this study, 17 autistic children receiving care in a multidisciplinary autism clinic were evaluated. We reviewed medical, developmental, behavioral records and family reported measures to determine baseline WCSC score at initial intake and then obtained a score at 6–11–months.

RESULTS: Improvements were seen in all domains at 6–11-months. The largest change was noted in the domains of Mental Health and Medication management where these domains saw a score decrease of 29% and 24%, respectively.

CONCLUSIONS: The Whole Child Scorecard is a novel approach to providing and tracking holistic autism care by allowing clinicians to assess clinical progress within and across wellness domains. By expanding upon standard assessment tools, this work addresses the need for high-quality, multidisciplinary treatment for autistic children.

KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Practice Parameters

204. Diverse Caregiver Perspectives on the Diagnostic Odyssey and Genetic Testing for Global Developmental Delay/Intellectual Disability: A Qualitative Study

Cole J (Aurora, CO), Killian E, Sellitto A D, Balls-Berry J, Gurnett C

OBJECTIVE: Genetic testing is recommended for all children with global developmental delay or intellectual disability (GDD/ID) without a readily-identifiable etiology, but there are many barriers to accessing it, contributing to the diagnostic odyssey. Prior qualitative studies investigating caregiver experiences and perspectives on genetic testing have been limited by inclusion of primarily White, highly-educated, high socioeconomic status participants. We aimed to understand experiences and perspectives of a more diverse group.
METHODS: Semi-structured qualitative interviews were conducted with 18 caregivers of children who were evaluated at pediatric neurology clinics at a single tertiary care institution in early 2023. Over half of participants (55.5%) identified with at least one historically underrepresented demographic (33.3% Black, 27.8% with high school or less education, 27.8% with high neighborhood-level area deprivation, and 11.1% rural). Both inductive and deductive thematic coding were used to perform content analysis. Content saturation was reached.
RESULTS: Six recurring themes emerged: the caregiver search for answers, advocacy, uncertainty, and empowerment; healthcare accessibility in a real-life context; financial strain and insurance coverage; trust and communication in healthcare; racial disparities and discrimination; and social support and community networks. Views on genetic testing were generally positive.
CONCLUSIONS: Lived experiences varied dramatically between caregivers, much related to social determinants of health including insurance type, job security/flexibility, rurality, family structure, and racism, but a significant degree related to provider/organizational barriers and facilitators. We identified caregiver-informed targets to improve the quality and equity of care for GDD/ID including insurance coverage, diagnostic efficiency, resource availability and awareness, healthcare navigation, and cultural humility.
KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Diversity, Equity, Inclusion

205. Perinatal Strokes Associated with Autism Spectrum Disorder Preferentially Impact Distinct Brain Networks Compared to Non-Autistic Peers

Sheikhi N (Boston, MA), Steeby C, Tripathy S, Miller G, Wu C, Lehman L, Cohen A

OBJECTIVE: Recent research from our institution suggests that children with venous versus arterial perinatal stroke are three times more likely to develop autism spectrum disorder (ASD). Here, we analyze the same patient cohort to identify whether this finding is explained by differences in affected brain networks.
METHODS: Children with perinatal stroke were identified from a retrospective registry with ($n = 20$) and without ($n = 20$) a confirmed diagnosis of ASD. These two groups were matched on sex, stroke subtype (arterial or venous), and lesion size. Lesions were segmented using the DeepNeuro software tool, then manually corrected before registration. Brain regions functionally connected to each patient's lesion were computed and functional connectivity (FC) maps were compared between ASD patients and matched controls.
RESULTS: 80% of ASD patients, compared to 65% of non-ASD patients, had lesions with positive lesion-connectivity to the midline cerebellum. 75% of controls demonstrated negative FC to the left temporal lobe, while over half of ASD patients demonstrated positive FC to the same location. Statistical comparison, controlling for stroke subtype and lesion size, found that lesions in ASD patients had distinct connectivity to the midline cerebellum, left temporal lobe, midline ventromedial prefrontal cortex, and right dorsolateral prefrontal cortex.
CONCLUSIONS: Our findings suggest that the observation that children with venous perinatal strokes are more likely to develop autism is driven by distinct and biologically meaningful differences in affected brain networks, particularly involving the cerebellum and left temporal lobe. These findings suggest a specific neuroanatomical substrate injury underlying the development of ASD.
KEYWORDS: Neurodevelopmental Disorders, Stroke, Neuroimaging

206. The Psychosocial Impact of Tourette Syndrome and Chronic Tic Disorder in Children and Adolescents

Arkalgud A (Memphis, TN), Jack J, Beard G, Ridley-Pryor T

OBJECTIVE: This study aims to examine the psychosocial impact of symptoms experienced in pediatric chronic tic disorder (CTD) and TS to optimize care.
METHODS: A single-center, retrospective chart review was conducted for 30 patients, diagnosed with CTD or TS, aged 5-18, referred for comprehensive behavioral intervention for tics (CBIT).
RESULTS: Tic severity reported by the Parent Tic Questionnaire (PTQ) was lower than the Yale Global Tic Severity Score (YGTSS). Over half of the patient sample reported having impaired sleep. Those with impaired sleep had more instances of depression and ADHD diagnoses. 23% of patients reported instances of Suicidal Ideation (SI) or Self Harm (SH). Mean age at evaluation was 12.7.
CONCLUSIONS: Patients with TS or CTD are thought to have greater support needs than patients without TS or CTD but were only granted school accommodations based on parent advocacy, though parents often underreport symptoms. Adolescents were more likely to report instances of SI and SH. This finding indicates the significance of incorporating psychoeducation, CBIT and other behavioral interventions, given the risk of co-occurring conditions.
KEYWORDS: Neurodevelopmental Disorders, Behavioral Neurology, Movement Disorders

207. Pathophysiology and Mitigation of Lumbar Radiculopathy in Patients Receiving GTX-102, an Investigational Antisense Oligonucleotide for the Treatment of Angelman Syndrome

Brandabur M (Novato, CA), Goodspeed K, Aquino P, Chen A, Myers K, Berry-Kravis E, Nouri M N, Sell E, Olugemo K

OBJECTIVE: Explore pathophysiology and risk mitigation strategies for lumbar radiculopathy events.
METHODS: Angelman syndrome (AS) is a rare neurodevelopmental disorder characterized by seizures, sleep

disorders, and severe impairment of speech, cognition, and motor function. GTX-102 is an intrathecally administered antisense oligonucleotide designed to target the UBE3A antisense transcript to inhibit silencing of the paternally inherited UBE3A allele in AS.

All 5 participants in cohorts 1-3 receiving high GTX-102 loading doses experienced serious adverse events (SAEs) of reversible leg weakness diagnosed as radiculopathy. Spine MRI predominantly showed enhancement restricted to the nerves and leptomeninges of the cauda equina. Cerebrospinal fluid (CSF) protein was elevated without pleocytosis. An exploration of inflammatory CSF markers using Olink® proteomic profiling and Quanterix SIMOA® technology was undertaken. CSF proteomic profiling showed elevated TNFα, IL-6, IL-8, CD244, CD5, and CD6; no autoantibodies to circulating nerve components were detected.

Mitigation measures were implemented to facilitate resumption of GTX-102 dosing, including use of lower GTX-102 doses, premedication with dexamethasone, aCSF flush immediately after GTX-102 administration, and post-flush Trendelenburg positioning.

RESULTS: Mitigation measures significantly reduced the incidence of radiculopathy from 100% (5/5) in the original high-dose cohorts to 4% (3/69) in lower-dose cohorts. All participants with prior radiculopathy safely redosed and continue to receive GTX-102 following recovery from the SAE or have recovered and are expected to redose.

CONCLUSIONS: Results show localized contact injury proximal to the injection site and increase our understanding of the local inflammatory profile associated with radiculopathy. Mitigation strategies substantially decreased the incidence of reversible lumbar radiculopathy.

KEYWORDS: Neurodevelopmental Disorders, Global Neurology, Behavioral Neurology

208. Beyond the Diagnosis: Evaluation of Quality-of-Life Measures in representing the clinical characteristics of SLC6A1-Related Neurodevelopmental Disorder

Kalvakuntla S R (Dallas, TX), Dahshi H, Goodspeed K, Armstrong D, Lee M

OBJECTIVE: SLC6A1 Neurodevelopmental Disorder (SLC6A1-NDD) is among the top genes within epileptic and autism spectrum disorder genetic databases. There is no established quality of life (QOL) measure that captures the impact of SLC6A1-NDD on patients and caregivers. This study investigates how clinical characteristics of SLC6A1-NDD correlate with QOL scores.

METHODS: We conducted univariable comparisons (n=52) of the Quality-of-Life Inventory-Disability (QI Disability), Quality of Life of Childhood Epilepsy (QOLCE, ages 5-18-years), and Pediatric Quality of Life Inventory Family Impact (PedsQL) with 45 clinical characteristics of SLC6A1-NDD. Given the non-normal score distributions of our sample, Spearman's Rank Order correlation coefficient and Wilcoxon rank-sum test were utilized.

RESULTS: The mean total scores were 73±12.3 (QI-Disability), 49±17.1 (QOLCE-55), and 51±17.6 (PedsQL). Lower QOLCE-55 total scores were associated with developmental and language regression, absence seizures, clinical severity, coordination difficulties, and male gender ($P < 0.039$). Autism severity was significantly associated with lower total scores on all three QOL measures ($P < 0.025$; $\rho = -0.473$ to -0.681).

CONCLUSIONS: Of the three measures utilized, QOLCE-55 had the largest representation of statistically significant clinical features driving subdomain and total scores. Autism severity was a driver of lower QOL in all three measures. While this could be suggestive of the utility of QOLCE-55 in capturing SLC6A1-NDD QoL, subdomain scores of all three measures captured various clinical features that were not represented in total scores. Future studies should utilize these measures in larger cohorts of patients while controlling for potential confounds to further explore these findings.

KEYWORDS: Neurodevelopmental Disorders, Epilepsy

NEUROGENETICS

209. Acute choreoathetosis, Multisystem Inflammatory Syndrome in Children (MIS-C), and malate dehydrogenase 2 deficiency (MDH2D)

Saringkarisate K (Baltimore, MD), Umland J I, Bégué R E, Abe K, Seaver L, Purohit P

OBJECTIVE: Increase consideration of genetic/metabolic testing in patients presenting with acute neurological symptoms in the setting of infectious illness.

METHODS: Case report of a 3-year-old male with history of speech delay who was admitted with fever and acute choreoathetosis.

RESULTS: He developed cardiogenic shock and respiratory failure requiring mechanical ventilation. He was diagnosed with MIS-C based on coronary artery dilatation, elevated inflammatory markers, shock, thrombocytopenia, and positive SARS-CoV-2 spike antibody. He was started on intravenous methylprednisolone, immunoglobulin, and anakinra. Despite overall improvement, his choreoathetosis returned after weaning sedation. Further work up included a repeat MRI of the brain showed new symmetric increased T2 signal and restricted diffusion in the globi pallidi. Metabolic screening tests were unremarkable. He was discharged with persistent but improved choreoathetosis.

He was readmitted after two months with respiratory failure from human metapneumovirus infection. He died from refractory cardiogenic shock and multiple organ failure. Exome sequencing posthumously identified a homozygous variant of uncertain significance in MDH2. Symptoms associated with MDH2 deficiency (MDH2D) include ataxia, global developmental delay, hypotonia, areflexia, movement disorder, and encephalopathy. Given his presentation, a diagnosis of MDH2D was suspected.

CONCLUSIONS: Choreoathetosis has been reported in acute COVID-19 infection but not MIS-C. MDH2D is associated with movement disorder and cardiomyopathy. It is possible that our patient was eventually going to develop

these manifestations, and MIS-C triggered it sooner. A genetic/metabolic etiology should be considered in patients with acute neurological symptoms and symmetric basal ganglia lesions on MRI, especially with a history of developmental delays.

KEYWORDS: Neurogenetics, Movement Disorders, Neurocritical Care

210. An antisense oligonucleotide that rescues in vitro and in vivo phenotypes of Timothy syndrome

Levy R J (Palo Alto, CA), Chen X, Birey F, Li M-Y, Revah O, Thete M, Reis N, Kaganovsky K, Onesto M, Sakai N, Hudacova Z, Hao J, Meng X, Huguenard J, Pasca S

OBJECTIVE: Timothy syndrome type 1 (TS1) is characterized by long QT syndrome, autism, epilepsy, and other neuropsychiatric disorders. TS1 is caused by one gain-of-function pathogenic variant in CACNA1C exon 8A, as opposed to the alternately spliced exon 8. We previously discovered that TS1 patient-derived neurons in 3D neural organoid cultures have delayed channel inactivation, prolonged calcium rise, impaired interneuron migration, and persistent expression of exon 8A. Our objective was to determine whether switching CACNA1C utilization from exon 8A to 8 represents a therapeutic strategy.

METHODS: We used human induced pluripotent stem cell-derived 3D neural organoids, assembloids, and transplantation of organoids into rodents to develop a potential TS1 treatment employing antisense oligonucleotides (ASO) to effectively decrease exon 8A splicing.

RESULTS: We discovered that ASOs that effect a switch from exon 8A to exon 8 rescued defects in channel inactivation and calcium rise in TS1 patient-derived neural organoids. Additionally, ASO effectively rescued interneuron migration in TS1 patient-derived forebrain assembloids. There is no animal model accurately recapitulating the TS1 variant. Leveraging our transplantation platform to integrate human neurons into rat neural circuits, we found that intrathecal ASO rescued calcium defects in TS1 patient-derived cortical neurons in vivo.

CONCLUSIONS: These results suggest that reducing CACNA1C exon 8A expression could be a possible treatment for TS1 neurologic and neurodevelopmental symptoms. Moreover, these experiments illustrate how a multi-level stem cell model approach can used to identify strategies to reverse neural pathophysiology in vitro and in vivo for neurogenetic disorders.

KEYWORDS: Neurogenetics, Experimental Therapeutics, Neurodevelopmental Disorders

211. Pediatric Genetic Ataxias: A Case Series from a Single Center Neurogenetics Clinic

D'Souza D (Washington, DC), Bouska C, Turner A, Wright S, Zea Vera A, Sen K

OBJECTIVE: Pediatric ataxias are genetically heterogeneous conditions. We aim to describe patients presenting to our neurogenetics clinic with ataxia as a primary symptom and a subsequently confirmed genetic etiology.

METHODS: All patients were seen by a pediatric movement disorder specialist, dual-boarded neurogeneticist, and certified genetic counselor. Data was collected by retrospective chart review.

RESULTS: We identified 5 patients with genetic etiologies: CACNA1A (15yo M), SCN2A (2yo F), ACBD6 (11yo M), and FRDA (6yo M, 15yo F). The CACNA1A patient had episodic cerebellar ataxia and slowly progressive ataxia. The SCN2A patient had episodic cerebellar ataxia, epilepsy, encephalopathy, and motor regression. The ACBD6 patient had static cerebellar ataxia, intellectual disability, and dystonia. The patients with FRDA had progressive cerebellar and sensory ataxia without exacerbations. The SCN2A patient had DWI changes on brain MRI during acute episodes. MRI was unavailable in one patient (ABCD6) and normal in the rest.

The median time from symptom onset to diagnosis was 3 (range: 1-13) years. Four patients were initially misdiagnosed with: a functional neurological disorder (CACNA1A), a potential mitochondrial disorder (SCN2A), birth-related ataxic cerebral palsy (ACBD6), and a primary orthopedic problem (FRDA). Genetic diagnosis resulted in management changes: initiation of disease-specific medication (CACNA1A, FRDA), family testing (CACNA1A), disease-specific surveillance (SCN2A), and clinical trial participation (FRDA).

CONCLUSIONS: Pediatric genetic ataxias are often misdiagnosed and the time to diagnosis is long. Frederich's ataxia, caused by FRDA trinucleotide repeats, is a common cause and can be missed in genetic panels and whole exome sequencing. A step-wise approach to genetic testing is critical.

KEYWORDS: Neurogenetics, Movement Disorders

212. Atad1 Gene Rescue of Zellweger Spectrum Disorders via Targeting of Shared Common Mechanism

Bonkowsky J (Salt Lake City, UT), Stevenson T J, Chang P, Baronio D, Nuebel E, Bradbury A, Pyne N

OBJECTIVE: Zellweger Spectrum Disorders (ZSDs) are caused by mutations in PEX genes. ZSDs present with severe clinical features, including seizures, leukodystrophy, hepatomegaly, and early death. There are no curative treatments for ZSDs. Development of gene therapies for ZSDs is limited by the size of the PEX genes which exceed AAV payload; and since each of the 14 PEX genes would require a lengthy gene therapy development process. Our goal was to test a novel approach through targeting of a shared mechanism common to ZSDs. We had shown that ATAD1, a mitochondrial chaperone AAA+ ATPase, could restore PEX3 phenotypes in a cell line. Use of ATAD1's small size (~1kb) allows it to package efficiently in AAVs; and ATAD1 could potentially rescue multiple different ZSDs.

METHODS: We characterized ATAD1 rescue in PEX1 patient fibroblasts. We tested AAV9-mediated gene therapy in PEX1 mouse model (G844D mutation) with P1 delivery. Genes (GFP, ATAD1, or PEX1) were subcloned into AAV9. We used the EFS (shortened EF1-a) or CAG promoter.

RESULTS: In PEX1 fibroblasts, we found that ATAD1 expression improved mitochondrial function; normalized

expression of VLCFAs; improved plasmalogen synthesis; and improved peroxin mislocalization.
In mice, the AAV9-CAG-GFP construct resulted in high expression levels throughout the neuroaxis wherease the EFS construct was significantly lower.
CONCLUSIONS: Our results suggest that ATAD1 gene therapy has potential to rescue mitochondrial and peroxisomal dysfunction in PEX1, PEX3, and potentially other ZSDs. We are currently engaged in experiments to test gene therapy rescue in mice with ATAD1.
KEYWORDS: Neurogenetics

213. Effect of bevacizumab on brain MRI and disease course in children with Coats plus syndrome

Sharayah S (St. Louis, MO), Arroyo M, Mange U, Mar S

OBJECTIVE: Cerebral microangiopathy with calcifications and cysts (CRMCC), also known as Coats plus syndrome (CPS), is a rare neurodegenerative disorder caused by autosomal recessive mutations in the CTC1 gene. There is currently no established treatment for this condition, which affects multiple organs, including the central nervous system. Bevacizumab, a vascular endothelial growth factor inhibitor, has been successfully used to varying degrees in the treatment of two disorders that share similar pathologies with a more limited distribution: Coats disease and Labrune syndrome. In this case series, we report three pediatric cases of CPS and their response to Bevacizumab.
METHODS: Institutional review board approval was obtained to retrospectively review cases of CPS cases who were treated with Bevacizumab at 2 different institutions.
RESULTS: We identified three pediatric cases of CPS featuring CTC1 gene mutations, all of which were treated with Bevacizumab. The patients were male, and treatment commenced at ages 2, 4, and 15 years, respectively. Two patients showed improvement in leukoencephalopathy on magnetic resonance imaging (MRI) after 4-6 months of treatment, while the third exhibited a reduction in cyst size and stable leukoencephalopathy. Intravenous Bevacizumab also contributed to stabilizing retinal disease progression in two patients and halting gastrointestinal bleeding in another patient.
CONCLUSIONS: CPS currently has no effective treatment. However, Bevacizumab shows promise in stabilizing disease progression across various organs, such as the retina, brain, and gastrointestinal tract. Longer-term follow-up and larger-scale studies are essential to establish the optimal dosing schedule, assess tolerability, and determine the efficacy of Bevacizumab in mitigating neurological decline.
KEYWORDS: Neurogenetics, Lifespan Manifestations of Childhood Onset Conditions

214. Familial Occurrence of Alternating Hemiplegia of Childhood: Novel Observations and Unique Genotype-Phenotype Correlations

Al-Yahia M (Tampa, FL), Prange L, Mikati M

OBJECTIVE: Characterize the genotype and phenotype manifestations of familial Alternating Hemiplegia of Childhood (AHC) patients seen in our referral center.
METHODS: Interrogation and analysis of the database and charts of the patients with two or more cases in one family who fulfilled the strict diagnostic criteria of AHC. All had comprehensive clinical and genetic workups including whole exome sequencing (WES).
RESULTS: Family #1: Daughter with ATP1A3 E815K mutation with a typical severe AHC phenotype. Mother with the same mutation and a mild AHC phenotype misdiagnosed til her thirties as epilepsy. Family #2: 3 siblings with severe AHC phenotype (one from a different father) each with ATP1A3 G89D which was not present on WES of the asymptomatic mother. Family # 3: A son with typical AHC and ATP1A2 c.1017+5G>A, IVS8+5G>A. Father with the same variant with hemiplegic migraine. The other three families had negative WES despite manifesting AHC phenotypes. Family #4: Two sisters with AHC, mother with hemiplegic migraine. Families #5 and #6: Each with two AHC male siblings (in family #5 mother has hemiplegic migraine).
CONCLUSIONS: We demonstrated: 1) ATP1A3 E815K mutation manifesting as familial AHC with mild manifestations in a parent (both novel findings). 2) Severe familial AHC occurrence in siblings with asymptomatic parents likely due to gonadal mosaicism in the mother. 3) Discrepant manifestations of an ATP1A2 mutation with AHC in child and hemiplegic migraine in father. 4) Negative WES in 3 families of which 2 mothers had hemiplegic migraine.
KEYWORDS: Neurogenetics, Epilepsy, Headache

215. Biallelic Variants in LIPT2 as a Cause of Infantile-Onset Dystonia: Understanding an Ultra-Rare Disorder using Lipoylation pathway in Yeast

Sen K S (Washington, DC), Zea Vera A, Gropman A G, Ganetzky R G, Wongkittichote P W, Puronurmi A P Autio K A, Kastaniotis A K

OBJECTIVE: Lipoyl transferase 2 is involved in biosynthesis of the lipoate. Lipoate is the cofactor for the glycine cleavage system and four dehydrogenase enzymes. Biallelic variants in LIPT2 cuasing severe neonatal encephalopathy was first described in 2017.
METHODS: Clinical data was collected by retrospective chart review after obtaining consent from parents. The pathogenicity of these variants was further delineated using a yeast model. The YEp352-LIPT2 plasmid was used as a template to generate the two patient variants using QuickChange Lightning Site-Directed Mutagenesis Kit.
RESULTS: Patient was an 11-month-old female who presented at 1 month with dystonia, developmental delay and feeding difficulties. MR Brain showed cortical malformations including colpocephaly, polymicrogyria and heterotopia. Patient had elevations in lactate (6.1 mmol/L) and glycine. Exome sequencing showed 2 variants of uncertain significance in trans in the LIPT2 gene: c.346 G>T and c.418C>T. Patient was started on lipoic acid, thiamine and COQ10. Yeast complementation experiments indicate that both patient mutation variants result in diminished function versions of the LIPT2 protein.
CONCLUSIONS: We report the fourth case of LIPT2-related disorder. Proband shared significant overlap

with previous patients, however had a distinct movement disorder and brain malformations which have not been previously described. Unlike most neurometabolic disorders where dystonia develops later after metabolic stroke in basal ganglia, LIPT2- related disorder seems unique due to early onset of dystonia due to energy deficit in the developing brain. Lipoic acid supplementation has not led to significant clinical improvement. Analyses in yeast indicate that novel variants are deleterious but have retained some functionality.

KEYWORDS: Neurogenetics, Neurometabolic, Movement Disorders

216. Unsupervised Clustering of Neuroanatomical Disease Progression in Untreated Adrenoleukodystrophy

Mallack E J (Baltimore, MD), Raymond G V, Goodman J, Fatemi A, Turk B

OBJECTIVE: Quantify the natural history of prelesional and untreated, early- to late-stage cerebral adrenoleukodystrophy (CALD) on MRI using unsupervised clustering.

METHODS: We performed hierarchical single-linkage clustering of disease progression across discrete neuroanatomical structures in 224 patients with prelesional and untreated early- to late-stage CALD. Patient age and patient-specific affected neuroanatomical structures as defined by the Loes Scoring (LS) system at first MRI were analyzed and visualized. The analysis was repeated on the same variables in the same patients at most recent MRI with clustering constrained by the neuroanatomical sorting at diagnosis.

RESULTS: The median LS at first MRI was 0.5 (IQR 0 – 10) which progressed to a LS of 2.0 (IQR 0 – 11.5) at last follow up MRI over a 2.0-year interval (IQR 1.7 – 2.4y). At baseline, the highest signal density occurred in splenium of corpus callosum, parietooccipital white matter, optic radiations, and lateral geniculate body. In patients 5 – 10yo, disease progressed significantly to include the auditory pathways, corticospinal tracts, subcortical parietooccipital white matter, Meyers loop, periventricular anterior temporal white matter, frontal white matter, and genu of corpus callosum.

CONCLUSIONS: Consistent with prior studies, we highlight age-related neuroanatomical susceptibility of disease progression in younger boys. Additionally, we demonstrate that younger patients may have multiple affected brain structures in addition to the classically reported predominance of splenial and parietooccipital disease progression.

KEYWORDS: Neurogenetics, Neuroimaging, Pediatric Demyelinating Disease

217. Pathogenic variants in genes associated with speech/cognitive delay and seizures show expression biases in excitatory neurons and microglia in developing human cortex

Russ J B (Durham, NC), Stone A C, Maney K, Morris L, Wright C, Hurst J, Cohen J

OBJECTIVE: Up to one third of neurodevelopmental disorders (NDDs) are attributable to single-gene pathogenic variants. However, we have little understanding of how variants contribute to neuronal pathophysiology. We therefore integrated phenotypic information from subjects with monogenic diagnoses with single-nucleus RNA-sequencing (snRNAseq) data from human cortex across developmental stages to investigate cell-specific biases in gene expression associated with distinct neurodevelopmental phenotypes.

METHODS: Phenotypic information was gathered from: 1) a single-institution cohort of 84 neonates with pathogenic single-gene variants, and 2) a cohort of 4,238 patients with pathogenic single-gene variants enrolled in the Deciphering Developmental Disorders (DDD) study. Variants were grouped by phenotype and their expression across cortical cell subtypes was compared within snRNAseq datasets from 86 human cortex samples spanning from 2nd trimester to adulthood.

RESULTS: Pathogenic variants associated with speech/cognitive delay or seizures involved genes that are more highly expressed in excitatory neurons or in microglia than variants associated with other NDDs. Variants enriched in excitatory neurons and associated with speech/cognitive delay without seizures tended to involve calcium regulatory pathways and showed greater corticothalamic expression, while those with seizures tended to involve synaptic regulatory machinery and less corticothalamic bias.

CONCLUSIONS: By combining phenotypic data from patients with single gene-related NDDs with human cortical snRNAseq datasets across developmental stages, we identified cell-specific expression biases for genes in which pathogenic variants cause speech/cognitive delay and seizures. The involvement of genes with enriched expression in excitatory neurons or microglia highlights the unique role both cell types play in sculpting the developing brain and potentially mediating neurodevelopmental symptoms.

KEYWORDS: Neurogenetics, Neonatal Neurology, Fetal Neurology

218. Age-related differences in the presentation of COL4A1/2-related disorders

Porcari G S (Philadelphia, PA), Rashid R N, Mulvihill C A, Beslow L, Dubbs H, Schindewolf E, Gebb J, Agarwal S, Whitehead M, Cristancho A

OBJECTIVE: COL4A1/2-related disorders have heterogeneous presentations across the lifespan. Here, we describe the spectrum of pediatric phenotypes.

METHODS: Patients evaluated at a single center with confirmed pathogenic variants and variants of uncertain significance in COL4A1 or COL4A2 with consistent clinical presentation were included. Patients were stratified by age at first sign or symptom into perinatal (prenatal-28 days), early childhood (>28 days-4 years), and late childhood/adolescence presentations (>4-18 years).

RESULTS: Thirty-one patients were included (25 with COL4A1 variants, 5 with COL4A2 variants, one with variants in both). Perinatal and early childhood COL4A1 cases (n=13, median age 0 years, IQR 0-0; n=6, median age 0.3 years, IQR 0.3-0.4) presented with moderate-severe developmental delays (12/13, 5/5) and epilepsy (6/13, 2/5). Late childhood presentations (n=7, median age 8.2 years,

IQR 5-11) featured mild delays (4/7) and migraines (2/7). Perinatal presentations of COL4A2 (n=2, median age 0 years, IQR 0-0) included moderate delays (2/2), and seizures (1/2). Early and late childhood presentations (n=2, median age 1.4 years, IQR 0.2-2.7; n=1, 16 years) featured mild delays (2/3), migraines (2/3), and epilepsy (1/3). Periventricular hemorrhagic infarction and brain malformations were frequent in perinatal/early childhood presentations (15/22, 5/22), while leukoencephalopathy was common in late childhood presentations (5/8).

CONCLUSIONS: The pediatric phenotype of COL4A1/2-related disorder varies by age at clinical presentation. Perinatal and early childhood presentations (<4 years) have a prominent neurologic phenotype with severe developmental delays and epilepsy with early brain injury sequelae on imaging. Late childhood presentations (>4 years) have a milder phenotype with leukoencephalopathy on imaging.

KEYWORDS: Neurogenetics, Stroke, Neuroimaging

219. Broadening the Clinical Spectrum Related to PACS2 Mutations: A Case Series.

Frueh J S (Basel, Switzerland), Czarnecka S, Szczaluba K, Aykanat A, Henzi B, Datta A, Buerki S, Olson H

OBJECTIVE: We aimed to further define the phenotypic spectrum of missense variant(s) in phosphofurin acidic cluster sorting protein 2 (PACS2). A recurrent missense variant p.E209K was first described in 2018 in association with early-onset seizures, developmental delays, cerebellar hypoplasia, facial dysmorphisms, and other malformations. Deletions are also reported.

METHODS: For this case series, data were obtained through retrospective chart review of patients with known PACS2 pathogenic or likely pathogenic variants.

RESULTS: Fifteen patients with pathogenic missense variants in the PACS2 gene were identified: Fourteen with the previously described recurrent variant c.625G>A (p.E209K), one with the same amino acid substitution but two amino acids away (c631.G>A). Mean age was 4.5 years (range 13m - 10y). Seizure onset occurred between day of life one and age 4 months. Age at last seizure ranged from 4m to 5y10m. Four patients had status epilepticus. Brain imaging showed cerebellar malformations in 8 patients. Developmental delays were present in 11 patients, 7 of whom had autism spectrum disorder. Most notably, four patients showed typical development at ages 13m, 21m, 27m and 3y6m respectively. Three patients with chromosomal deletions including PACS2 were also identified (ages 15m, 28m, and 8y). All three had refractory epilepsy and a range of developmental disabilities.

CONCLUSIONS: Patients with PACS2 recurrent missense variant c.625G>A (p.E209K) present with epilepsy and developmental delays of variable severity. Mild phenotypic presentation including normal development is seen in a subset, and seizures resolve in most by 5 years as previously reported. Deletions can be associated with refractory epilepsy.

KEYWORDS: Neurogenetics, Epilepsy, Neurodevelopmental Disorders

220. A Novel MT-TW Gene Mutation Associated with Suspected Pyridoxine-Responsive Epilepsy

Elaasar H (New Orleans, LA), Tuttrup G, Pence K

OBJECTIVE: To describe a rare mitochondrial mutation with a potential pyridoxine-responsive epilepsy phenotype.

METHODS: A 37 weeks gestational age male with a with a history of intrauterine growth retardation was born via vaginal delivery complicated by an umbilical cord knot. APGARS were 9 and 9 at birth. The patient was hypoglycemic after delivery with anemia, metabolic acidosis, elevated lactate, and cholestatic jaundice. On day of life eight, the neonate developed seizures. Electroencephalogram (EEG) demonstrated severe background discontinuity and asynchrony with numerous electrographic seizures arising from the left temporal region with localized spread and bisynchrony. Seizures continued despite multiple anti-seizure medications. Pyridoxine challenge was administered on day of life eleven with cessation of seizures on subsequent EEG.

RESULTS: MRI revealed diffusion restriction of the bilateral corticospinal tracts and posterior limb of the internal capsule. Subsequent MRI showed diffusion restriction of perirolandic subcortical and deep white matter. Whole exome sequencing revealed a homoplasmic, likely pathogenic, rare variant in MT-TW m.5559 A>G.

CONCLUSIONS: This mutation has previously been found in four patients with Leigh's syndrome, three siblings with symptoms including developmental delay with regression, lactic acidosis, and failure to thrive, with multiorgan dysfunction including hypertrophic cardiomyopathy, hepatosplenomegaly, cholestatic hepatitis, and seizures.The fourth patient exhibited psychomotor delay, vomiting, and lactic acidosis. This case report demonstrates that a pyridoxine response is not limited to patients with pyridoxine deficiency, which may also present with profound hypoglycemia and lactic acidosis. It additionally points to a possible pyridoxine-responsive component of epilepsy related to this mitochondrial mutation that has not been previously described.

KEYWORDS: Neurogenetics, Epilepsy, Neonatal Neurology

221. Biallelic variants in BCS1L cause a novel neuromuscular phenotype with motor neuronopathy

Orbach R (Bethesda, MD), Maio N, Donkervoort S, Foley A, Chao K, Lehky T, Silverstein S, Potticary A, Rouault T, Butterfield R, Bönnemann C

OBJECTIVE: To define a novel phenotype and the biochemical consequences of BCS1L-related disorder.

METHODS: Deep phenotyping, research-based whole genome sequencing, and studies in patient-derived fibroblasts and cells were applied to characterize and identify the underlying genetic cause in siblings with undiagnosed complex neurologic condition.

RESULTS: The index case is a 13-year-old boy who presented at age 16 months with progressive motor difficulties. He gradually developed hand dystonia, dysarthric speech, muscle weakness, and scoliosis. The older sibling, a 16-year-old male, was diagnosed in early childhood with depression,

anxiety, and ADHD. His motor difficulties emerged later in childhood. Both siblings have learning disabilities, lifelong difficulty gaining weight, and report significantly low stamina. Their physical examinations were notable for mild proximal and moderate-severe distal muscle weakness; muscle ultrasound and electrodiagnostic studies confirmed a predominantly motor neuropathy/neuronopathy. We identified in both a paternally inherited missense variant (c.838C>T; L280F) and a maternally inherited 5' UTR variant (c.-122G>T) in BCS1L. Biochemical characterization of fibroblasts from the patients compared to control showed decreased BCS1L levels, decreased respiratory complexes I and III, and reduced basal oxygen consumption rates and respiratory spare capacity. Characterization of the homozygous L280F variant in cells was equivalent to the homozygous S78G variant causing the classic GRACILE syndrome. Thus, the milder phenotype is likely the result of the compound heterozygous state with the 5' UTR variant.

CONCLUSIONS: This study expands the clinical spectrum of BSC1L-related disorders to now include a milder phenotype with CNS and PNS involvement and combines genetic and biochemical characterization of the disease pathomechanism.

KEYWORDS: Neurogenetics, Neuromuscular, Neurometabolic

222. A rare case of LAMA1-related Poretti-Boltshauser syndrome involving supratentorial brain abnormalities

Beriwal N (Chicago, IL), Yano S

OBJECTIVE: We report a 12-year-old patient with ultra-rare Poretti-Boltshauser syndrome (PBS) due to compound heterozygous pathogenic variants in LAMA1.

METHODS: An undiagnosed proband was evaluated in neurogenetics clinic. Consent from the family was obtained for a case report.

RESULTS: We evaluated a 12-year-old female with learning disability, multiple vision impairments (cortical visual loss, bilateral optic atrophy, and high myopia), staring spells with previous diagnosis of epilepsy (now off anticonvulsants), and motor hand tics. She had a prior working diagnosis of congenital muscular dystrophy due to cerebellar abnormalities and developmental delay in infancy, but no known genetic cause.

Duo exome sequencing of the patient with mother's sample showed three heterozygous pathogenic variants, two associated with LAMA1-related PBS and one with TTR-related amyloidosis. One LAMA1 variant, c.8192C>A, p.(S2731*), was maternally inherited while the other, c.7050+1G>A, p.?, was not, suggesting occurrence in trans although paternal sample was unavailable. Brain MRI showed inferior vermian hypoplasia, dysplastic cerebellar hemispheres with cerebellar cyst, and scattered supratentorial white matter lesions, which together with her LAMA1 variants were diagnostic for PBS.

CONCLUSIONS: PBS syndrome is an ultra-rare disorder, reported in approximately 40 patients to date, which explains our patient's neurological and ocular findings. PBS is inherited in an autosomal recessive fashion with loss-of-function in LAMA1.The supratentorial brain abnormalities in our patient contribute to the known phenotypic spectrum: they are not common in PBS but have been reported in a few patients. This case highlights the genetic differential diagnosis of syndromic intellectual disability involving vision and cerebellar abnormalities.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders, Neuroimaging

223. Characterization of Progressive Neuroimaging Changes in Canavan Disease

Nagy A (Boston, MA), DeLa Rosa Abreu L, Maciel S, Peregoy C, Martinez-Lage Alvarez M, Bredow J, Bley A, Rapalino O, Eichler F

OBJECTIVE: Canavan Disease (CD) is a devastating leukodystrophy characterized widespread CNS demyelination. This study aims to characterize the spatiotemporal progression of neuroimaging changes in patients with CD.

METHODS: All patients with CD evaluated in a leukodystrophy clinic were included. Measurements were taken of the genu and splenium of the corpus callosum and 4th ventricle (mid-sagittal plane), 3rd ventricle (axial plane); the Evans Index was calculated. Published normative data was used for comparison.

RESULTS: Forty-three MRIs from 23 individuals were included for analysis. Age at MRI ranged from 1.8 months to 13.6 years. Twelve participants (52%) were male. The majority (86%) of MRIs were obtained at < 2.5 years. Corpus callosum measurements started in the normal range, increasing near the end of the first year before decreasing after 1.5 years. Splenium size peaked earlier than genu size. The Evans Index, a measure of ventriculomegaly, decreased in the second half of the first year and then progressively increased again after 1 year of age. The 3rd ventricle showed an inverted pattern, starting in a more typical range before decreasing in size after 6 months and then increasing after 1 year. Only the 4th ventricle deviated from this pattern, below average initially due to early edema before increasing in size with age.

CONCLUSIONS: MRI changes in this cohort varied by age, showing evidence of typical structure size initially followed by edema and ultimately atrophy. The spatiotemporal distribution involved first the brainstem and then supratentorial areas, progressing from posterior to anterior following the typical pattern of developing myelination.

KEYWORDS: Neurogenetics, Neuroimaging, Early Stage Investigator

224. Characterization of Childhood Neurodegeneration and Associated Ataxia in UBTF-Related Disorder

Nagy A (Boston, MA), Luddy A, Molay F, DeLa Rosa Abreu L, Becker C, Gupta A, Eichler F

OBJECTIVE: Childhood-onset Neurodegeneration with Cerebellar Atrophy (CONDBA), caused by heterozygous mutations in UBTF, is characterized by initially typical or mildly delayed development followed by regression and onset of movement disorders. This study aims to clarify the natural history of CONDBA and to understand movement patterns

extracted from continuous wrist and ankle accelerometer data.

METHODS: An online REDCap survey of families of patients with CONDBA was conducted. Patients with CONDBA evaluated in a neurogenetics clinic were enrolled for data collection using wearable wrist and ankle accelerometers. Movement during typical activities was collected remotely for one-week periods every 3 months and compared to data from patients with Ataxia-Telangiectasia (A-T) and controls. Motor activity was compared with clinical severity using the Brief Ataxia Rating Scale (BARS).

RESULTS: Between March 2021 and June 2023, 56 surveys were started, 11 of which were fully submitted and included for analysis. Median age of the 11 survey subjects was 11 years (range 2-20), with symptom onset at a median of 2.3 years. All participants experienced motor regression, with 82% reporting ataxia. Ankle and wrist motor data were collected from 5 participants (median age 12 years, range 8-12 years) over one year with high test-retest reliability, showing similarities to A-T over controls across multiple measures and correlating with BARS. Participants with CONDBA showed decline in motor activity over one year.

CONCLUSIONS: Ataxia is common in CONDBA. Motor activity collected via wrist and ankle accelerometers is a reliable measure correlated to disease severity, showing decline over time, indicating potential as a motor biomarker.

KEYWORDS: Neurogenetics, Movement Disorders, Early Stage Investigator

225. Modulation of somatic repeat expansion with small interfering RNAs

Belgrad J (Worcester, MA), Summers A, Sapp E, Luu E, O'Reilly D, Yamada N, Fakih H, Echeverria D, McHugh N, Allen S, Furgal R, Gaston N, Maebuis A, Gross K, Bramato B, Aronin N, DiFiglia M, Khvorova A

OBJECTIVE: Huntington's disease (HD) is a genetic neurodegenerative disorder affecting children, adolescents, and adults, with no treatment available. HD is caused by CAG trinucleotide repeats in exon 1 of the huntingtin gene. Symptoms including chorea and depression present at >37 CAG repeats, with the age of disease onset decreasing as CAG repeat length increases. Lifelong somatic CAG expansion in the striatum contributes to HD neurodegeneration. Human GWAS have associated multiple mismatch repair (MMR) pathway components in HD onset and rates of somatic expansion. Thus, MMR-driven somatic expansion is a therapeutically targetable modifier of HD. The goal of this work is to evaluate the impact of RNAi-mediated silencing of MMR genes on the somatic CAG repeat expansion of huntingtin.

METHODS: CNS-active therapeutic siRNA are currently under clinical investigation for many indications offering promise for neurological disorders. Here, we have screened and validated CNS-active chemically stabilized divalent siRNA silencing key MMR genes. Top siRNA were intracerebroventricularly injected into 3-month-old HD mice (n=10/group). 2 months post-injection, target mRNA, protein, and the striatal somatic repeat expansion were assessed.

RESULTS: RNAi-based interventional lowering of MSH3, PMS1, MLH1, MLH3, and MSH2 each block somatic CAG expansion, and FAN1 increases expansion with more targets under investigation.

CONCLUSIONS: This work dissects the key players facilitating somatic expansion in HD and represents a therapeutic category of repeat-expansion-blocking agents. Further, the work presented here informs novel, RNAi-based treatment options for HD and similar triplet repeat disorders including spinocerebellar ataxias, myotonic dystrophy, fragile X, and more, where somatic triplet expansion is a contributing factor.

KEYWORDS: Neurogenetics, Movement Disorders, Experimental Therapeutics

226. Diagnostic Yield of Whole Genome Sequencing for Patients with Epilepsy

Neogi A (New Haven, CT), Rigobello R, Chibuk J M, Andrews C, Meng L, Vossaert L, Eng C, Xia F

OBJECTIVE: Whole genome sequencing (WGS) is increasingly being adopted as a first-tier diagnostic tool for various neurodevelopmental disorders per guidelines from the American College of Medical Genetics and Genomics (ACMG). However, there is limited information on the utility of WGS for epilepsy disorders. In this study, we reviewed the diagnostic yield of WGS for patients presenting with epilepsy.

METHODS: We conducted a retrospective analysis of over 1100 consecutive patients tested by WGS and rapid WGS in our clinical laboratory. Patients with a clinical indication of epilepsy were included in the analysis. The study focused on determining the frequency of positive results (defined as pathogenic and likely pathogenic) and the variant types detected by WGS.

RESULTS: 24% of patients had epilepsy as part of their phenotype. The overall diagnostic yield of WGS in this cohort was 35.6%. Most of the patients with positive results were under 18 years old and 81% of positive results were obtained from rapid WGS. Positive results included two patients with tandem repeat disorders (TRDs) (CTSB and ATXN8OS), two with findings in the mitochondrial genome (MT-TV and MT-TL1), and two with Down Syndrome. Copy number variants (CNVs) contributed to the diagnosis for ~7% of patients with epilepsy.

CONCLUSIONS: WGS identified a genetic diagnosis in over 1/3 of patients with epilepsy. Most positive results came from rapid WGS, which is a time-sensitive option for critically ill patients. WGS detected genetic variations that are often missed by targeted or panel testing. Altogether, these data support the use of WGS for patients with epilepsy.

KEYWORDS: Neurogenetics, Epilepsy

227. Pediatric Neurologic Phenotypes in Individuals with SLC16A2 Variants in MCT8 Deficiency

McWalter K (Gaithersburg, MD), Zghal Elloumi H, Sidlow R, Berrens M, Willis B, Bauer A

OBJECTIVE: Variants in SLC16A2 cause MCT8 deficiency, an X-linked condition associated with a wide spectrum of

pediatric neurologic findings in conjunction with underlying thyrotoxicosis. Pathogenic SLC16A2 variants are known in ~320 individuals, with genotype-phenotype correlations suggested. Here, we report on phenotypic spectrum of MCT8 deficiency in a cohort with SLC16A2 variants.

METHODS: By approved IRB protocol, we queried genetic testing laboratory deidentified data for SLC16A2 variants. Clinical abstraction of medical records was performed using Human Phenotype Ontology (HPO) terms summarizing clinical findings. Descriptive statistics were generated to define cohort characteristics.

RESULTS: We identified 57 individuals with likely pathogenic or pathogenic variants in SLC16A2 and 47 individuals with variants of uncertain significance (VUS). At time of testing, 49 individuals were ≤3yrs old; 10 were adults (≥20yrs). Most cases (101/104) were identified by exome sequencing (ES). In total, 506 different HPO terms were associated with 99 individuals (332/506 terms seen only once). Common pediatric neurologic HPO terms included: 'global developmental delay' (75/99); 'generalized hypotonia' (37/99); 'seizure' (30/99); 'delayed speech and language development' (30/99); 'failure to thrive' (28/99); 'intellectual disability' (27/99) and 'delayed gross motor development' (20/99). Non-neurologic HPOs included gastrointestinal and thyroid-related terms.

CONCLUSIONS: This study indicates that pediatric neurologic deficits are a prominent part of the overall phenotype of SLC16A2 genotypic variation causing MCT8 deficiency. Since this is fundamentally a disorder of T3 metabolism, confirmatory thyroid function testing, including TSH, free T4, and T3 are warranted in individuals with neurologic features suspicious of MCT8 deficiency.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

228. Neurological Phenotypes presenting to the Pediatric Undiagnosed Diseases Program (PUDP): Clinical and Genomic Approach to Identifying a Diagnosis

Acosta M T (Bethesda, MD), Macnamara E, D'Souza P, Wolfe L, Gahl W, Adams D, Tifft C J

OBJECTIVE: Nearly 75% of applicants to the PUDP present with features of neurologic disease. However neurological manifestations vary from case to case; some cases are primarily or only neurologic while others have neurologic concerns as a feature of their condition. Here we present a spectrum of neurological phenotypes and discuss how subclassification of neurologic phenotypes impacts our diagnostic rate and informs our diagnostic pathway for rare and undiagnosed cases

METHODS: A total of nearly 1500 patients have applied to the PUDP and 39% were classified, at application, as having a primarily neurologic phenotype. After an accepted patient's clinical evaluation, the patient's neurologic symptoms are reclassified into more specific categories, i.e., autism spectrum disorder (ASD), developmental delays with additional findings, seizures with or without additional features, movement disorders, and complex cases with atypical presentations.

RESULTS: We present the different categories of neurological phenotypes in our cohort as they relate to the research and clinical pathways used for identifying a molecular diagnosis. Case examples are used to illustrate and describe the different pathways and to highlight the success rate for identifying a diagnosis within the different neurologic phenotypic categories. From clinical evaluation, neurodevelopmental assessments, genetic studies and bioinformatic analysis, to functional studies and use of animal models, each group required a tailored diagnosis pathway design.

CONCLUSIONS: In pediatric patients with undiagnosed diseases, neurological manifestations are highly prevalent. A detailed clinical evaluation that further clarifies the phenotype is fundamental to reaching a successful molecular diagnosis.

KEYWORDS: Neurogenetics

229. Wearable sensors characterize impairment in body sway and gait across an international leukodystrophy cohort

Fine A S (Baltimore, MD), Turk B, Yska H, Rannila E, Ylikallio E, Engelen M, Keller J, Fatemi Ali

OBJECTIVE: Leukodystrophies are rare neurologic disorders that feature progressive sensorimotor dysfunction. In a subset there is prominent myeloneuropathy. These patients experience significant ataxia that leads to loss of independence in walking and daily activities, and severely diminishes quality of life. The variable progression rate complicates disease monitoring and identification of outcome measures for clinical trials. Deploying wearable sensors for remote assessment allows for accessible and frequent sway and gait variable collection. Multi-center cohorts are often required to sufficiently power leukodystrophy research studies and trials. We trained investigators in the U.S., the Netherlands, Finland and Brazil in a universal protocol of balance and gait testing using wearable sensors.

METHODS: Sway and gait variables measured with wearable accelerometers were collected from patients with Leukoencephalopathy with Brainstem and Spinal Cord Involvement and Lactate Elevation (LBSL) at multiple institutions after a training program. Ataxia and quality of life scales were obtained.

RESULTS: Sway area during stance with feet together and eyes closed distinguishes LBSL participants from controls (5.0m/s2 vs. 025m/s2, $p<0.001$). Lateral step variability (6.0cm vs. 3.7cm, $p<0.001$), gait speed (0.9m/s vs. 1.2m/s, $p<0.01$) and turn angle (235° vs. 210°, $p<0.05$) also distinguish LBSL participants from controls and indicate an ataxic gait pattern. We explore relationships between sway and gait with quality of life.

CONCLUSIONS: We demonstrate feasibility of a study to characterize sensorimotor impairment in leukodystrophy patients using wearable sensors across international sites. These measures will be further investigated as primary outcomes for clinical trials to assess myeloneuropathy and monitor disease progression.

KEYWORDS: Neurogenetics, Telemedicine, Lifespan Manifestations of Childhood Onset Conditions

230. Speech Delay in presymptomatic boys with xALD

Rhee J (Washington, DC), Shin M, Mahoney D, Fraser J L, Tochen L

OBJECTIVE: In this study, we describe the incidence of speech delay in a series of pre-symptomatic boys with X-linked adrenoleukodystrophy that were identified through newborn screening or known familial testing, in the absence of cerebral findings on imaging.

METHODS: Subjects gave informed consent for participation in natural history and biorepository data collection through the ongoing Myelin Disorders Biorepository Project. Clinical data was extracted from medical records. All subjects received biochemical and molecular confirmation of X-ALD.

RESULTS: Four of the eight subjects were diagnosed with X-ALD through state level newborn screening, and the remainder were identified through familial variant testing. Eight out of fifteen subjects exhibited speech delay prior to age 3 years. Speech delay was first notable between 11 months to 3 years of age. None of the subjects had cerebral changes related to X-ALD at the time of speech delay recognition.

CONCLUSIONS: Speech impairments are reported in males with cerebral X-ALD associated with ongoing progressive motor loss. However, we have identified eight subjects with speech delay without any cerebral changes on neuroimaging. Further research is needed to determine if early speech delay are an isolated finding, or if it may be predictive of future cerebral disease versus other X-ALD features.

KEYWORDS: Neurogenetics, Lifespan Manifestations of Childhood Onset Conditions

231. From Last Resort to First Choice: The Ascension of Exome Sequencing in Isolated NDD Diagnostics

Gasser B (Aliso Viejo, CA), Schultz C, Carraway C, Rea H, Gallegos M, Hoffer D, Suslovitch V, Towne M

OBJECTIVE: Historically, exome sequencing (ES) was used for complex, multisystem cases that remained undiagnosed after other testing methods. While professional guidelines now recommend ES as a first-tier test for neurodevelopmental disorders (NDD), many clinicians still opt for multigene-panel tests (MGPT). Here, we describe patients with isolated NDD undergoing ES and assess diagnostic outcomes compared to MGPT.

METHODS: We performed a retrospective analysis of consecutive ES cases at a single clinical laboratory between 2018 and 2023. Clinical records provided at the time of testing were mapped to Human Phenotype Ontology (HPO) terms. Based on the comprehensive set of assigned HPO terms, cases were categorized as 'isolated NDD' if they had intellectual disability, developmental delay, seizures, and/or autism spectrum disorder without major involvement of other organ systems. Ordering trends and diagnostic yield for ES and MGPT were evaluated.

RESULTS: In total, 2244 cases with isolated NDD were included in the analysis. Between 2018 and 2023, the proportion of ES cases with isolated NDD exhibited a 37% relative increase (from 27% to 37%) and emerged as the most prevalent clinical category ordered for ES. There was a significantly higher diagnostic rate (20% v. 11%; p<.0001) and a lower rate of variants of uncertain significance (VUS; 16% v. 21%; p=.0002) for isolated NDD cases on ES compared to MGPT.

CONCLUSIONS: The trend toward ordering ES for isolated NDD reflects evolving clinical practices. ES demonstrates improved diagnostic yield and lower rates of VUS compared to MGPT for NDD, underscoring its utility as a first-tier diagnostic test in neurology.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

232. How many diseases can one gene cause? Why mechanism matters for gene curation, variant classification, and patient counseling.

Huang J M (Portland, OR), Wayburn B, Rossi M, Alcaraz W, Towne M, Horton C, Herrera-Mullar J, Thrush D, Radtke K

OBJECTIVE: The "one gene-one disease" paradigm has evolved through recognition that genes may cause multiple disorders. The multiple disease model requires variant interpretation for all associated disorders, which can result in divergent classifications for different disorders. We aim to assess and define the scope of this phenomenon and its impact on variant curation and clinical reporting.

METHODS: We reviewed a large set of neurodevelopmental disorder (NDD) genes and all associated monogenic gene-disease relationships (GDR), curating them by mode of inheritance (MoI), mechanism of disease (MoD), and/or clinical presentation. Genes associated with multiple disorders were grouped into four categories based on these attributes.

RESULTS: We curated 1679 distinct disorders associated with 1502 genes (range: 1-4 disorders/gene). 10.1% (153/1502) of genes are associated with >1 genetic disorder, totaling 19.7% (330/1679) of all the disorders reviewed. Approximately 53% (81/153) of these genes are associated with disorders with different MoI, 70% (108/153) with different MoD, and in 41% (63/153) both MoI and MoD were different. Genes associated with >1 genetic disorder were categorized as: 1) Dosage Effect (13%; 21/153): distinct presentations with different MoI; 2) Multimodal (12%; 18/153): similar presentation despite differences in MoI/MoD; 3) Allelic (56%; 86/153): distinct presentations with different MoD; and 4) Unknown (31%; 48/153): unique presentations with insufficient MoD information.

CONCLUSIONS: A significant number of NDD genes are associated with >1 distinct genetic disorder. Dosage Effect, Multimodal, Allelic, and Unknown are four proposed GDR categories that can optimize variant curation, clinical reporting, and patient counseling for variants in genes associated with multiple disorders.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

233. Male Rett Syndrome: Clinical characteristics and the diagnostic journey

Ananth A L (Birmingham, AL), Thompson T, Gurfinkel D, Klamut N, Ferdinandsen K, Fu C, Lane J, Marsh E, Percy A, Neul J, Benke T

OBJECTIVE: Pathogenic variants in the MEPC2 gene are well known to cause Rett syndrome. However, the

misconception remains that Rett syndrome occurs exclusively in female patients, with limited survival in males. Broader use of next-generation genomic sequencing has lead to more males with pathogenic variants in the MECP2 gene being identified (male RTT)

METHODS: This study utilized a mixed methods study design with electronic surveys and qualitative interviews to review the diagnostic journey, clinical characteristics, and quality of life of male RTT.

RESULTS: Parents to 36 male RTT patients completed surveys, and 32 interviews were completed. 28 males were living, and 8 deceased. In the deceased cohort, the median age of death was 4.5 years. Parents reported a range of motor abilities with or without assistance: 33 (92%) reported seating ability, 22 (61%) reported ambulation, and 34 (94%) reported functional hand use. 33 (92%) reported some communication with sounds or spoken language. Age of diagnosis was variable with a mean of 3 years (IQR=5.04, min/-max=0.33/16 yrs). The diagnostic experience was mostly negative with 25% reporting the worst experience ever, 14% as very negative, and 11% mostly negative. 17% reported a neutral experience, 14% reported mostly positive, 14% very positive, and 6% the best possible. Most parents report receiving little guidance at time of diagnosis, and often were faced with disbelief by medical teams.

CONCLUSIONS: Male RTT patients have varied clinical outcomes. Challenges faced by families during and after diagnosis highlight the need for increased awareness and continued study of this population.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

234. The Clinical and Genetic Landscape of Epilepsy in Individuals with Dual Diagnoses

Neogi A (New Haven, CT), Chau M, Lau S A, Rigobello R, Chibuk J, Meng L, Vossaert L, Eng C, Xia F

OBJECTIVE: Previous studies have shown that 2-7% of individuals undergoing whole genome sequencing (WGS) receive a dual molecular diagnosis. However, the clinical and genetic landscape of specific indications associated with dual diagnoses remains underexplored.

METHODS: We retrospectively examined the clinical and genetic findings of 44 consecutive patients with dual diagnoses detected through WGS to identify patients with epilepsy. Additionally, we assessed epilepsy gene panels from 9 commercial laboratories to determine if patients with dual diagnoses and epilepsy would receive a complete diagnosis through panel testing.

RESULTS: 12 patients (27%) with dual diagnoses had a clinical indication involving epilepsy. All exhibited a complex multisystemic phenotype, with common indications being brain imaging abnormalities (83%), facial dysmorphisms (50%), cardiac issues (42%), neurodevelopmental delays (33%), and pulmonary issues (33%). 11 patients had at least 1 diagnostic finding in genes with established epilepsy associations; of these, 5 had a second finding related to epilepsy, and 6 had a second finding related to additional clinical features. The twelfth patient had findings in two genes with preliminary evidence for epilepsy. Multiple variant types were detected (including copy number and mitochondrial variants). Notably, only one of the 12 patients would receive a complete genetic diagnosis through panel testing.

CONCLUSIONS: Panel testing would provide a complete diagnosis for only one of the above 12 patients with dual diagnoses. The phenotypic complexity amongst patients with epilepsy and the specific gene findings from their dual diagnoses highlight the diagnostic utility of WGS.

KEYWORDS: Neurogenetics, Epilepsy

235. Title: Bioenergetic defects and reduced coenzyme A levels in a C. elegans model of TANGO2 deficiency disorder suggest a dual role for TANGO2 in coenzyme A maintenance and redox homeostasis

Sandkuhler S E (Rochester, NY), Youngs K S, Owlett L D, Leonardi R, Wojtovich A, Mackenzie S

OBJECTIVE: TANGO2 Deficiency Disorder (TDD) is a severe neurogenetic disease affecting children. We hypothesize that TANGO2 protein is implicated in the degradation and salvage of coenzyme A (CoA), possibly through the hydrolysis of pantetheine. In this study we investigated the effect of TANGO2 homolog deficiency in a C. elegans model and whether this phenotype could be rescued with pantothenate and cysteamine, the two byproducts of pantetheine cleavage.

METHODS: We first sought to replicate key experiments related to heme trafficking in double knockout (hrg-9-/-, hrg-10-/-; DKO) nematodes. We then performed expanded phenotyping of these worms and investigated the potential therapeutic effects of pantothenate and cysteamine.

RESULTS: DKO worms demonstrated a 62% decrease in median survival, a 66% reduction in brood size, poor swim motility, 20% slower pharyngeal pumping, and significant lawn avoidance. Strikingly, HPLC analysis revealed a 65% decrease in total CoA levels in DKO worms after 24 hours of fasting, whereas wildtype worms maintained CoA levels. Pantothenate and cysteamine were able to partially rescue the brood size and lawn avoidance phenotypes in DKO worms. We were unable to validate previous experiments implicating TANGO2 as a heme chaperone. RT-qPCR analysis of wildtype worms revealed marked 12.1-fold enrichment of hrg-9 and modest 1.3-fold enrichment of hrg-10 in response to paraquat, a superoxide generator.

CONCLUSIONS: C. elegans harboring deletions in TANGO2 homologs demonstrate a phenotype reminiscent of bioenergetic dysfunction. This study is the first to show CoA depletion in a model of TDD, potentially implicating this condition as the first disorder of CoA salvage.

KEYWORDS: Neurogenetics, Neurometabolic, Movement Disorders

236. BAF complex perturbation affects activity-dependent gene expression in human stem cell derived neurons

Trowbridge S K (Boston, MA), Choi G, Carter A C, Petrocelli J, Davis C, Harmin D, Griffith E, Greenberg M

OBJECTIVE: Pathogenic variants affecting the BAF chromatin remodeling complex lead to neurodevelopmental

disorders, but the factors that regulate the BAF complex in neurons remain poorly understood. The BAF complex interacts with the transcription factor FOS in mouse fibroblasts, suggesting that FOS may regulate BAF function. In neurons, FOS is rapidly transcribed in response to neuronal activity and activates gene programs critical for neurodevelopment and learning/memory. We hypothesized: (1) FOS and the BAF complex cooperate to regulate neuronal activity-dependent gene programs; and (2) mis-regulation of these programs drives symptoms in BAF complex-associated disorders.

METHODS: Using an in vitro system with human stem cell-derived excitatory neurons, we identified FOS and BAF complex binding sites before and after neuronal depolarization. With CRISPR/Cas9 technology, we generated cell lines to model pathogenic variants in different BAF complex subunits and profiled changes in gene expression in response to neuronal activity.

RESULTS: We find that neuronal activity leads to co-binding of FOS and the BAF complex at distal enhancer regulatory regions, many of which are near known autism-associated genes. In neurons with pathogenic variants in ARID1A or SMARCA4, there were numerous gene expression changes. Strikingly, a subset of the genes predicted to be activated by FOS had decreased expression in these models.

CONCLUSIONS: This study suggests that FOS directs the BAF complex to regulate key activity-dependent genes and that perturbation of the BAF complex leads to decreased activation of these gene programs. Thus, modulation of activity-dependent transcription could represent a novel therapeutic target in BAF complex-associated disorders.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

237. Adverse Events Across Gene Therapy Trials in the Leukodystrophies: A Single Center Experience

Santhakumar V (Boston, MA), Winter E, Drummond E, Lee S, Rosa Abreu L, Eichler F, Higuera C, Nagy A, Thompson R, Li Y

OBJECTIVE: Gene therapy (in-vivo, ex-vivo) and antisense oligonucleotides (ASOs) continue to be employed in trials of leukodystrophies, inherited progressive conditions affecting the white matter of the brain. Yet there is little awareness of the adverse event (AE) profile of these new emerging technologies. AE monitoring is crucial for ensuring patient safety and identifying potential risks. We set out to review the records of leukodystrophy gene therapy trials.

METHODS: AE logs from each gene therapy clinical trial enrolling at the Leukodystrophy Clinic at Massachusetts General Hospital were reviewed to identify the nature and timing (acute versus chronic) of AEs.

RESULTS: An average of 41 AEs and 2 SAEs per participant were identified across 4 trials. An ex-vivo gene therapy trial included side effects from myeloablation and immune suppression (acute) and events of insertional mutagenesis (chronic). Two in-vivo gene therapy studies reported both (acute) innate and (subacute) adaptive immune responses. These were managed with glucocorticosteroids and more common with systemic gene delivery. An ASO trial reported transient complications related to lumbar puncture. In most cases interdisciplinary management across several specialties was needed to address adverse events.

CONCLUSIONS: The nature of AEs in gene therapy trials differs by modality used and highlights the need for specialized training of physicians to manage these treatments effectively. Training should focus on patient monitoring, genetic data interpretation, and collaboration with multidisciplinary teams to ensure safe implementation of gene therapies in clinical practice.

KEYWORDS: Neurogenetics

238. Genetic Testing in an Unselected Cohort of Patients with Cerebral Vascular Malformations - A Single Center's Experience

Mithal D (Chicago, IL), Ivanisevic J, Salazar C, Yap K-L, Rathbun P, Ing A, Drackley A, Rose S, Patel P, Vazquez D, Moum S, Shaibani A, Lam S, Barry M, McGinnis E

OBJECTIVE: Pediatric patients with cerebral vascular malformations (CVM) are at risk to have germline pathogenic variants in genes that play a role in the development of vasculature. In adult patients, the frequency of genetic variants is low, but the frequency in children remains unknown. We offered genetic testing to all patients in our pediatric neurovascular clinic from 2019-2023 to determine the frequency of variant-positive CVM.

METHODS: Patients in the pediatrics neurovascular CVM genetic testing program were sorted into two groups based on likelihood of a germline genetic etiology. Patients with multiple cerebral and cutaneous vascular lesions or a relevant family history were classified as high risk for a germline variant. A two-sampled t-test was performed to determine statistical significance in genetic testing outcome between the two groups.

RESULTS: 39 patients underwent genetic testing. Six cases were positive (15.4%), three were inconclusive (7.7%), and thirty were negative (76.9%). All patients with a positive test had additional risk factors which was statistically significant compared to patients with a negative test (P=1.89E-06). All genetic diagnoses resulted in adjusted medical management, mostly related to surveillance guidelines. In all families of affected individuals, familial testing was offered and several affected family members were identified.

CONCLUSIONS: Approximately 15% of all patients in our neurovascular clinic had a positive genetic test. Genetic testing impacts medical management in patients and has a significant impact on familial risk stratification as well. Genetic testing should be considered for any pediatric patient with a CVM if they have a family history or multiple vascular lesions.

KEYWORDS: Neurogenetics, Stroke, Neurocritical Care

239. RNA Sequencing of Human Subject Tissue Transdifferentiated into Neurons Improves Diagnostic Yield and Gene Discovery

Clark G D (Houston, TX), Li S, Zhao S, Sinson J, Lee B, Mokry J, Liu P

OBJECTIVE: Examination of variants of unknown significance and of candidate genes for neurological disorders often requires RNA sequencing, especially when these variants are noncoding and in the splice region. Complicating the examination of these variants by RNA sequencing is the lack of expression of RNA in blood and fibroblasts for neurologically specific genes.
METHODS: Implementation of direct transdifferentiation of fibroblasts and of white blood cells into neurons or neuron-like cells was utilized to explore RNA sequencing for heretofore undiagnosed patients.
RESULTS: RNA sequencing of transdifferentiated neural cells led to recognition of compound heterozygote TMEM161b as a genetic cause of diffuse polymicrogyria in a child. The same strategy led to the recognition that a male with frontal pachygyria and a DOUBLECORTIN intronic variant, not predicted to lead to splicing or other transcriptional issues, resulted in an intronic inclusion in the RNA derived from this allele. Further, his mother was found to be mosaic for this variant only by RNA sequencing from her transdifferentated fibroblasts.
CONCLUSIONS: Given the nervous tissue exclusivity of expression of many genes implicated in neurological disorders, a workflow of RNA sequencing from transdifferentiated fibroblasts and white blood cells can improve diagnostic yield and gene discovery.
KEYWORDS: Neurogenetics

240. Expanding the Phenotypic Spectrum of TCF20-Associated Neurodevelopmental Disorder: A Case Emphasizing the Role of Comprehensive Genetic Testing

Varnet M (Dallas, TX), Goodspeed K

OBJECTIVE: To describe a case of TCF20-Associated Neurodevelopmental Disorder (TAND) presenting as Autism Spectrum Disorder (ASD) requiring little support (level 1) and late-onset developmental regression. The case presented here expands the TAND phenotype, adds a previously unreported pathogenic variant, and supports generalized genetic testing in autism.
METHODS: Retrospective chart review.
RESULTS: A 13-year-old girl presented to the neurodevelopment clinic for management of ASD. History was significant for speech delay and social skill regression at 3-4 years old. She became difficult to engage, no longer made direct eye contact, and preferred isolation. She is currently in general education classes with speech therapy. She has a history of physical therapy to address muscle tightness in her legs. She was uncoordinated and mildly dysmorphic with high-arched eyebrows. There was no family history of neurologic or developmental disorders.
Comprehensive genetic testing was performed revealing a pathogenic variant in TCF20 (p.Glu29*, c.85G>T) consistent with TAND. This variant was inherited from her asymptomatic mother.
CONCLUSIONS: TAND presentation is variable, including intellectual disability, ASD, facial dysmorphisms, abnormal tone, etc.; similar to Smith-Magenis syndrome (gene structure and products of TCF20 and RAI1 display significant overlap). Variants are typically de novo but have been reported to be inherited in an autosomal dominant pattern from symptomatic parents. This case demonstrates inheritance from a purportedly asymptomatic mother (impacting both reproductive choices and physical and mental health monitoring), a novel pathologic variant, and regression occurring outside the typical age expected for ASD; suggesting an expanded phenotype and supporting genetic evaluation in patients with level-1 ASD.
KEYWORDS: Neurogenetics, Neurodevelopmental Disorders, Lifespan Manifestations of Childhood Onset Conditions

241. A case of a rare HK1 mutation associated with thalamic, midbrain, pontine, and cerebellar abnormalities

Jackson S M (New York, NY), Jandhyala N R, Garcia M R, Segal D

OBJECTIVE: To describe a case of a 6-year-old female with progressive neurologic deficits found to have a rare missense variant in the HK1 gene.
METHODS: Birth and developmental histories were collected through parental report and medical records. Clinical examinations were completed at 6.5 years of age. Magnetic resonance imaging (MRI) with and without contrast were reviewed. Trio whole genome sequencing (WGS) was completed to identify potential pathogenic variants.
RESULTS: The patient is an ex-37-week female dizygotic twin born via normal spontaneous vaginal delivery following an uncomplicated pregnancy. Newborn period was significant for hypotonia. She had recurrent urinary tract infections, a hoarse voice, and articulation difficulty in early childhood. At age 6, she developed progressive fatigue, weight gain, and abnormal ocular movements over 4 months. Her mental status declined, and she was admitted in hypercapnic respiratory failure requiring intubation. MRI showed abnormal signal in the hypothalamus, medial thalami, posterior midbrain, and posterior pons, with contrast-enhancement in the cerebellum and leptomeninges. An EEG showed diffuse cerebral dysfunction without epileptiform activity or seizures. Cerebrospinal fluid revealed oligoclonal bands. Rapid trio WGS identified a rare likely de novo heterozygous missense pathogenic variant, c.1241 G>A, p.(G414E) in the HK1 gene.
CONCLUSIONS: We describe a case of a 6-year-old female with progressive brainstem and cerebellar deficits found to have a missense variant in the HK1 gene. This variant was previously identified in one adult patient. This case expands the neurologic presentation associated with HK1 mutations and extends the findings to include pontine abnormalities on MRI.
KEYWORDS: Neurogenetics, Neuroimaging, Early Stage Investigator

242. Expanding the Phenotypic Spectrum: A Novel GRIA4 Mutation Associated with Agenesis of the Corpus Callosum and Colpocephaly in Monochorionic Twins

Ferrer M (New York, NY), Jandhyala N, Nelson A

OBJECTIVE: To describe a case of monochorionic female twins with agenesis of the corpus callosum and colpocephaly found to carry a novel missense variant in the GRIA4 gene.

METHODS: Pre-natal and birth history was collected through parental report and medical record review. Clinical examinations were performed on both patients at 7 months of age. Pre-natal and post-natal magnetic resonance imaging (MRI) was performed. Whole exome sequencing (WES) was carried out for both twins and their mother to identify potential pathogenic variants.

RESULTS: The infants are ex-37 week monochorionic female twins born via primary C-section due to breech presentation. The infants are a product of consanguineous parents (first cousins). Pre-natal imaging at 24 week gestational age was notable for absent corpus callosum and ventriculomegaly. Post-natal imaging at day of life (DOL) 1 confirmed agenesis of the corpus callosum and showed colpocephaly. There were no clear signs of obstruction. EEG at DOL 1-2 revealed decreased interhemispheric synchrony; however, no clinical or subclinical seizures were observed. There were no parental concerns regarding development and at 7 months of age, both infants were developmentally appropriate. WES identified a novel likely de novo heterozygous missense variant, c.1086 G>T, p.(Gln362His) in the GRIA4 gene.

CONCLUSIONS: We describe a novel heterozygous missense variant in the GRIA4 gene (c.1086 G>T), expanding the genotypic and phenotypic spectrum of GRIA4-associated disorders. As both twins presented with consistent findings of agenesis of the corpus callosum on MRI, this case further supports the association of corpus callosum malformations with GRIA4 mutations.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders, Neuroimaging

243. Evaluation of Corticogenesis in NuRDopathies using mouse and human cerebral organoid models

Pierson T M (Los Angeles, CA), Otero G G, Zhao S, Dahlgren W, Delgado K, Walz K, Young J

OBJECTIVE: NuRDopathies are a group of neurodevelopment disorders associated with the Nucleosome Remodeling and Deacetylase (NuRD) Complex with overlapping phenotypes. We have modeled NuRDopathies using mouse and human IPSC-derived cerebral organoid models of a "pan-NuRDopathy": GATAD2B-associated Neurodevelopmental Disorder (GAND).

METHODS: IPSC-derived dorsal and ventral forebrain organoids were generated and studied with immunochemistry and transcriptomics. Gatad2b-heterozygous (GAND) and -Null mice were studied in parallel to determine cognitive ability, cortical structure, and single-cell transcriptomic profiles.

RESULTS: GAND-IPSCs were capable of differentiating into neuro-progenitor cells (NPCs) and cortical neurons (CNs) in the context of 2-D cultures and cerebral organoids. GAND cells with loss-of-function variants had haploinsufficient expression of GATAD2B mRNA and protein. Transcriptomic analysis of GAND-IPSCs and -NPCs indicated GATAD2B played a major role in NPC function, while GATAD2A was more likely playing a role in IPSCs. GAND neurons had altered temporal and quantitative expression of cortical laminar markers (TBR1, CTIP2, SATB2) in vitro. GAND mice were shown to have significant cognitive and behavioral deficiencies, as well as altered cortical morphology and abnormal patterning of cortical laminar markers. Single-nucleus transcriptomics of E16.5 mouse cortices had similar changes as the human IPSC and also noted that GATAD2B was more highly expressed throughout the cortex during this time that its paralog, GATAD2A.

CONCLUSIONS: The NuRD complex is an important regulator of laminar-specific gene expression during corticogenesis and GATAD2B is the prevalent GATAD2 paralog during this process.

Because of this and GAND's significant phenotypic overlap with other NuRD-related disorders, GAND serves as a pan-NuRDopathy model to best study these disorders.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

244. Discriminating Incidental and Pathological Findings on Brain MRIs for Boys with X-linked Adrenoleukodystrophy

Van Haren K P (Palo Alto, CA), Mallack E, Srivastava I, Gauna J

OBJECTIVE: Boys with X-linked adrenoleukodystrophy (ALD) undergo serial brain MRIs to allow prompt identification and treatment of inflammatory demyelinating brain lesions.

We sought to identify MRI features capable of differentiating between incidental and pathological MRI findings among ALD boys.

METHODS: We conducted a retrospective chart review at two expert ALD centers, cataloging intracranial findings included on MRI reports among ALD boys who had at least one surveillance brain MRI prior to age 12.

RESULTS: Among the 187 individuals with ALD in our databases, 69 males with 387 MRI reports met inclusion criteria. The cohort was racially diverse. Thirty-six (52%) had pathogenic mutations in ABCD1; the remainder had variants of uncertain significance. Median age at MRI was 6.6 (IQR 4-10.3). Most boys (51/69; 74%) had no incidental findings on at least one brain MRI. The most common findings were: frontal lobe punctate T2 hyperintensities (n=19; 27%), non-enhancing curvilinear T2 hyperintensities in splenium or genu (n=11; 16%), anomalous T2 hyperintensity in myelination zones (n=17; 25%), delayed myelination (n=8; 12%), and cerebral ALD lesion (n=7; 10%). Delayed myelination and anomalous, regional T2 hyperintensities tended to resolve with age while punctate and curvilinear T2 hyperintensities persisted indefinitely without further evolution. In contrast, pathologic ALD brain lesions were T2 bright, T1 dark, exhibited interval growth, eventually developed contrast enhancement, and appeared in classically described locations.

CONCLUSIONS: Most ALD boys undergoing MRI surveillance had incidental or ambiguous findings reported at least once. Ambiguous findings typically resolved on subsequent studies or persisted stably without enhancement, distinguishing them from pathological ALD lesions.

KEYWORDS: Neurogenetics, Neuroimaging, Pediatric Demyelinating Disease

NEUROIMAGING

245. Dynamic Diaschisis is Behaviorally Correlated in Pediatric Nonfatal Drowning

Razaqyar M S (San Antonio, TX), Deng S, Franklin C G, Ishaque M, Manning J, Chiang F, Woolsey M, Fox F

OBJECTIVE: After pediatric nonfatal drowning (PnFD) incidents, children often experience brain injuries and associated alterations in consciousness. While acute brain injuries are commonplace, previous studies in this population has demonstrated selective recovery of perception and cognitive functional networks during the chronic phase, even as motor function tends to remain impaired. This study aimed to characterize local tissue integrity and evaluate the influence of diaschisis on cortical areas in pediatric brain injuries using dynamic voxel-based BOLD metrics obtained through functional magnetic resonance imaging (fMRI).
METHODS: Previously acquired fMRI time-series data from 10 PnFD patients and 10 age and gender-matched healthy controls were analyzed. Data from each voxel was used to calculate metrics such as the amplitude of low-frequency fluctuations (ALFF), fractional amplitude of low-frequency fluctuations (fALFF), and regional homogeneity (ReHo) with time-varying dynamics.
RESULTS: In group-wise comparisons, the time-varying dynamics of BOLD-based voxel-wise metrics revealed abnormal regions distant from the structural lesions in the thalamus. Increased temporal variability in fALFF was observed within atrophic thalamic regions. Conversely, there was a notable decrease in temporal variability of ReHo in cortical regions functionally connected to the thalamus. These dynamic metric changes were found to be correlated with motor and perception functions but not with cognition.
CONCLUSIONS: This study unveiled a temporal dynamic decline in regions distal to the primary basal ganglia/thalamus lesion, potentially indicating diaschisis. Furthermore, the findings underscore the concept of temporal diaschisis in resting-state connectivity, depicting a phenomenon involving anatomically remote but temporally altered effects of focal brain lesions.
KEYWORDS: Neuroimaging, Neurocritical Care, Early Stage Investigator

246. A Rare and Treatable Cause for Unexplained White Matter Lesions: Partial Biotinidase Deficiency

Lai S (Jacksonville, FL), Franchi M, Gallo G, Aldana P, Trapane P, Galan F

OBJECTIVE: We report an unusual cause of a cerebral peduncle MRI lesion in a teenager with well-controlled idiopathic generalized epilepsy. To date, only a handful of cases exist on partial biotinidase deficiency. Our objective is to highlight the clinical presentation and increase awareness of this disorder to facilitate early diagnosis and improve neurological outcomes.
METHODS: A 14-year-old previously healthy girl was diagnosed with idiopathic generalized epilepsy. Her physical exam was non-focal including symmetric reflexes in the extremities and a thorough motor and sensory examination. As part of her epilepsy evaluation, MRI brain showed a hyperintense FLAIR signal in the right cerebral peduncle with no abnormal postcontrast enhancement. Given her physical exam and MRI brain findings, she was evaluated for neurofibromatosis type 1 (NF1). Whole exome sequence revealed compound heterozygosity for two pathogenic variants in the BTD gene suggesting a diagnosis of partial biotinidase deficiency.
RESULTS: Her regimen included Keppra (750mg twice daily) and Biotin (5mg daily). No further seizure episodes were observed, although the relationship to her epilepsy is unknown. Repeat MRI brain is pending.
CONCLUSIONS: This report showcases a rare but treatable cause for unexplained MRI lesions. Prior cases have reported both white matter lesions within the brain and spinal cord (Bhat et al., 2015). In cases of unexplained white matter lesions, we encourage consideration of genetic testing of the BTD gene as partial deficiency may be missed on newborn screening due to its significant residual enzyme activity and treatment may reverse identified lesions and prevent further complications (Gowda et al., 2020).
KEYWORDS: Neuroimaging, Neurogenetics, Epilepsy

247. Headache and Cranial Nerve Palsy: An Unusual Presentation of Renal Cell Carcinoma in a Pediatric Patient

Shams S (Sunnyvale, CA), Broughton A G, Lambeth K M, Dove K

OBJECTIVE: Considering Renal Cell Carcinoma (RCC) in the differential for pediatric patients presenting with headaches and acute-onset cranial nerve palsy.
METHODS: Background:
Renal cell carcinoma (RCC) in pediatrics is rare, and brain metastasis occurs in only 4-11% of cases within one to five years of renal symptom onset. Patients with metastasis may exhibit atypical site-specific symptoms alongside typical urological manifestations.
RESULTS: A 14-year-old previously healthy female presented with 3 weeks of left-sided headache, dysphagia, and left-sided tongue deviation. Review of systems was negative for weight loss, abdominal pain, and hematuria. Blood work, urinalysis, and CSF studies were normal except for an elevated ESR. Two initial brain MRIs, MRI cervical spine, and CT angiogram of the head and neck, all with and without contrast were normal. Given concern for additional cranial nerve involvement, MRI brain with and without contrast with Fast Imaging Employing a Steady-state Acquisition (FIESTA) sequence was performed, revealing an aggressive infiltrative osseous lesion on the clivus of the left occipital bone near the hypoglossal canal. MRI spine showed metastatic deposits on T3, T8, and L3 vertebral bodies and a 10-centimeter left renal mass. A biopsy of the mass confirmed TFE3-Rearranged RCC.
CONCLUSIONS: This atypical presentation of metastatic renal cell carcinoma highlights the necessity of maintaining a broad differential diagnosis, pursuing a thorough evaluation of the cranial base and foramina with high-resolution imaging

in cases involving cranial neuropathies, and facilitating early oncologic intervention to improve patient outcomes.
KEYWORDS: Neuroimaging, Neuro-oncology, Headache

248. Comparing Structural and Functional Brain Network Architectures in Children with ASD

Zielinski B A (Gainesville, FL), Farmer A, Traiser C, Nelson S

OBJECTIVE: Functional connectivity MRI (fcMRI) and structural covariance MRI (scMRI) have begun to reveal the brain's multiple network architectures. Previous work in children identified structural covariance networks (SCNs) that recapitulate previously identified resting-state connectivity networks (RSNs)1. A subset of SCNs has been shown to be atypical in ASD2,3. We examined known RSNs and SCNs in children with autism, to determine convergence of architectures and characterize relative contributions of these intrinsic connectivity networks (ICNs) to our understanding of ASD.
METHODS: MRI MPRAGE volumes of 106 children (57 ASD) aged 5-12 years were included. We derived eight 4-mm radius spherical seed regions-of-interest known to anchor large-scale ICNs, including sensorimotor, visual, auditory, speech, semantic, emotional salience, default mode, and executive-control networks. Whole brain condition-by-covariate analyses were performed using the General Linear Model, accounting for brain volume and age. Covariance maps were thresholded at $p < 0.01$. We then compared similarities and differences between brain architectures ($p<0.05$, two-tailed T-test) across major ICNs.
RESULTS: RSNs and SCNs were consistent with prior reports using fcMRI and scMRI in children with ASD. Between-group differences suggest domain-specific patterns of atypical network architecture in ASD. We observed a high degree of consistency between structural and functional data sources, with some differences in fcMRI not apparent in structural network architecture at this developmental stage, indicating complementary contributions.
CONCLUSIONS: 1. Children with ASD demonstrate atypical network structure and function in some, but not all, of ICNs studied.
2. Structural and functional ICNs demonstrate a high degree of overlap, suggesting convergence of biological mechanisms driving network development.
KEYWORDS: Neuroimaging, Neurodevelopmental Disorders

249. Brain hemodynamics in patients with MSUD using fNIRS

Khaksari K (Washington, DC), Sen K, Moreno Chaza A, Taylor A, Tucker K, Regier D, Dolins K, Bulcher S, Gropman A

OBJECTIVE: Maple Syrup Urine Disease (MSUD) is an inherited disease resulting in neurological impairment due to the accumulation of branched-chain amino acids (leucine, isoleucine, and valine) along with their associated ketoacids, along with depletion of essential amino acids and neurotransmitters (glutamate, tryptophan). Prefrontal cortex (PFC) impairment was reported in previous studies using fMRI. Functional Near-Infrared Spectroscopy (fNIRS) is a noninvasive imaging modality with low sensitivity to motion, thus more feasible, especially in children. It can produce activation maps and monitor neurocognitive function.
METHODS: We evaluated brain hemodynamics during a cognitive task in 2 siblings with MSUD using an fNIRS device (NIRSport2, NIRx). Patients are full siblings with a genetically confirmed diagnosis of MSUD (DBT Exon 2 deletion and c.916T>C). P1 is a 5-year-old male who presented with decreased oral intake and hypoglycemia at birth. He currently has speech delay, and epilepsy and has had multiple admissions for emesis and concern for hyperleucinemia. P2 is a 4-year-old female who presented on day 15 of life in a metabolic crisis. Her medical history includes global developmental delay and a history of brain edema requiring PICU admission. Both patients watched a baseline video of the Timmy Time cartoon for 5 minutes.
RESULTS: Oxy and deoxyhemoglobin signals of the PFC were analyzed throughout the task. Strong motion artifact was detected and removed using wavelet motion artifact removal. The result signals revealed a similar pattern of deoxyhemoglobin in both patients compared to BOLD signals from fMRI.
CONCLUSIONS: This work presents the feasibility of fNIRS in young individuals with MSUD.
KEYWORDS: Neuroimaging, Neurodevelopmental Disorders, Neurogenetics

250. Geometric morphometrics in pyridoxine-dependent epilepsy: Shape analysis of skull, cerebellum, and corpus callosum.

Masi S (Seattle, WA), Mercan E, Friedman S, Wright J, Doherty D, Oesch G, Shelkowitz E, Gospe S

OBJECTIVE: To evaluate presence of additional morphologic differences in sagittal skull and cerebellar shape in patients with pyridoxine-dependent epilepsy (PDE-ALDH7A1), extending past work demonstrating posterior corpus callosum difference in age- and sex-matched controls.
METHODS: A database of brain MRIs in PDE-ALDH7A1 patients and controls was employed; the sample reduced ($N=25$ pairs) to subjects with optimal mid-sagittal plane for cerebellum and no other morphometric features altering cerebellar results. For shape analysis, 300 semi-landmarks as a trace were used for the corpus collosum (as previously published); 100 semi-landmarks for the skull, and 8 in a "constellation" distribution for the cerebellum. Statistical analyses were used to compare patients based on age of seizure onset, sex, and pyridoxine treatment lag.
RESULTS: In this curated sample, posterior thinning of the corpus collosum ($P<0.001$) was observed, as in previous work. No differences were noted in skull shape between groups ($P=0.8$). For the cerebellum, the PDE-ALDH7A1 group demonstrated altered shape ($P <0.001$) reflective of reduced superior and anterior extent. Posthoc evaluation revealed no difference with regards to age of onset, sex, and treatment-lag status of the patients.

CONCLUSIONS: In midsagittal plane, PDE-ALDH7A1 patients exhibit altered posterior corpus callosal and cerebellar shape. The neuronal migration origins of these important structures are distinct without direct tracts or pathways connecting them. Thus, these results may reflect the common dysfunction in antiquitin, the ALDH7A1 product, or shared developmental features. Further studies evaluating the role of antiquitin on the development and growth of the brain in animal models could expand these results.

KEYWORDS: Neuroimaging, Epilepsy, Neurogenetics

251. Cantu syndrome is associated with increased cerebral blood flow but not increased cerebral oxygen utilization

Lim M (St.Louis, MO), Lewis J B, Dedkov I, Quartuccio H, Hoke T, Fields M, Couteranis S, Aggarwal M, Lee J-M, Nichols C, Grange D, Guilliams K

OBJECTIVE: Cantu syndrome (CS) is a genetic gain-of-function KATP channelopathy that reduces membrane excitability in multiple tissues, including vascular smooth muscle. Individuals with CS have chronically decreased vascular resistance, resulting in dilated and tortuous cerebral vessels, and common neurologic sequelae including migraines and developmental delay. We hypothesized that decreased vascular resistance in patients with CS may increase cerebral blood flow (CBF), which may affect cerebral oxygen metabolism.

METHODS: Participants with genetically confirmed CS and healthy controls underwent a brain MRI measuring: 1) CBF via pseudocontinuous arterial spin labeling and 2) Oxygen extraction fraction (OEF) via asymmetric spin echo. Arterial oxygen content was calculated as $CaO2 = 1.36* Hb*SpO2$. Cerebral metabolic rate of oxygen utilization (CMRO2) was calculated as CBF x CaO2 x OEF. Non-parametric statistics compared controls and participants with CS.

RESULTS: We scanned 23 participants with CS, ages 6–46 years (12 female), and 29 age- ($p=0.09$) and sex- ($p=0.21$) matched controls, ages 6–35. Participants with CS had significantly higher CBF (78.2 [58.1, 98.3] mL/100g/min compared to controls (58.1 [52.7, 63.7] mL/100g/min; $p=0.0008$), but lower OEF (Cantu 22.4% [19.3, 23.6] vs controls 24.9% [24.1, 26.0] $p<0.0001$). CMRO2 was not different between CS participants (1.8 [1.5, 2.0] mL/100g/min) and controls (1.7 [1.4, 2.4] mL/100g/min; $p=0.50$).

CONCLUSIONS: Participants with Cantu syndrome have higher cerebral blood flow, consistent with known vascular dilation. However, this does not appear to alter cerebral oxygen utilization as it is offset by a compensatory decrease in oxygen extraction.

KEYWORDS: Neuroimaging, Neurogenetics, Headache

252. Beyond One Size Fits All: Personalizing Brain Registration Techniques in Perinatal Stroke

Steeby C J (Boston, MA), Miller G N, Chui C, Sullivan A, Alhadid K, Musolino P, Cohen A

OBJECTIVE: Studying brain lesions can help localize brain function, but registration of patients' anatomy to a standard template can be difficult for highly distorted brains, like those seen in chronic imaging after perinatal strokes. Here, we compared the performance of multiple lesion compensation techniques and registration algorithms in registering chronic perinatal stroke lesions.

METHODS: Data from 11 patients with perinatal stroke from a single-site cohort were registered to an MNI template using three state-of-the-art algorithms (ANTS, FNIRT, and EasyReg) with two lesion compensation techniques (brain grafting and built-in compensation). To compare methods, we utilized Dice Similarity scores of ROIs between the registered brain and the MNI template and conducted a three-way mixed-design ANOVA examining the main effect of method, lesion compensation technique, and lesion size.

RESULTS: We found both a significant main effect of method ($F(2, 1469)=3.265$, $p=0.04$), where FNIRT performed worse than ANTS and EasyReg, and lesion size ($F(2,1469)=32.320$, $p<0.001$), where larger lesions caused poorer registration, but no significant main effect of lesion compensation technique. During visual inspection, a blinded expert tended to prefer FNIRT-registration for small lesions and EasyReg- or ANTS-registration for medium to large lesions, regardless of lesion compensation technique.

CONCLUSIONS: Our data suggests that ANTS and EasyReg are appropriate for data with large lesions, either with built-in lesion compensation or with brain grafting, while FNIRT may still outperform for patients with smaller lesions. Highly deformed brains may yet require manual correction.

KEYWORDS: Neuroimaging, Stroke

253. Dentate Nucleus Hyperintensity: a potential MRI biomarker for GNB1-Encephalopathy Identification - A Case Report

Cheung C (Elk Grove, CA), Choi W, Dahmoush H, Chen K, Manning M, Mackenzie K

OBJECTIVE: GNB1 encephalopathy classically presents with global developmental delay, intellectual disability, abnormal muscle tone, and distinctive MRI abnormalities. These MRI findings typically include abnormal/delayed myelination, abnormal corpus callosum, cerebral volume loss, ventriculomegaly, or bilateral polymicrogyria. However, T2/FLAIR hyperintensity of the dentate nucleus was noted for our patient, a finding that has not yet been described in the literature.

METHODS: We present a 9-year-old right-hand dominant male diagnosed with GNB1 encephalopathy (c.239T>C, p.-Ile80Thr), with resulting global developmental delay, generalized dystonia with spasticity, truncal ataxia, left hemiparesis, behavioral challenges, epilepsy, and feeding difficulties.

RESULTS: On review of our patient's 3T MRI at age 8, symmetric, hazy, ill-defined hyperintense signals of bilateral dentate nuclei on T2/FLAIR were noted. On retrospective review, this same finding was also present but had not been recognized in prior imaging conducted at 2 years of age.

CONCLUSIONS: Diagnosis of GNB1 currently requires molecular genetic testing, but advancements in neuroimaging interpretation can enhance our recognition of these disorders. The dentate nucleus is associated with the planning and

execution of voluntary movement, and hyperintensity on T2 imaging has been associated with symptoms of dystonia, ataxia, seizures, and a few other rare genetic disorders. Clinically, some patients with GNB1 encephalopathy experience hyperkinetic movements including dystonia, tics, ataxia, and chorea. Further research exploring the presence of dentate nucleus hyperintensity on neuroimaging could serve as a valuable diagnostic tool in identification and implementation of reported beneficial treatments for individuals with GNB1 encephalopathy.

KEYWORDS: Neuroimaging, Movement Disorders

NEUROIMMUNOLOGY

254. Brain Puzzle: Decoding a case of LGI-1 autoimmune encephalitis

Bacus P (Lexington, KY), Chalkley J

OBJECTIVE: Leucine-rich glioma-inactivation 1 (LGI 1) encephalitis is the second most common autoimmune neurological disorder. It is marked by cognitive impairment or rapid progressive dementia, psychiatric disorders, epileptic seizures, faciobrachial dystonic seizures and refractory hyponatremia. It has been described mostly in adults however several pediatric cases reports have been noted.

METHODS: Literature review performed on PubMed and Cochrane review using terms "LG 1 encephalitis" and chart review.

RESULTS: A 16 year-old female with a history of spells which were being worked up for generalized epilepsy versus psychogenic non-epileptic seizure. While tapering lamotrigine the patient presented with an event concerning for status epilepticus alongside encephalopathy, fever, hyperreflexia and hemodynamic instability. The patient was started on levetiracetam in addition to lamotrigine. Venlafaxine was held due to concerns for serotonin syndrome. MRI head with and without contrast was normal, MRV normal, CSF unremarkable. EEG normal initially, later with mild slowing. Mayo PCDES confirming diagnosis of LG-1 encephalitis. Screening for malignancy including CT Abdomen/Pelvis and ultrasound pelvis was normal. The patient was treated with 5 days of IVIG and IV methylprednisolone. She continues on rituximab and mycophenolate with improvements.

CONCLUSIONS: A review identified 25 other children with LGI-1 encephalitis with presenting symptoms of seizures, encephalopathy, psychobehavioural changes and movement disorders. In comparison to adults, children have been reportedly less likely to have faciobrachial dystonic movements and hyponatremia. This is the first case that has presented similarly to serotonin syndrome and adds to the growing body of literature of LGI 1 encephalitis.

KEYWORDS: Neuroimmunology, Neurocritical Care, Behavioral Neurology

255. Relapses in Pediatric Anti-MOG-associated Disease and their predictors: A single center experience of 24 patients

Gupta A (Louisville, KY), Neofidov N, Sweeney M

OBJECTIVE: The primary objective of this study was to find proportion of pediatric MOGAD patients with relapses and mortality. Secondarily, we analyzed different factors associated with unfavorable outcomes/relapse.

METHODS: We retrospectively reviewed pediatric patients (0-18 years) with the diagnosis. Variables included demographics, clinic-radiological data, Anti MOG titers, CSF and nerve fiber layer data as well as the treatments performed during relapses and in between.

RESULTS: We identified 24 patients (13 patients without relapses and 11 with relapses), one of the 24 subjects (4%) passed away due to malignant cerebral edema. There were no differences in mean age of onset or race between groups; however, the non-relapsing group was male-dominated (9: 4) and the relapsing group was female-dominated (2: 9), ($p = 0.019$). All the patients <6 years at onset had ADEM as their initial presentations and majority (70%) had monophasic course, while most patients with age at onset >6 years had ON as their major phenotype (5/13) and 69% had relapsing type. 11 out of 17 patients who received IVIG had relapses ($p = 0.014$). Steroid taper was not associated with reduced odds of relapse on binomial regression ($p=0.185$).

CONCLUSIONS: Pediatric MOGAD can be associated with a relapsing phenotype in patients with onset > 6 years of age and female sex. Maintenance IVIG treatment and steroid taper treatment did not prevent relapses in our cohort.

KEYWORDS: Neuroimmunology

256. Bickerstaff brainstem encephalitis in a pediatric patient with Aicardi-Goutières syndrome

Mandle Q (Columbus, OH), Mangold S, Cartwright K, Ream M, Poisson K

OBJECTIVE: Bickerstaff brainstem encephalitis (BBE) is a putative variant of Guillain-Barre syndrome associated with serum immunoglobulin-G against the ganglioside GQ1b (GQ1b-IgG). Aicardi-Goutières syndrome (AGS) is a rare genetic autoinflammatory leukodystrophy and has been associated with a higher incidence of acquired autoimmune diseases. We report a patient with AGS who presented with encephalopathy, dysphagia and left-sided weakness and was ultimately diagnosed with BBE.

METHODS: Chart review identified relevant patient information.

RESULTS: A six-year-old boy with AGS presented with one week of diminished responsiveness, decreased use of the left arm and difficulty swallowing. His baricitinib was temporarily discontinued five days prior to symptom onset due to influenza infection. The neurologic exam was pertinent for encephalopathy and 2/5 strength in the left upper extremity proximal muscle groups, both representing changes from the patient's neurologic baseline. MRI of the brain with contrast demonstrated T2-hyperintense lesions of the ventral pons with associated enhancement, edema, and diffusion

restriction. Lumbar puncture displayed albuminocytologic dissociation. Infectious workup was unrevealing. He was treated with five days of IV methylprednisolone. After discharge, serum anti-GQ1b-IgG resulted positive at a titer of 1: 100. In light of inadequate improvement he was started on monthly intravenous immunoglobulin twelve days later with great response.

CONCLUSIONS: To the authors' knowledge, this is the first case report of a patient with AGS developing BBE. This case demonstrates that patients with AGS may be prone to rare antibody-mediated autoimmune disorders, especially if chronic immunosuppressive medication is discontinued.

KEYWORDS: Neuroimmunology, Neurogenetics

257. Early Blood Pressure Differentiates Pediatric NMDA Receptor Encephalitis from Non-Encephalitic Patients

Ledbetter E (Houston, TX), Kass N, Imoh K, Erikson T, Yarimi J, Zoghbi A, Muscal E, Murray K, Shukla N, Fisher K, Sandweiss A

OBJECTIVE: Pediatric NMDA receptor encephalitis (NMDARE) is an autoantibody-mediated neurological condition characterized by seizures, psychosis, movement disorder and autonomic dysfunction. Detection of anti-NMDAR antibodies in cerebrospinal fluid obtained by an invasive lumbar puncture (LP) is required for definitive diagnosis. The disorder frequently requires long hospitalizations including intensive care and prolonged inpatient rehabilitation with complete recovery often involving months to years. Symptoms of NMDARE are heterogeneous and may mimic other non-encephalitic disorders, but early diagnosis portends faster recovery with better outcomes, so non-encephalitic patients are often subjected to unnecessary LPs. Since early autonomic dysfunction is a cardinal feature of NMDARE, we aimed to leverage vital signs as a non-invasive biomarker to screen for appropriate escalation of workup.

METHODS: This is a single-center, retrospective, case-control study comparing pediatric patients with NMDARE to control patients with similar symptoms who were worked up—and ultimately negative for—NMDARE between 2021-2023. We compared demographics, past medical history, presenting symptomology, and early vital signs including blood pressure percentile (BP%).

RESULTS: Children with NMDARE (n=24) had significantly higher average absolute and relative systolic and diastolic BP% compared to controls (n=53) (95.0 +/- 2.3 percentile vs 68.8 +/- 4.4 percentile, p<0.0001). Pulse pressure was also different between the two groups, but average heart rate was not. The most common non-encephalitic diagnosis in patients worked up for NMDARE was "primary psychiatric condition."

CONCLUSIONS: NMDARE is characterized by autonomic dysfunction reflected by early elevated BP, providing both a non-invasive variable to leverage the screening process and insight into the underlying pathogenic mechanisms of NMDARE.

KEYWORDS: Neuroimmunology

258. Neuroimaging findings during pediatric immune effector cell associated neurotoxicity syndrome (ICANS) - a CARNIVAL study

Gust J (Seattle, WA), McGuire J, Pinto S, Bhatia A, Oztek M, Vossough A, Wright J, Erdogan E, Taylor J, Annesley C, Diorio C, Dolan G, Epperly R, Hsieh E, Gardner R, Myers R, Naik S, Shah N, Shalabi H, Taraseviciute A, Talleur A, Yates B

OBJECTIVE: To systematically describe neuroimaging findings in immune effector cell associated neurotoxicity syndrome (ICANS), we collected all brain MRIs obtained in patients receiving chimeric antigen receptor (CAR) T cell therapy for hematologic malignancies at 6 pediatric institutions.

METHODS: Brain MRIs obtained at baseline (most proximal pre-CAR T study), acute (day 1-28 after CAR T), and follow up (any time >28 days post CAR T) studies were centrally reviewed by pediatric neuroradiologists.

RESULTS: Acute MRIs were available for 121 patients treated from 2014-2022. 90% of them had cytokine release syndrome, and 79% had ICANS. In patients with ICANS, the acute MRI showed ICANS-related abnormalities in 41%, most commonly white matter edema (16%) and brainstem edema (12%). ICANS grade strongly predicted the likelihood of acute abnormalities on brain MRI, ranging from 4% for patients with no ICANS, to 29% for grade 2, and 73% for grade 4 (P<0.001). Acute MRI abnormalities were not associated with patient age, CRS grade, prior radiotherapy, or neurologic comorbidities. ICANS-specific and non-specific imaging pattern incidence, correlation with apparent diffusion coefficient, reversibility, and association with ICANS grade, CAR product and patient characteristics will be presented.

CONCLUSIONS: The CARNIVAL database provides a unique resource for studying the neuroimaging findings in CAR-T-associated toxicity and is open to additional participating institutions worldwide. We found a higher than expected prevalence of brainstem and thalamic edema in ICANS. Limitations include the lack of systematic baseline and follow up imaging, as well as a bias toward more severely ill patients for whom imaging was obtained.

KEYWORDS: Neuroimmunology, Neuro-oncology, Neuroimaging

259. Use of Immunotherapy in Down Syndrome Regression Disorder: A Single Center Retrospective Analysis

Sofela O (Houston, TX), Shukla N M

OBJECTIVE: Down Syndrome Regression Disorder (DSRD) is becoming a more frequently recognized entity. It is characterized by the decline of previously acquired adaptive, cognitive, or social abilities in adolescents or young adults with Down Syndrome. While the precise underlying mechanisms remain unclear, there have been reports of immunotherapies showing efficacy. Our aim is to delineate the specific immunotherapeutic approaches utilized in

individuals suspected of having DSRD, contributing to the existing understanding of this condition.

METHODS: Patients with Down Syndrome who were diagnosed with DSRD or seronegative autoimmune encephalitis between 2018-2023 were included in this analysis. Age at onset of regression, regression symptoms, presence of any potentially pathogenic antibodies, age at initiation of immunotherapy, and subjective response to immunotherapy were collected and analyzed.

RESULTS: Median age of onset of regression: 10

Common regression symptoms: Global mutism, Mixed expressive-receptive aphasia, catatonia, social withdrawal, loss of previously developmental acquired milestones, inability to perform ADLs.

Potentially pathogenic antibodies found: Type I and Type II interferon, Thyroid peroxidase (TPO) antibodies and Thyroglobulin antibodies.

Median age at initiation of immunotherapy: 13

Types of immunotherapies used: Monthly IVIG, IV steroids, plasmapheresis, rituximab and tocilizumab

Mean duration of immunotherapy: 19

Subjective response to immunotherapy: Many were reported to return to either their pre-morbid baseline or 70% or above of their pre-morbid baseline. Plateau was noted in 2/7 of the cases.

CONCLUSIONS: Though limited by small patient cohort and retrospective analysis, our analysis shows some reported benefit with various immunotherapies. Further studies with more objective neuropsychological testing are needed to quantify this benefit.

KEYWORDS: Neuroimmunology, Experimental Therapeutics

260. Pediatric Acquired Neuroinflammatory and Demyelinating Disorders at a Pediatric Tertiary/ Quaternary Medical Center

Arellano J L (Orange, CA)

OBJECTIVE: Pediatric acquired neuroinflammatory and demyelinating disorders is a growing field in neurology. These disorders are heterogeneous and rare. It is important to diagnose and manage these patients early in the disease course and to identify patients who are at higher risk for relapse.

METHODS: This is a single-center retrospective review of patients less than 21 years old who presented with new onset neuroinflammatory and demyelination disorders from October 1, 2015 to October 1, 2022.

RESULTS: In the patients who met the inclusion criteria, the average age was 11.2 years (SD= 5.2), 62.5% were female, 56.3% had public health insurance, and 47.5% were Hispanic. The diagnoses included were 15.0% multiple sclerosis, 21.0% acute disseminated encephalomyelitis (ADEM), 1.3% neuromyelitis optica spectrum disorder, 23.8% clinically isolated syndrome (CIS), 18.8% autoimmune encephalitis (AE; 73.3% had N-methyl-D-aspartate receptor antibodies), 3.8% acute flaccid myelitis, and 16.3% acute or chronic inflammatory demyelinating polyneuropathy. Myelin oligodendrocyte glycoprotein antibody disease was included in the ADEM and CIS groups. Factors associated with relapse included the diagnosis, hospital length of stay, and the number of immunotherapy medications administered ($p<0.05$). 22.5% of the patients did not have antibody testing, and out of those 61.1% relapsed. None of the patients who experienced a relapse had been diagnosed with autoimmune encephalitis, compared to 29.2% of those who did not relapse ($p<0.05$).

CONCLUSIONS: Patients diagnosed with AE and ADEM were less likely to relapse, which is congruent with the current literature. This data shows the importance of antibody testing in establishing the diagnosis and relapse risk.

KEYWORDS: Neuroimmunology, Pediatric Demyelinating Disease

261. A Case of Isolated Multiple Cranial Nerve Enhancements in Pediatric Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD)

Hinkley L (Baltimore, MD), Caceres J A

OBJECTIVE: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a demyelinating disease which features cerebral and optic nerve involvement and spinal lesions. Other clinical forms such as cortical encephalitis have been reported. Here we present a case of multiple cranial nerve enhancements without any other associated lesions in the setting of MOGAD in a pediatric patient.

METHODS: A previously healthy 16-year-old female presented with an unprovoked generalized tonic colonic convulsion. After a week, this was followed by significant headaches, blurry vision, and eye discomfort. An initial brain MRI 8 days after her seizure was normal. Outpatient EEG after 2 weeks showed focal epileptiform discharges. Due to persistent headaches and lethargy, a new MRI done 45 days later showed right CN III, left CN V and bilateral CN VII and VIII enhancement. Serum MOG antibody was positive at 1: 100 and lumbar puncture was unremarkable.

RESULTS: She was admitted 72 days after her initial symptom and was treated with 3 days of high dose IV-Methylprednisolone. At that time, multiple interleukins were elevated including IL-6 levels more than 10 times above normal. Repeat (third) MRI showed residual bilateral enhancement of CN V. Repeat MOG antibody was negative. At follow up, all symptoms resolved completely. She was able to perform all activities and returned to school.

CONCLUSIONS: To our knowledge, this is the first case of pediatric MOGAD presenting with isolated multiple CN enhancements. Her symptoms highlight the important inflammatory state of this condition and expands the range of possible presentations of MOGAD in pediatrics.

KEYWORDS: Neuroimmunology, Pediatric Demyelinating Disease

262. HLA Types Associated with Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD)

Ahsan N (Los Angeles, CA), Santoro J D, Saucier S, Mitchell W, Jafarpour S

OBJECTIVE: To prospectively study HLA types in children with MOGAD to determine if HLA-types were associated with relapsing disease.

METHODS: We enrolled 36 patients less than 21 years of age who met Banwell criteria for MOGAD. A buccal swab test kit was used to collect the sample. The samples were analyzed at CHLA HLA laboratory through Next Generation Sequencing.
RESULTS: The majority of patients were female (69%), with a median age of 13 years (IQR: 9.2-15). Twenty-one patients (58 %) were Hispanic/LatinX. Optic neuritis was the most common phenotype (55%) followed by ADEM (44%), Transverse myelitis (16 %) and cortical encephalitis (5%). Nine patients (25%) had mixed phenotype. Thirteen (36%) patients had relapsing disease. There was no difference in race/ethnicity between the relapsing and non-relapsing patients (Fisher's exact test: 2.19, p=0.356).
Overall, 210 distinct HLA Class I alleles and 377 Class II alleles were identified in this study. The most frequent HLA-A allele was 24: 02: 01 (18.1 %), HLA-B 40: 02: 01 (9.7 %), HLA-C 04: 01: 01 and 06: 02: 01 (5.3%). The most frequent alleles in Class II loci were HLA-DRB1* 07: 01: 01 (11.1%), HLA-DRB4*01: 03: 01 (25 %), HLA-DQB1* 03: 01: 01 (19.4%), HLA-DQA1*03: 01: 01 (18%), HLA-DPA1* 01: 03: 01 (48.6%) and HLA-DPB1*04: 01: 01 (26%). No significant association between HLA Class I or II alleles and relapsing disease was observed.
CONCLUSIONS: Risk of relapse in individuals with MOGAD was not associated with HLA-clustering in a small single institution cohort.
KEYWORDS: Neuroimmunology, Pediatric Demyelinating Disease, Early Stage Investigator

263. Biomarker utility of extracellular vesicles in pediatric myelin oligodendrocyte antibody-associated disease

Mandle Q (Columbus, OH), Cabal Herrera A, Hade M D, Purnell B, Poisson K, Gombolay G, Reategui E, Talisman T, Magana S

OBJECTIVE: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a recently described acquired demyelinating disease (ADS) of the central nervous system. Neither the initial titer of antibodies to myelin oligodendrocyte glycoprotein (MOGAD-Ab) nor persistent seropositivity predict relapse or treatment response. Extracellular vesicles (EVs) have emerged as novel biomarkers of a diverse array of diseases, including ADS. The aim of this study is to characterize circulating EVs in patients with MOGAD compared to other ADS and explore the biomarker utility of EV-omics in MOGAD.
METHODS: A total of 20 MOGAD patients and 20 non-MOGAD ADS will be enrolled (current total MOGAD n=16). Biofluids will be processed for EV isolation via tangential flow filtration and characterized through our established multiparametric bulk and single EV pipeline. Bulk RNA will be isolated and sequenced for miRNA analysis. Differential gene expression, target prediction, functional annotation and pathway analysis will be performed. EV-miRNA data will be evaluated for association with clinical parameters (e.g. MOGAD topographical phenotype, monophasic vs. multiphasic, MOGAD-Ab titer, treatment response, MRI features). Single EV analysis for MOG+EVs will be performed using our established MOG+EV assay.
RESULTS: Preliminary studies have established the presence of small EVs in the circulation of ADS patients, including MOGAD patients. As a proof-of-concept, we have also characterized MOG+EVs from the plasma of ADS patients. Next steps include repeating our proof-of-concept experiments in a larger cohort and evaluating the biomarker potential of EV-omics and single EV analytics.
CONCLUSIONS: Bulk and single EV-omics may provide disease-specific insights into MOGAD clinical phenotype, course and possibly treatment response.
KEYWORDS: Neuroimmunology, Pediatric Demyelinating Disease

264. Immunotherapy-responsive Epilepsy without Antibody Markers: Clinical Presentation and Response to Treatment in 8 Children.

Mahasamudram P (Dallas, TX), Forschner C, Keough K,

OBJECTIVE: Autoimmune encephalitis presents with acute mental status changes, seizures, and other neurologic deficits, confirmed by positive anti-neuronal antibodies. We report a series of patients with subacute or chronic drug-resistant epilepsy who benefitted from immunotherapy despite lacking anti-neuronal antibodies.
METHODS: Chart review included 8 immunotherapy-responsive pharmaco-resistant epilepsy patients without CSF anti-neuronal antibodies. Data included: age at onset, semiology, epilepsy diagnosis, seizure frequency, developmental status, genetic and antibody testing, current and prior ASMs, immunotherapies, MRI and EEG findings.
RESULTS: 7/8 patients had normal brain MRI's. Median age at seizure onset was 2.5 years, with 6 months to 7 years of seizures before immunotherapy. All patients had multiple daily seizures at initiation. Median number of failed ASM was 6. After immunotherapy, 5/8 patients achieved seizure freedom, 1 patient has seizures only with illnesses and 2 had substantial frequency reduction. Six patients continue immunotherapy at 7 to 138 (median 40) months. Four of these 6 reduced ASM by 66.6 to 100%. Two remain seizure-free off all therapy. Developmental regression reversed in all patients. Abnormal EEGs improved in all patients, including 3 normalized EEGs.
CONCLUSIONS: In this review, all patients showed reversal of developmental regression and improved EEG findings and seizure control, including two patients being seizure-free and off medication. These outcomes demonstrate that immunotherapy can be beneficial despite the absence of autoimmune antibodies, suggesting an antibody-negative form of autoimmune epilepsy. Clinicians should consider an empiric trial of immunotherapy in patients with high seizure burden and developmental regression who have failed multiple conventional ASM.
KEYWORDS: Neuroimmunology, Epilepsy

265. Early use of Tocilizumab in Suspected MOGAD with Malignant Cerebral Edema: A Case Report

Varnet M (Dallas, TX), Wang C

OBJECTIVE: To describe a case of MOGAD with early tocilizumab use after development of malignant cerebral edema with excellent subsequent recovery.

METHODS: Retrospective chart review.
RESULTS: A 4-year-old boy presented with 24 hours of lethargy progressing to somnolence. MRI brain was concerning for ADEM, possible MOGAD; IV methylprednisolone was initiated. He was admitted to the ICU, developed focal seizures, and intubated. On day 4, intermittent extension of his limbs, vital sign changes, and intermittent electrodecrements on EEG raised concern for increased intracranial pressure; confirmed with CT. Tocilizumab (8 mg/kg IV) was administered. Within 24 hours, seizures halted and vital signs stabilized. On day 11, positive MOG antibody titers (1: 100) and elevated CSF interleukin-6 (20.8 pg/mL, normal range <7.5) resulted. Over 45 days of hospitalization, he received 5 days IV steroids, 7 PLEX sessions, 5 days IVIG, repeated tocilizumab on day 23, regaining baseline cognitive and motor function with mild right-sided weakness. He was discharged on a prolonged prednisone taper. On day 68, he was at physical baseline and near cognitive baseline, oral steroids discontinued, and MRI brain demonstrated signal abnormalities approaching resolution with minor gliosis.
CONCLUSIONS: Regarding MOGAD, Tocilizumab (IL-6 receptor antagonist) is used chronically for relapse prevention with good efficacy. Rarely used acutely, case reports discuss use of tocilizumab after insufficient response to routine therapies (IV corticosteroids, IVIG, PLEX). This case argues for earlier tocilizumab in severe ADEM cases with increased ICP, before conventual therapy failure. Considering cerebral edema severity and symptoms intensity, our patient demonstrated remarkable recovery with minimal neurological sequalae.
KEYWORDS: Neuroimmunology, Pediatric Demyelinating Disease, Experimental Therapeutics

266. Sjogren's syndrome presenting with cranial polyneuritis in a pediatric patient

Das A R (Houston, TX), Plaud Gonzalez J, Sudheendra M, Parnes M, Muscal E, Lotze T

OBJECTIVE: To present a case of pediatric Sjogren's syndrome presenting with cranial polyneuritis
METHODS: Case report, imaging, pathology
RESULTS: A previously healthy 14 year-old male initially presented with periorbital swelling, conjunctivitis, and left-sided neck swelling. He was also noted to have fevers and weight loss. Infectious workup was unremarkable. Over the following weeks, he developed bilateral facial weakness, ageusia and hearing loss. MRI of the brain and orbits revealed panuveitis as well as cranial neuritis with involvement of the facial and vestibulocochlear nerves. He was then transferred to our institution for subspecialty care. Though his initial eye exam had been unremarkable, repeat exam revealed bilateral grade 3 disc edema with conjunctivitis. He also began to exhibit saccadic intrusions at this time. Repeat brain MRI was unchanged while LP revealed an opening pressure of 9 with unremarkable CSF studies. Biopsy of the submandibular gland revealed chronic lymphoplasmacytic inflammation with acute sialadenitis without evidence of granuloma or malignancy, leading to a diagnosis of Sjogren's syndrome despite negative anti-SSA/SSB antibody testing. Steroid treatment was initiated, and he was eventually started on rituximab with improvement in his hearing and facial strength on follow-up
CONCLUSIONS: While Sjogren's syndrome is most frequently associated with dry eye and xerostomia, there are reports of various neurologic presentations of Sjogren's syndrome, including demyelination, optic neuritis and abducens palsy. While cranial polyneuritis can be seen in various systemic inflammatory conditions, such as sarcoidosis, this case presents a novel presentation of cranial polyneuritis with Sjogren's syndrome in a pediatric patient.
KEYWORDS: Neuroimmunology, Neuroimaging

267. MOGAD presenting as OMAS in a 16-Year-Old Male: A Case Report

Salazar K P (Houston, TX), Sudheendra M, Gill J, Fisher K

OBJECTIVE: Myelin oligodendrocyte glycoprotein antibody disease (MOGAD) is a heterogeneous disorder that can present with phenotypes of demyelinating diseases or autoimmune encephalitis. Here we present a case of it presenting as opsoclonus-myoclonus-ataxia syndrome (OMAS), which has not been reported in literature.
METHODS: Case report.
RESULTS: A 16-year-old male presented to the emergency department after a month of unsteady gait with new-onset opsoclonus, ataxia, and tremor. Screening PET and full body CT with and without contrast revealed no signs of underlying malignancy. MRI brain with and without contrast was also normal. CSF studies, urine catecholamines, vanillylmandelic acid and homovanillic acid were all within normal range. Serum paraneoplastic panel was only positive for MOG antibody, with a titer of 1: 100.
He received five days of high-dose intravenous steroids and intravenous immunoglobulin (IVIg), with improvement of symptoms but some ongoing deficits at time of discharge. Given persistent symptoms including ataxia and cognitive symptoms, he was further treated with rituximab and monthly IVIg per consensus treatment for OMAS.
CONCLUSIONS: Here we present a case of OMAS in a teenager with findings of positive MOG antibodies. It is unclear at this time if the presence of MOG antibodies are causative of his clinical presentation or positive due to the primary inflammatory process of OMAS. We suspect given the known association of MOG antibodies with autoimmune encephalitis that these antibodies play a role in his clinical presentation. This case highlights the need for broader antibody testing in patients with atypical presentations of disease to help guide clinical management decisions.
KEYWORDS: Neuroimmunology

268. Diagnosis of Epilepsy Following MOGAD in Pediatric Patients

Salazar K P (Houston, TX), Yarimi J, Fisher K S

OBJECTIVE: To define clinical characteristics of a cohort of pediatric patients with MOGAD who were subsequently diagnosed with epilepsy.

METHODS: Case series. Patients under age 18 who met the 2023 diagnostic criteria for MOGAD were included in a retrospective analysis.
RESULTS: Of 88 MOGAD patients, 21 presented with acute symptomatic seizure (24%). Seven patients (33% of those with seizure at onset, 8% of overall cohort) went on to receive a diagnosis of epilepsy, of which three had drug resistant epilepsy. Initial presentation of status epilepticus was more common in those who were given an epilepsy diagnosis (71.4%) in comparison to those with solely acute symptomatic seizures (28.5%). Epilepsy diagnosis was more frequently seen in those presenting with FLAIR-hyperintense Lesions in Anti-MOG related Encephalitis with Seizures (FLAMES) (42.8%) and tumefactive MOG (28.6%), and additionally more frequent in comparison to those of the same clinical phenotype presenting with acute symptomatic seizures (50% and 66.7% respectively). Comparatively, 8 patients (20%) with ADEM presented with acute symptomatic seizures, but only one patient (2.5%) was given epilepsy diagnosis.
CONCLUSIONS: This study highlights the need for further investigation of pediatric MOGAD to determine predictors of epilepsy diagnosis. Our study suggests a 33% risk of epilepsy diagnosis if presenting with acute symptomatic seizures. In addition, those with MRI findings of FLAMES and tumefactive MOG may be at further increased risk in comparison to other clinical phenotypes. This limited data can help provide possible guidance in epilepsy risk for pediatric MOGAD patients and families.
KEYWORDS: Neuroimmunology, Epilepsy, Neurocritical Care

269. Azathioprine Prolongs Return of B-cells Following Rituximab Infusion: A Case Series

Peraino J (Kansas City, MO), Mullin N, Hoffart C, Harris J, Allison T

OBJECTIVE: INTRODUCTION: Rituximab is a chimeric anti-CD20 monoclonal antibody (MAB) used in autoimmune disorders. It depletes peripheral CD20-presenting B-cells, often to undetectable levels. Duration of depletion is variable but return generally occurs within 2-12 months1. Ocrelizumab is another anti-CD20 MAB that is humanized rather than chimeric. Although efficacy between the two is debated, rituximab is generally not inferior. For this case series, we will be considering the anti-CD20 MABs as one therapeutic class. At our center, when literature on persistent use of anti-CD20 MABs is lacking, azathioprine is often added for sustained immunosuppression. Azathioprine works by inhibiting purine synthesis leading to decreased production of white cells.
CASES: A series of five patients with autoimmune neurological disorders who received azathioprine following administration of an anti-CD20-MAB showed prolonged time to recovery of B-Cells. Of the five patients, two had myasthenia gravis (MG), two had chronic inflammatory demyelinating polyneuropathy (CIDP), and one had neuromyelitis optica spectrum disorder (NMOSD). One of the patients with CIDP had a reaction with initial rituximab infusion and was switched to ocrelizumab infusion without further event. B-cells returned over a year after final rituximab infusion in all but one patient, whose return was 10 months from final infusion. Patients had well controlled symptoms and no hospitalizations during the depletion and recovery of B-cells.
CONCLUSION: This case series demonstrates that azathioprine as an adjunct therapy to anti-CD20 MAB leads to prolonged B-cell recovery correlating with better symptom control, leading to decreased use of acute treatment interventions such as steroids and hospitalization.
METHODS: n/a
RESULTS: n/a
CONCLUSIONS: n/a
KEYWORDS: Neuroimmunology

270. Immune-mediated Neuropathy with Tri-sulfated Heparin Disaccharide or Fibroblast Growth Factor Receptor 3 Antibodies in Pediatric Patients: A Case Series

Nguyen T (Cincinnati, OH), Wilson E, Zygmunt A

OBJECTIVE: Novel antibodies to tri-sulfated heparin disaccharide (TS-HDS) and fibroblast growth factor receptor 3 (FGFR-3) have been identified in cryptogenic neuropathy cases. There is limited information regarding these antibodies in pediatric patients. The goal of this case series is to illustrate the clinical presentation and treatment in 2 patients with novel antibodies to TS-HDS and FGFR-3.
METHODS: Two pediatric patients with acquired neuropathy were identified to have antibodies against TS-HDS or FGFR-3. Each chart was reviewed for presentation, diagnosis, intervention, and outcome.
RESULTS: Case 1: 15-year-old female with juvenile myoclonic epilepsy presented with back pain, bilateral hand and leg paresthesia, and shuffling gait. Exam notable for diminished sensation in the extremities, absent lower extremity reflexes, and sensory ataxia. Testing was positive for IgM against TS-HDS antibodies (31,000; normal is < 12,000).
Case 2: 12-year-old male with ADHD presented with worsening leg pain, bilateral foot paresthesia, and hand twitching. Exam notable for intact strength, sensation, reflexes, and gait. Testing was positive for IgG against FGFR-3 antibodies (4,600; normal is < 3,000).
Both patients were found to have axonal neuropathy on EMG. Treatment was initiated with monthly intravenous immunoglobulin (IVIG). There is subjective and objective improvement in one patient with monthly IVIG treatment.
CONCLUSIONS: There is limited data for treatment of immune-mediated neuropathy in pediatric patients. Further investigation is needed to determine the role of these antibodies in pediatric cases and whether IVIG will be beneficial.
KEYWORDS: Neuroimmunology, Neuromuscular

271. Pediatric neuroinflammatory and demyelinating disorders require significant inpatient resources

Sandweiss A J (Houston, TX), Truong C, Murray K, Russell H

OBJECTIVE: Neuroinflammatory disorders such as encephalitis, encephalomyelitis, transverse myelitis, ADEM, multiple sclerosis (MS) and neuromyelitis optica (NMO) are a significant burden on pediatric patients and payors. Inpatient

admissions for children with a primary diagnosis of these neuroinflammatory disorders may be longer and more costly than other pediatric admissions but little is known about healthcare requirements needed to support these patients in the United States. We therefore characterized the drivers of inpatient resource use for neuroinflammatory disorders to understand what qualities of hospitalization lead to greater burden.

METHODS: We used the Texas Public Use Data File (Tx-PUDF) to explore drivers of inpatient resource use for neuroinflammatory disorders. This dataset contains patient demographic, clinical, administrative and charge information on Texas hospital discharges. Discharges with the above primary ICD diagnoses in children between 2016-2022 were identified (n=1,933).

RESULTS: There were 276.1 +/- 7.2 pediatric neuroinflammatory admissions per year in Texas. The cost of hospitalization was $57,610.30 +/- $7,960.23 per admission with a primary neuroinflammatory disorder compared to roughly $8,900 per nationwide pediatric hospitalization in 2019 according to Healthcare Cost and Utilization Project (HCUP). Length of stay in our cohort was 12.1 +/- 0.4 days per hospitalization compared to roughly 4.1 days nationwide. These admissions cost $15.4M/year in Texas which we estimated to cost The US payors $139.9M/year.

CONCLUSIONS: Pediatric neuroinflammatory disorders require significant inpatient resources and utilization. Our data from Texas indicate a disproportionate utilization of resources are expended on a narrow range of childhood neurologic disorders necessitating further research into the specific mechanisms of high cost.

KEYWORDS: Neuroimmunology, Pediatric Demyelinating Disease

NEUROINFECTIOUS DISEASE

272. Human Parechovirus Meningoencephalitis and Seizure Frequency - a Multi-Center Retrospective Case Series

Shah N S (Wichita, KS), Fortin O, Sheth A, Calardo S, Oren M, Souverbielle C, Erdem G, Hauger S, Katragkou A, Solaiman A, Harik N, Mulkey S, Downey R, Angelis D, Teran P

OBJECTIVE: To evaluate the 2022 national outbreak of Parechovirus (PeVA) meningoencephalitis (ME) cases associated with neurologic complications and MRI findings.

METHODS: Retrospective chart review was performed at seven children's hospitals. PeVA cases were identified by CSF RT-PCR. Seizures included clinical and/or EEG-confirmed ictal events. Standardized data collection utilized RedCap®. Data were analyzed using t-test for continuous variables and chi-squared test for categorical variables. Significance was determined at p<0.05. The study was deemed IRB-exempt.

RESULTS: 103 infants were diagnosed with PeVA ME. 24 patients (23.3%) experienced seizures. Seizures were associated with younger age, premature birth, increased length of stay and intensive care utilization. Seizures were less likely in patients with fever and irritability/fussiness and more likely with hypothermia, hemodynamic instability, apnea, and focal neurologic deficits (p<0.05). MRIs were obtained in 55 cases; 31 (56.4%) demonstrated abnormalities with diffusion restriction involving white matter and thalami [seizure group: 19/21 (90.5%) abnormal; non-seizure group: 12/34 (35.3%) abnormal; p<0.001]. EEGs were obtained in 40 cases; 22 revealed abnormalities [seizure group: 18/24 (75%) abnormal; non-seizure group: 4/16 (25%) abnormal; p=0.002]. There were low rates of CSF pleocytosis and elevated inflammatory markers. Thirteen patients were discharged with anti-seizure medications and ten required follow-ups with developmental therapies.

CONCLUSIONS: The 2022 PeVA ME outbreak led to a high rate of seizures and abnormal brain imaging. Classic laboratory signs of invasive infection were uncommon. Clinicians must maintain a high index of suspicion for PeVA ME and patients at risk for neurologic injury.

KEYWORDS: Neuroinfectious Disease, Neuroimaging, Neonatal Neurology

273. Brain MRI structural and diffusion abnormalities in a mouse model of congenital Zika virus infection

Liu E (St. Louis, MO), Quirk J, Kohn B, Neil J, Agner S

OBJECTIVE: To evaluate whether young adult mice with in utero Zika virus exposure with known behavioral and cognitive abnormalities have structural or diffusion abnormalities on brain MRI.

METHODS: Pregnant humanized STAT2 knock-in (Jax: 031630) dams underwent footpad injection with 104 focus forming units of Zika virus or mock solution at embryonic day 6.5. Pups were weaned in accordance with approved IACUC protocol (Washington University in St. Louis). In vivo MRI was obtained at postnatal day 60 (P60). 6 mock- (3 male, 3 female) and 6 Zika-infected (3 male, 3 female) mice underwent T2- and diffusion weighted brain imaging.

RESULTS: The apparent diffusion coefficient (ADC) of the somatosensory cortex, barrel field in Zika-infected mice was decreased compared mock-infected controls (6.29e-4±.5.74e-5 vs. 7.21e-4 ±.6.88e-5, $p = 0.03$). Some brain region volumes showed trends toward increased size in Zika-infected compared to mock-infected mice, but none were statistically significant (anatomy: mock vs. infected, p value; total brain volume: 453±6.80 mm3 vs. 462±11.6 mm3, $p = 0.16$; lateral ventricles: 1.57±0.124 mm3 vs. 1.73±.0.150 mm3, $p = 0.07$. Motor and somatosensory cortex volumes were not different between Zika- and mock-infected mice. All data were compared by unpaired t-test.

CONCLUSIONS: In a mouse model of congenital Zika virus, P60 mice with in utero Zika virus exposure show differences in MRI diffusion but not structural brain volumes compared to controls. This data suggests that the phenotype of this mouse model may accurately mirror the large proportion of Zika-exposed infants without abnormal brain imaging at birth that later have neurodevelopmental abnormalities.

KEYWORDS: Neuroinfectious Disease, Neuroimaging, Neonatal Neurology

274. Characterization and Novel Observations of Uncommon Pediatric Viral Meningoencephalitides

Perry Z (Houston, TX), Ballou E, Johnson J, Erickson T, Ronca S, Murray K, Demmler-Harrison G, Sandweiss A

OBJECTIVE: Pediatric viral meningoencephalitis is a rare condition that often affects immunocompromised patients. Herpes simplex virus, enterovirus, and adenovirus are the most common causative viral agents with literature to support clinicians in their management. However, other causative agents together make up a large proportion of viral meningoencephalitis cases with limited literature describing them.

METHODS: This is a single-center, retrospective observational study of pediatric patients with viral meningoencephalitis between 2012-2023. We compared clinical data from electronic medical records of children without a previously existing immunodeficiency by pathogenic agent isolated in the CNS. We focused on the three next-most-common viral agents isolated.

RESULTS: Our analysis revealed Ebstein Barr virus (EBV, n=7), Human Herpes virus 6 (HHV-6, n=3), and West Nile virus (WNV, n=5) as prevailing CNS viral agents in immunologically normal hosts. 12/15 (80.0%) were male; EBV only affected males and WNV predominantly affected males. The patient demographics mirrored those of Harris County, Texas. Patients with CNS HHV-6 were youngest (1.6 +/- 0.5 years) while EBV and WNV patients were adolescents. Children with CNS EBV had the highest CSF cell count while HHV-6 produced the highest CSF protein. While 13/15 patients required ICU admission, WNV cases necessitated the longest hospitalization.

CONCLUSIONS: Viral meningoencephalitis is an uncommon but important cause of acquired brain injury and hospitalization. Our preliminary data in previously healthy children demonstrate EBV, HHV-6, and WNV as important causes and should be considered in children presenting with signs and symptoms concerning for meningoencephalitis.

KEYWORDS: Neuroinfectious Disease

NEUROMETABOLIC

275. Antibody Response to the Pneumococcal Vaccine in Children with Mitochondrial Disease

Gordon-Lipkin E (Bethesda, MD), Schlein M, Kruk S, McGuire P

OBJECTIVE: Mitochondrial diseases(MtD) are multisystemic disorders caused by genetic defects in mitochondrial metabolism. Infection is a major cause of morbidity in MtD, and the most common causes of death are sepsis and pneumonia. We analyzed pneumococcal titers to determine if MtD patients respond appropriately to the pneumococcal(PC) vaccine.

METHODS: Blood samples from children with "probable"/"definite" MtD by revised Walker criteria were collected. Total immunoglobulin levels and antibodies against the 23 PC serotypes included in the vaccine were measured. Per clinical standards, sufficient immune response was defined as positive titers against >50% of the serotypes for age <6y and >70% for ages 7-18y. In a subset, PhIPSeq measured environmental exposure to PC in 2020 and 2021.

RESULTS: 43 patients were included with an average age of 9.3 years old. Overall, 58% had sufficient response and 42% did not. Longer time since last vaccination was correlated with a higher incidence of insufficient immune response. For patients who received the vaccine within 5y, 18% had insufficient response but for those who received it >5y prior, 67% had insufficient response($p<0.05$). On PhipSeq, MtD had a downward trend in PC protein antigen binding between timepoints. This indicates waning natural immunity/lack of re-exposure during the pandemic.

CONCLUSIONS: While the majority of patients produce titers against the pneumococcal vaccine, 2/3 have insufficient response after 5y. Natural immunity due to community exposures wanes quickly. These patients may be vulnerable to PC disease and require revaccination. Providers should consider including PC titers in their clinical evaluation.

KEYWORDS: Neurometabolic, Neurogenetics, Neurodevelopmental Disorders

276. The 50-meter timed test as a longitudinal functional outcome measure in CLN3 Batten disease

Abreu N J (New York, NY), Powers B P, Yildiz V, Sveda M, Peifer D, Khuhro Z, O'Neal M, Alfano L, Scherr J, de los Reyes E

OBJECTIVE: We examined the use of a 50-m timed test (50MTT) in CLN3 Batten disease, an autosomal recessive typically juvenile-onset neurodegenerative lysosomal storage disorder.

METHODS: Individuals with CLN3 Batten disease were followed from August 2019 to May 2023 at a single institution. The primary outcome was time to complete independent travel over 50 meters. Baseline performance was compared to healthy age- and sex-matched children. Linear mixed-model analyses using repeated measures were conducted for affected individuals.

RESULTS: Twenty-six children with CLN3 Batten disease (10 females) ranging between 65-193 months of age (median 104.5 months) completed at least one assessment. All had baseline vision impairment. Affected individuals performed worse compared to controls on the 50MTT (median 89.3 v. 40.2 seconds, Mann–Whitney $U = 1971.0$, $p < 0.001$). Linear mixed model analyses within CLN3 Batten disease revealed a positive association between 50MTT performance and age as well as total physical score on the Unified Batten Disease Rating Scale ($\beta = 0.45$, confidence limits 0.20-0.70, $p < 0.001$; $\beta = 2.31$, 1.33-3.29, $p < 0.0001$). There was a negative association with the Stanford-Binet knowledge subtest ($\beta = -8.83$, -12.74 - -4.91, $p < 0.001$).

CONCLUSIONS: The 50MTT captures gross motor dysfunction over time in CLN3 Batten disease demonstrating slower performance with increasing age, increasing neurological severity and decline in cognitive performance. Given the short assessment time with less attentional demands compared to the 6-minute walk test, the 50MTT may be an

appealing functional outcome measure in future clinical trials in CLN3 Batten disease.

KEYWORDS: Neurometabolic, Neurogenetics, Neurodevelopmental Disorders

277. Expanded Clinical and Metabolomic Spectrum of AICA Ribosiduria

Walimbe A S (Houston, TX), Gonzalez M, Gijavanekar C, Wilson T, Elsea S, Katyayan A, Emrick L

OBJECTIVE: To expand the clinical spectrum of 5-aminoimidazole-4-carboxamide-ribosiduria (AICAR).

METHODS: Case report including untargeted metabolomic profiles that were generated from plasma derived from venous whole blood, urine, and CSF. Individual patient samples were compared to a set of invariant anchor specimens included in each batch to achieve semi-quantitative analysis of metabolites. Raw spectral intensity values were normalized to the anchor samples, log-transformed, and compared to a normal reference population to generate Z-scores.

RESULTS: AICAR is an ultra-rare inborn error of metabolism caused by biallelic pathogenic variants in ATIC (MIM #601731), which lead to defects in the last two steps of de novo purine synthesis. The classic phenotype includes hypotonia, severe visual impairment, epilepsy, dysmorphology, and growth retardation. A 5-year-old girl with cortical visual impairment was first evaluated at nine months of age for global developmental delay and abnormal movements. An EEG revealed epileptic spasms. Exome Sequencing identified compound heterozygous pathogenic variants in ATIC, c.1277A>G (p.K426R) and c.1113C>A (p.Y371*). Untargeted metabolomic analyses in urine, plasma, and CSF revealed elevations of N6-succinyladenosine (Z-score >= +6.0) and reductions in hypoxanthine, indicating a defect in purine metabolism, consistent with a diagnosis of AICAR. Spasms continued despite ACTH and Vigabatrin. Ultimately, she started a ketogenic diet, which resolved her spasms and improved her overall development.

CONCLUSIONS: Our case is notable for a positive response to a ketogenic diet and the absence of dysmorphic features. Our work highlights the utility of untargeted metabolomic analyses in establishing a diagnosis of AICAR and should help identify more patients with this condition.

KEYWORDS: Neurometabolic, Neurogenetics, Epilepsy

278. Expanded Clinical Phenotype and the Role of Untargeted Metabolomics Analysis in Confirming the Diagnosis of Sodium-Dependent Multivitamin Transporter Deficiency

Walimbe A S (Houston, TX), Waskow E, Mackay L, Miller M, Gijavanekar C, Elsea S, Scaglia F

OBJECTIVE: To expand the clinical spectrum of Sodium-dependent Multivitamin Transporter Deficiency (SMVTD, MIM # 618973).

METHODS: Single case report including untargeted metabolomic profiles generated from plasma derived from venous whole blood. Individual patient samples were compared to a set of invariant anchor specimens included in each batch to achieve a semiquantitative analysis of metabolites. Raw spectral intensity values were then normalized to anchor samples, log-transformed, and compared to a normal reference population to generate Z-scores.

RESULTS: Severe biallelic loss-of-function variants in SLC5A6 (MIM #604024) impair the absorption of biotin, pantothenate, and lipoic acid, leading to SMVTD. Reported phenotypes include developmental delays, brain atrophy, epilepsy, peripheral neuropathy, and gastrointestinal, immunological, and cutaneous abnormalities. We describe a twenty-four-year-old female with autism spectrum disorder (ASD) who presented at fifteen years of age with altered mental status and rhabdomyolysis (CK >15,000 U/L) in the setting of a metabolic crisis. Exome Sequencing identified compound heterozygous variants in SLC5A6; NM_021095.4: c.1865_1866del (p.Gln622fs), a known pathogenic variant, and NM_021095.4: c.814G>A (p.Gly272Arg), an unpublished variant of uncertain significance. Plasma untargeted metabolomics analysis demonstrated reductions in pantothenate (z-score -2.6), lipid, and CoA metabolism, indicating impaired fatty acid oxidation, consistent with SMVTD. Replacement with biotin, lipoic acid, and pantothenic acid improved her metabolic and neurocognitive function.

CONCLUSIONS: Our patient is the oldest reported at the time of diagnosis of SMVTD and indicates that metabolic decompensations may not develop until the teenage years. Our work identifies ASD and rhabdomyolysis as novel features of SMVTD and suggests that untargeted metabolomics analyses may help establish a diagnosis.

KEYWORDS: Neurometabolic, Neurogenetics, Neurodevelopmental Disorders

279. Qualitative Assessment of the Validity and Standardization of the Swallow Domain in the 5-Domain Niemann-Pick disease type C Clinical Severity Scale (5DNPCCSS)

Berry-Kravis E (Chicago, IL), LaGorio L A, í Dali C, Gallo D

OBJECTIVE: Niemann Pick disease type C (NPC) is a rare, progressive neurodegenerative disorder. The 5DNPCCSS is a validated clinician-reported outcome tool assessing clinical severity and disease progression across 5 domains (ambulation, fine motor, speech, swallow, and cognition). The 5DNPCCSS was the primary endpoint in the arimoclomol phase 2/3 study in NPC (NCT02612129). We reassessed the relevance of individual swallow domain scoring options, scoring guidance and linearity of the scoring algorithm via qualitative interview study in response to health authority feedback.

METHODS: Qualitative semi-structured interviews were conducted by an independent research organization with 12 NPC and swallow experts. Interview questions were designed to capture insights on swallow domain assessment and structure, followed by cognitive debriefing to evaluate swallow domain content validity.

RESULTS: Clinical experts indicated that swallow domain scoring instructions yield clear, consistent interpretation of

response categories, without the need for performance-based measures of swallow. Expert feedback yielded a more linear scoring algorithm of the swallow domain, which reranked score categories for dysphagia by frequency (intermittent=2 vs consistent=3), applied a supplemental tube-feeding score of 4 and a tube-feeding-only score of 5. Applying this algorithm to NCT02612129 outcomes yielded a rescored 4-Domain NPCCSS (omitting cognition based on health authority guidance) treatment difference for change in score from baseline to 12 months of -1.51 (P=0.0413) in favor of arimoclomol vs placebo.

CONCLUSIONS: Data from a qualitative swallow study indicate that the 5DNPCCSS swallow score reflects the patient's level of dysfunction and that a change in score reflects actual improvement or worsening in a patient's swallowing function.

KEYWORDS: Neurometabolic, Experimental Therapeutics, Neurodevelopmental Disorders

280. Leukoencephalopathy Secondary to Fentanyl Toxicity in an Infant

Devaraj A D (Brooklyn, NY), Fidaan E F, Chari G C

OBJECTIVE: To underscore the importance of considering toxic exposures, particularly fentanyl, in the differential diagnosis of mental status changes and respiratory compromise.

METHODS: This case highlights a complex presentation of a 12-month-old normally developed female who was admitted to PICU with acute hypoxic respiratory failure, altered mental status, and metabolic acidosis. Initial clinical findings included saturation in the 60s, initial hypothermia followed by fever, fluctuating blood glucose levels, transaminitis, elevated INR, and acute kidney injury (AKI). A comprehensive workup confirmed fentanyl in the urine, indicating opioid exposure as a significant contributing factor. Chest X-ray findings suggested pulmonary edema, a recognized complication of opioid toxicity. Other investigations were non-contributory. The patient gradually improved and returned to baseline after four days. MRI of the brain revealed multiple areas of signal abnormality with peripheral enhancement in the subcortical and periventricular white matter seen in leukodystrophy, however, the pattern was atypical for such a diagnosis, especially in the absence of clinical features in the past. Notably, similar MRI findings have been reported in adult cases of certain opiate exposures.

RESULTS: Post-discharge, the patient followed up at pediatric neurology clinic. Her growth and development were deemed appropriate for age, and her neurological examination was normal. A repeat MRI has been scheduled to monitor long term changes.

CONCLUSIONS: This case highlights the challenges of detecting fentanyl ingestion in children due to often unrevealing clinical histories and the absence of fentanyl screening in standard toxicology tests. Prompt identification and naloxone administration as needed are vital to effectively counteract opioid-induced effects.

KEYWORDS: Neurometabolic

NEUROMUSCULAR

281. RGX-202, an investigational gene therapy for the treatment of Duchenne Muscular Dystrophy: interim clinical data

Dastgir J (Rockville, MD), Veerapandiyan A, Rao V, Tesi-Rocha C, Harper A, Iannacone S, Falabella P, Pakola S, Phillips D, Wilson C, Boulos N, Gilmor M, Patel H, Fiscella M, Danos O

OBJECTIVE: Duchenne is a severe, progressive, degenerative muscle disease caused by mutations in the DMD gene which encodes for dystrophin, without which muscles degenerate and become weak, eventually leading to loss of movement and independence, required support for breathing, cardiomyopathy, and premature death.

Investigational RGX-202 is designed to deliver a transgene for a novel microdystrophin that includes functional elements of the C-Terminal (CT) domain, imparting RGX-202 microdystrophin with important biology similar to naturally occurring dystrophin.

METHODS: The multicenter, open-label phase I/II AFFINITY DUCHENNE® trial is evaluating the safety, tolerability, and clinical efficacy of a one-time intravenous (IV) dose of RGX-202 in patients with Duchenne.

RESULTS: As of February 28, 2024, RGX-202 has been well tolerated with no drug-related serious adverse events in five patients, aged 4 yrs 4 mo to 12 years 0 mo at dosing who received either dose level 1 (1x1014 genome copies (GC)/kg body weight) or dose level 2 (2x1014 GC/kg body weight). Patients who reached the three-month follow-up completed the protocol immunosuppression regimen.

Patients across both dose levels demonstrated robust RGX-202 microdystrophin expression three months following RGX-202 administration. Among patients aged 8 to 11 years old at screening, RGX-202 microdystrophin levels were higher in dose level 2 than 1. In the first patient who received RGX-202 dose level 2 (12 yrs 0 mo at dosing), RGX-202 microdystrophin expression (western blot Jess) was 75.7% compared to control.

CONCLUSIONS: At both dose levels, RGX-202 has been well tolerated and demonstrated robust RGX-202 microdystrophin expression in boys with DMD 4-12 years of age.

KEYWORDS: Neuromuscular, Experimental Therapeutics, Movement Disorders

282. Risdiplam clinical trial outcomes in individuals with spinal muscular atrophy (SMA) and four SMN2 copies

Toy F (San Francisco, CA), Bertini E, Chiriboga C A, Mercuri E, Dickendesher T, Li Y, Martin C, Palfreeman L, Tam S, Yeung W

OBJECTIVE: SMA is a genetic, progressive neuromuscular disease characterized by motor neuron loss. Three disease-modifying therapies (DMTs) are available for SMA, including risdiplam (EVRYSDI®), an orally administered SMN2 pre-mRNA splicing modifier. SMN2 copy number does not fully predict the disease phenotype; some individuals with

SMA and four SMN2 copies continue to decline with age and have significant comorbidities. Evidence suggests earlier treatment with an SMA DMT leads to better outcomes. This research presents results from risdiplam clinical trials that explore the impact of risdiplam on outcomes in individuals with SMA and four SMN2 copies.

METHODS: Data from SUNFISH Part 2 (NCT02908685), JEWELFISH (NCT03032172) and RAINBOWFISH (NCT03779334) were analyzed. Motor function outcomes, as measured by 32-item Motor Function Measure, Revised Upper Limb Module and Hammersmith Functional Motor Scale–Expanded from SUNFISH and JEWELFISH, and Bayley Scales of Infant and Toddler Development, third edition, Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders and Hammersmith Infant Neurological Examination, Module 2 from RAINBOWFISH, were assessed. Outcomes in individuals with four SMN2 copies (≥4 SMN2 copies for RAINBOWFISH) were compared with their corresponding overall study population.

RESULTS: Treatment outcomes with risdiplam for individuals with four SMN2 copies were consistent with the overall study populations. Data from SUNFISH, JEWELFISH and RAINBOWFISH also showed a consistent risdiplam safety profile between individuals with four SMN2 copies and overall study populations.

CONCLUSIONS: Individuals with SMA and four SMN2 copies showed benefit from risdiplam in various clinical endpoints, although sample size for this subgroup is small in the risdiplam clinical trial program.

KEYWORDS: Neuromuscular

283. ACTA1-related cardiomyopathy: emerging genotypic and phenotypic patterns among patients with ACTA1-related myopathy with cardiac involvement

McAnally M M (Bethesda, MD), Potticary A, Hayes L H, Clayton J, Haliloğlu G, Donkervoort S, Yang M, Gibbons M, Gross B, Matesanz S, Medne L, Yum S, Yun P, Ghaoui R, Haberlová J Quinn C, Dilley R, Leach M, Chatfield K, Saade D, Foley A, Guglieri M, Lee T, Munot P, Sarkozy A, Muntoni F, Straub V, Laing N, Beggs A, Bönnemann C

OBJECTIVE: ACTA1 encodes skeletal muscle α-actin, the principal actin isoform and central component of sarcomeric thin filaments necessary for producing skeletal muscle contraction. Heterozygous pathogenic variants in ACTA1 cause myopathy with histopathologic features ranging from nemaline rods or actin aggregates to non-specific myopathic findings. The clinical spectrum ranges from severe congenital weakness and respiratory failure to milder childhood or adult-onset myopathy. Cardiac involvement is not commonly recognized, as the predominant cardiac actin isoform is encoded by ACTC1, separate from skeletal actin. Nonetheless, rare, published reports describe cardiomyopathy related to ACTA1. Here we present clinical, genetic, and histopathologic data for 25 patients with ACTA1-related cardiomyopathy (CM), representing the largest single cohort to date, establishing ACTA1 as a causative cardiac disease gene.

METHODS: We performed a retrospective cohort analysis of patients with ACTA1-related myopathy and cardiomyopathy.

RESULTS: The present study comprises 18 dilated cardiomyopathy (DCM), four hypertrophic cardiomyopathy (HCM), one mixed DCM/HCM, and two unclassified CM cases. We report four novel ACTA1 variants previously unreported in either skeletal or cardiac myopathy and 13 novel cardiac variants previously reported in ACTA1-myopathy without associated cardiac phenotype. Isolated congenital fiber type disproportion (CFTD) emerges as the predominant histopathologic feature in those with ACTA1-CM. Two distinct phenotypes surface, namely those with neonatal-onset profoundly severe congenital myopathy with associated early-onset HCM and those with childhood or adult-onset mild skeletal myopathy with rigid spine and severe, rapidly progressive DCM often necessitating transplantation.

CONCLUSIONS: Recognizing the possibility of ACTA1-related cardiac involvement is critical to promoting investigation into the pathophysiologic underpinnings of this disease.

KEYWORDS: Neuromuscular, Early Stage Investigator, Lifespan Manifestations of Childhood Onset Conditions

284. When the strong become weak: Myasthenia Gravis in an elite female teen athlete

Chakrapani T L (Portland, OR), Finanger E

OBJECTIVE: We report a case of juvenile myasthenia gravis with delayed diagnosis due to under recognized weakness in an elite female athlete.

METHODS: A retrospective chart review was conducted on a 15-year-old elite female swimmer presenting with exercise-induced shortness of breath, decreased sports performance, air hunger when racing, low PO2, voice change, and post race slurring of speech. Clinical documentation, laboratory evaluation and objective treatment response measures are recorded.

RESULTS: The patient presented with shortness of breath (SOB) when swimming and PO2 in the low 90s as measured by her Apple watch. Symptoms began after suspected COVID and Flu illnesses. Before this, the patient had just won regionals for the 1650-yard freestyle. Despite normal PFTs and laryngoscopy, she was diagnosed with exercise-induced asthma and vocal cord dysfunction. She was prescribed prednisone, budesonide/formoterol, and albuterol. Her SOB improved. Subsequent methacholine challenge PFT was done to evaluate for exercise-induced asthma. Budesonide/formoterol was stopped 10 days prior. The PFTs noted an unusual 71% drop in FEV1 at the 2nd tested dose. The subsequent week the patient experienced extreme weakness after swimming with the inability to pull herself out of the pool. She had ptosis and facial asymmetry which prompted a referral to pediatric neurology. Labs were ordered demonstrating high ACHr blocking, binding, and modulating antibodies. She was diagnosed with Juvenile Myasthenia Gravis.

CONCLUSIONS: This case highlights an unusual presentation of Myasthenia Gravis and demonstrates how young athletes can have significant reserves making diagnosis more challenging.
KEYWORDS: Neuromuscular, Early Stage Investigator

285. UGDH Variants Cause Congenital Muscular Dystrophy with Hypoglycosylation of α-Dystroglycan

Reelfs A M (Iowa City, IA), Stephan C M, Czech T M, Cox M, Joseph S Darbro B, Moore S, Campbell K, Mathews K

OBJECTIVE: Biallelic variants in UGDH have been associated with hypotonia, developmental delay, and epilepsy. The UGDH protein product generates substrates for synthesis of matriglycan on α-dystroglycan (α-DG). We report the first pathologic evidence of congenital muscular dystrophy (CMD) due to hypoglycosylation of α-DG in siblings with UGDH variants.
METHODS: We reviewed electronic medical records of two siblings followed for CMD. Clinical whole exome sequencing from both siblings and parents was independently analyzed with VarSeq v2.5.0 (including annotation, segregation, and minor allele frequency filtering) and PhoRank gene ranking. A diagnostic muscle biopsy from patient 1 was evaluated with immunofluorescence and western blotting.
RESULTS: Both brothers (current ages 10 and 5 years) presented at approximately 6 months with developmental delay and elevated creatine kinase (771-2108 U/L). They walked at 2 and 4 years, respectively, and have acquired minimal language. Patient 1 developed seizures at age 9; his brain MRI was normal. They shared two UGDH variants in trans. In silico analysis predicted that c.305G>A (p.R102Q) alters UGDH function and c.265-6C>G causes nonsense-mediated decay secondary to a splicing defect. The muscle biopsy showed necrotizing myopathy with reduced glycospecific α-DG immunostaining; α-DG hypoglycosylation was confirmed with western blot.
CONCLUSIONS: While studies of protein function imply UGDH variants could cause dystroglycanopathy, this is the first evidence of dystroglycanopathy pathology in muscle. We hypothesize that our reported UGDH variants alter synthesis of UDP-glucuronate and downstream UDP-xylose (substrates for α-DG glycosylation) and suggest that UGDH is a new dystroglycanopathy gene. Our CMD cases best fit a muscle-eye-brain phenotype.
KEYWORDS: Neuromuscular, Neurogenetics, Epilepsy

286. Early-Onset RAPSYN-Related Congenital Myasthenia Syndrome Responsive to Oral Albuterol

Consing K (Gainesville, FL), Zingariello C

OBJECTIVE: A newborn male born 38w4d was admitted to the neonatal intensive care unit with retrognathia, high-arched palate, arthrogryposis multiplex congenital, hypotonia and hypoxic respiratory failure. Based on family history, his symptoms were suggestive of RAPSYN-related congenital myasthenic syndrome (CMS) which was confirmed with genetic testing. His course was complicated by hypoventilation and poor oral feeding requiring a second-line agent after pyridostigmine. We present a unique case of early-onset RAPSYN-related congenital myasthenic syndrome responsive to oral albuterol.
METHODS: N/A
RESULTS: Pyridostigmine was started immediately with high suspicion of CMS. At 2 weeks old, oral liquid albuterol (2mg/5 ml) was started at 0.1 mg/kg/day divided three times a day after frequent admissions for acute respiratory failure and poor oral feeding. At 3 months old, tracheostomy was performed. A gastrostomy tube was placed at 3 months of age. At 5 months, he demonstrated marked motor improvements in the ability to mildly elevate his head, good head control when seated, kicking his feet antigravity, and reaching for toys with his hands with attempts to transfer while lying supine.
CONCLUSIONS: Albuterol has been studied previously in symptomatic management of gene-related CMS including DOK7 myasthenia and end-plate acetylcholinesterase deficiency but has not been evaluated in RAPSYN-related CMS. The physiology behind the improvement of neuromuscular transmission with albuterol in this condition is unknown. There are no current guidelines on the management of RAPSYN-related CMS. This case study shows that oral albuterol may have beneficial effects in the treatment of RAPSYN-related CMS.
KEYWORDS: Neuromuscular

287. Assessing Concordance Between Electronic Medical Record-Sourced Clinical Data Registry and Caregiver-Reported Patient Outcomes in Pediatric Spinal Muscular Atrophy

Welsh E F (Elk Grove Village, IL), Whitmire S M, Belter L, Curry M, Schroth M

OBJECTIVE: This study aims to assess the concordance of electronic medical record (EMR) data from a spinal muscular atrophy (SMA) clinical data registry (CDR) and caregiver-reported patient-outcomes from an annual SMA community update survey (CUS).
METHODS: Pediatric SMA patients (<18 years) from the CDR were deterministically matched with CUS respondents from 2021-2023, excluding individuals with non-5q SMA, international residence, and limited data sharing in the CDR. Surgical history data, including scoliosis intervention, gastrointestinal surgeries, and tracheotomies, were compared. Concordance was assessed using positive and negative percent agreement (PPA; NPA) and Cohen's kappa statistic.
RESULTS: Analysis included 132 pediatric patients with SMA from 19 care centers; was 48% female, 52% male, a mean current age of 7.6 (s.d. 4.3) years, and SMA type distribution of 41% Type 1, 35% Type 2, 11% Type 3, and 13% unknown. Substantial agreement was found for gastrointestinal surgeries (PPA = 92.68%; NPA = 96.43%; kappa = 0.78), and perfect agreement for tracheotomies (PPA = 100%; NPA = 100%; kappa = 1). Scoliosis intervention analysis included 104 individuals at 16 care centers with procedure data and showed substantial agreement (PPA = 71.43%; NPA = 100%; kappa = 0.78). Additional analyses will be presented.

CONCLUSIONS: The EMR-sourced CDR demonstrates significant agreement with caregiver-reported data from the CUS, suggesting its close representation of the pediatric SMA population. While discrepancies highlight the need for further exploration, overall concordance supports the utility of both sources for comprehensive understanding and management of SMA.
KEYWORDS: Neuromuscular

288. Impact of Vamorolone, Prednisone, and Placebo on Linear Growth in VISION-DMD (VBP15-004) Study, as Measured by Changes in Height Over 6 Months

de Vera A (Pratteln, Switzerland), Rooman R, Hoffman E P, Clemens R, Kasun K, Guglieri M

OBJECTIVE: Corticosteroids are recommended as standard of care for patients with Duchenne muscular dystrophy (DMD). However, children with DMD are on average shorter than the general population by age 5, and daily dosing with prednisone or deflazacort leads to further stunting of growth. In the phase 2b VISION-DMD study (NCT03439670), height percentile was shown to decline from baseline to month 6 in patients treated with prednisone, but not those treated with the dissociative corticosteroid vamorolone at 6mg/kg/d. We aim to study the impact on linear growth by reporting unadjusted and patient-level changes in height (cm) over 6 months.
METHODS: Boys aged 4 to <7y were randomized to placebo, prednisone 0.75mg/kg/d, vamorolone 2mg/kg/d, or vamorolone 6mg/kg/d. Height was recorded at baseline and 12-week intervals. This analysis included 118 participants in the safety population.
RESULTS: At baseline, median height was 106-111cm across treatment groups. After 6 months of treatment, increases were lower in the prednisone group (n=30, 2.60cm) than placebo (n=28, 3.55cm, P=0.03) or vamorolone 6mg/kg/day group (n=26, 3.50cm, P=0.009). There were no significant differences in median height increase between the vamorolone group and placebo (P>0.1). In the prednisone group, 30.0% of children showed reductions in height z-score ≥0.2 SDs after 6 months compared with 18.5% in the vamorolone 2mg/kg/d group, 10.7% in the placebo group, and 0 children in the vamorolone 6mg/kg/d group.
CONCLUSIONS: In patients with DMD aged 4 to <7y, absolute height (cm) values after 6 months of treatment showed similar increases with vamorolone and placebo, while growth stunting was observed with prednisone.
KEYWORDS: Neuromuscular

289. Evaluation of behavioral problems in the VISION-DMD study of vamorolone vs prednisone in Duchenne muscular dystrophy (DMD)

de Vera A (Pratteln, Switzerland), Rooman R, Hoffman E P, Clemens P, Kasun K, Guglieri M

OBJECTIVE: Psychiatric adverse effects during systemic corticosteroid therapy are common and well-documented. Here we report the frequency of behavioral problems in the phase 2b VISION-DMD study (NCT03439670) using the Personal Adjustment and Role Skills (PARS) III Scale, a validated index of youth psychosocial adjustment in DMD.
METHODS: During the trial, patients were randomized to placebo, prednisone 0.75 mg/kg/day, or vamorolone at 2 or 6 mg/kg/day. PARS III subscales assessed by parents were normalized as z-scores using historical data. Clinically relevant worsening in PARS III subscales was defined as a shift from normal baseline adjustment score (z-score <1) to an abnormal score (z-score ≥1) at week 24.
RESULTS: Moderate or severe behavioral adverse events (BAEs) were more frequent in the prednisone group (22.6%) than in any other arm (≤3.4% in all other groups). One patient on prednisone discontinued due to a severe BAE. Clinical worsening in hostility was more frequent with prednisone (26.1%) than vamorolone 6 mg/kg/day (15.4%) or 2 mg/kg/day (9.1%) or placebo (8.0%). Clinical worsening in dependency and productivity was reported in >20% of patients with prednisone (24.0% and 26.9%, respectively) compared with <10% in any other group.
CONCLUSIONS: Vamorolone 6 mg/kg/day was associated with an increase in mainly mild BAEs compared with placebo, but with a lower frequency and severity of BAEs reported compared with prednisone. PARS III subscales showed a reduced risk for psychosocial adjustment/functioning in hostility, dependency, and productivity with vamorolone compared with prednisone.
KEYWORDS: Neuromuscular

290. Vamorolone dose titration in expanded access protocols (EAPs) and its impact on rates of weight change in patients with Duchenne muscular dystrophy (DMD)

de Vera A (Pratteln, Switzerland), Rooman R, Hoffman E P, Clemens P, Kasun K, Guglieri M

OBJECTIVE: Vamorolone, recommended at 6mg/kg/day in children with DMD, is associated with a dose-dependent risk of weight gain. We report the EAPs experience with vamorolone dose titration and impact on weight percentiles.
METHODS: Patients completed studies VBP15-LTE, VBP15-004, or VBP15-006 and enrolled in 1 of 3 EAPs (US, Canada, or Israel). Available data were pooled. The down-titration set (DTS; N=17) included patients with ≥3 weight measurements on vamorolone 6 mg/kg/day, followed by ≥3 weights after down-titrating to 4 mg/kg/day. The up-titration set (UTS; N=16) included patients with ≥3 weight measurements on vamorolone 2 mg/kg/day followed by ≥3 weights after up-titrating to 4 mg/kg/day. Annualized changes in weight percentiles were estimated using mixed models.
RESULTS: Median duration of vamorolone exposure in EAPs (N=99) was 2.1 years. Most patients received vamorolone 4 mg/kg/day (58/99 [58.6%]) or 6mg/kg/day (57/99 [57.6%]), with a smaller proportion dosed at 2 mg/kg/day (21/99 [21.2%]). Adverse events leading to dose reduction, mainly weight gain, were reported by 14% of patients who received vamorolone 6 mg/kg/day. In the DTS, annual rate of change (ARC) in weight percentiles (95% CI) decreased from 19.0 (7.5-30.5) at 6 mg/kg/day to 4.6 (–

0.8-9.9) at 4 mg/kg/day. In the UTS, ARC in weight percentiles (95% CI) remained stable despite dose increase, changing from 12.4 (0.4-24.3) at 2 mg/kg/day to 10.6 (3.8-17.4) at 4 mg/kg/day.
CONCLUSIONS: Down-titration from vamorolone 6 to 4mg/kg/day resulted in a reduction of further weight gain. No evidence of increased weight gain risk was observed in patients up-titrated from 2 to 4 mg/kg/day.
KEYWORDS: Neuromuscular

291. A Clinical Nomogram that Predicts Creatine Kinase Elevation in Dried Blood Spot Newborn Screening Not Attributable to Duchenne Muscular Dystrophy

Falk E N (Boston, MA), Chrzanowski S, Coyne F, Sheldon Y, Cherkerzian S, Parad R

OBJECTIVE: Early diagnosis of Duchenne Muscular Dystrophy (DMD) is needed as disease modifying therapies become available. If DMD NBS with CK is implemented, all newborns will have CK levels reported at birth. Numerous parturitional and newborn factors unrelated to DMD may transiently elevate CK above established cutoffs. Predictive modeling may aid the clinician in positive DMD NBS interpretation.
METHODS: 8385 newborns receiving the DMD NBS in this prospective cohort study were used for derivation and internal validation of a predictive model for elevated CK values. Candidate predictors were evaluated using unadjusted logistic regression. The multivariable prediction model was derived using backward stepwise logistic regression. The final model was externally validated in a subsequent cohort of 2653 newborns. None of the infants in either the derivation or external validation datasets met criteria for DMD after DMD diagnostic testing.
RESULTS: Univariate analyses revealed multiple maternal and neonatal demographic and parturitional predictors associated with elevated CK including: neonatal sex, gestational age, birth weight, APGAR scores, resuscitation need, sample collection time, maternal ethnicity, primiparity, prior C-section, C-section indication, labor and delivery complications, oxytocin, forceps or vacuum assisted delivery, and duration of ruptured membranes. Results of the final multivariable prediction model were summarized in a clinical nomogram and included: gestational age, time of DBS collection, parity, shoulder dystocia, resuscitation, and forceps or vacuum use in delivery.
CONCLUSIONS: Consideration of elevated CK predictors during labor and birth can help to interpret elevated CK that could be screened as concerning for DMD on NBS but attributable to other factors.
KEYWORDS: Neuromuscular

292. Juvenile ALS masquerading as an acquired inflammatory neuropathy

Massrey C (Houston, TX), Walimbe A, Das A, Fisher K, Avula S, Lotze T

OBJECTIVE: To describe a patient with juvenile ALS initially presenting with features suggestive of an acquired inflammatory neuropathy.
METHODS: Case report
RESULTS: A 16-year-old female with a learning disability initially presented with seven months of proximal muscle weakness. She had preserved reflexes, but cerebrospinal fluid (CSF) showed albumino-cytologic dissociation. Post-contrast MRI of the spine demonstrated peripheral nerve root enhancement, suggesting an acquired inflammatory neuropathy. There was little clinical improvement with IVIG, steroids, and PLEX. An EMG demonstrated fibrillation potentials, severely decreased motor amplitudes, and prolonged motor latencies, consistent with axonal neuropathy. A muscle biopsy corroborated these findings. Chromosomal Microarray (CMA) and duo-whole exome sequencing (WES) reported no pathogenic variants related to the described phenotype of chronic, progressive weakness with neuropathic features. With non-diagnostic genetic studies, an inflammatory neuropathy remained a consideration, and rituximab and monthly IVIG were started. She presented to our institution with acute respiratory failure requiring tracheostomy, flaccid quadriplegia, areflexia, tongue atrophy, fasciculations, and polyminimyoclonus. WES re-analysis was performed with updates to the phenotype, including concern for motor neuron disease. This revealed de novo homozygous pathogenic variants in the FUS gene (c.1573C>T, p.P525S), consistent with juvenile Amyotrophic Lateral Sclerosis (ALS) Type 6.
CONCLUSIONS: We demonstrate a clinical presentation of juvenile ALS that began with progressive weakness accompanied by CSF albumino-cytologic dissociation, nerve root enhancement on MRI, and an initially non-diagnostic genetic work-up mimicking an acquired inflammatory neuropathy. Our study highlights how features of juvenile ALS can mimic an inflammatory neuropathy and the benefit of WES re-analysis when the clinical phenotype has evolved.
KEYWORDS: Neuromuscular

293. Phenotypic Variability of Seronegative Myasthenia Gravis in Children

Fay A J (San Francisco, CA), Strober J

OBJECTIVE: This study aims to retrospectively characterize a cohort of children with seronegative myasthenia gravis (17), compared to those with seropositive disease (18).
METHODS: We analyzed patients' symptoms, co-existing diagnoses, exam findings, results of antibody and electrodiagnostic testing, and response to treatments among a cohort of 35 children with myasthenia gravis over 7 years, and compared seronegative to seropositive patients. Diagnosis of seronegative myasthenia required a pattern of fluctuating weakness and one or more of the following: positive response to an acetylcholinesterase inhibitor such as pyridostigmine and/or a > 10% decremental response with low-frequency RNS or positive SFEMG.
RESULTS: We identified several distinct phenotypes among seronegative patients. These include children with autoinflammatory disorders, children with pain-associated myasthenia, those with a slow channel syndrome-like phenotype, and ocular myasthenia. Several children in the seronegative group required ICU care and plasma exchange, underscoring the severity of seronegative MG. Furthermore, some seronegative children without characteristic 10 %

decremental response on repetitive nerve stimulation showed severe symptoms and a robust response to immunotherapies, including IVIg, plasma exchange and rituximab. We also discuss use of several medications not reported in the pediatric MC literature, including eculizumab, efgartigimod, daratumumab and obinutuzumab.
CONCLUSIONS: Children with seronegative myasthenia may manifest with diverse phenotypes, and sometimes do not have characteristic findings on repetitive nerve stimulation, making diagnosis more challenging. Nonetheless, they can suffer from severe disease and may respond well to immunotherapy, including monoclonal antibody treatments, highlighting the need to correctly diagnose children with MG early in their disease course.
KEYWORDS: Neuromuscular

294. Pediatric FSHD in the US: Results from the US National Registry for FSHD

Katz N (Durham, NC), McHan L, McDermott M, Tawil R, Statland J

OBJECTIVE: Pediatric-onset FSHD accounts for approximately 20% of individuals with facioscapulohumeral muscular dystrophy (FSHD), approximately half of whom meet criteria for early-onset FSHD. Few prospective studies exist to inform our understanding of disease progression in pediatric FSHD, which creates a barrier to clinical care and drug development.
METHODS: We analyzed prospectively collected data from participants in the US National Registry for FSHD who were diagnosed ≤ 18 years of age. Early-onset was defined as diagnosis ≤ 10 years of age.
RESULTS: A total of 166 individuals with genetically confirmed FSHD were identified. Individuals with 1-3 D4Z4 repeats were diagnosed ($p < 0.001$) and progressed to wheelchair use ($p < 0.001$) at a younger age than those with 4+ D4Z4 repeats. When separated by sex, females were more likely to: be diagnosed at a younger age than males ($p < 0.001$), independent of D4Z4 repeat size ($p < 0.001$); be diagnosed ≤ 10 years of age ($p < 0.001$); report facial weakness as their initial symptom ($p = 0.001$); progress to wheelchair use ($p < 0.001$) and at a faster rate ($p = 0.007$) than males, independent of genetics.
CONCLUSIONS: This is one of the largest analyses of prospectively collected data from individuals diagnosed with pediatric onset FSHD in the US. These data suggest that females with pediatric-onset FSHD may be more severely than males. Larger, prospective studies are needed to further understand disease progression and sex differences in pediatric FSHD.
KEYWORDS: Neuromuscular, Early Stage Investigator, Lifespan Manifestations of Childhood Onset Conditions

295. The Efficacy of Givinostat in patients with Muscular Dystrophy: A Systematic Review

Al Shouli R (Sharjah, United Arab Emirates), Sohal A

OBJECTIVE: Muscular Dystrophy (MD) is a group of hereditary disorders characterized by progressive generalized muscle weakness and degeneration. Recent studies evaluated the role of givinostat in treating MD. So, we aimed in our systematic review to assess the efficacy of givinostat in MD.
METHODS: PubMed, ScienceDirect, and Cochrane databases were searched using a pre-defined search strategy from inception until April-2024 following the standard method of Cochrane Handbook and the PRISMA-statement guidelines. All clinical trials studying Givinostat in patients with MD were included.
RESULTS: Three clinical trials with a total of 250 participants were included, two of these tested givinostat efficacy in DMD and the other in BMD. One of these primarily investigated the givinostat histological effect in DMD and revealed that it increased the fraction of muscle tissue by 29.1%, and cross-sectional area by 77%. And reduced the amount of necrosis by 43.5% and fatty replacement by 37.5%. The second study tested its effect in BMD and reported that mean total fibrosis didn't change in the treatment or placebo group, and the two groups didn't differ at Month-12 (least squares mean [LSM] difference 1.04%; $p = 0.8282$). MRI fat fraction didn't change as well. The third study tested the effect of givinostat in DMD and indicated the geometric LSM ratio at 12-months of treatment was 1·27 (95% CI 1·17–1·37) in givinostat group and 1·48 (1·32–1·66) in placebo group ($p=0·035$).
CONCLUSIONS: Our systematic review revealed that givinostat has favorable outcomes in functional tests and histological findings in DMD patients, but not in patients with BMD.
KEYWORDS: Neuromuscular

NEURO-ONCOLOGY

296. Oncolytic Adenoviral Treatment of Primary Brain Tumors: A Scoping Review

Horak V J (Chicago, IL), Alleman K, Bae G, Gulsuna B, Jimenez M J, Kucera A E, Wang R, Wescott A B, Marr R, Peterson D A, Eliot L, DeCuypere M G

OBJECTIVE: Oncolytic virotherapy (OVT) is a promising cancer treatment. Adenovirus (AdV) is modified to target and destroy tumor cells, triggering cytokine release to boost the immune response. This potentially complements other therapies without added side effects. Our scoping review gathers literature on adenoviral OVT for primary brain cancer and evaluate quantitative and qualitative patient outcomes.
METHODS: Following PRISMA-ScR protocol, articles were obtained from PubMed, Embase, Scopus, The Cochrane Library, CINAHL, and ProQuest Dissertations & Theses Global. Independent screeners reviewed titles, abstracts, and texts. Screener bias was calculated with a Fleiss' Kappa. We included reports published in English until March 1, 2023, and articles related to randomized clinical trials, case studies, and case series.
RESULTS: We included 14 of the 1199 screened reports published from 2004-2023 containing 14 clinical trials related to primary brain tumor AdV OVT. Ten clinical trials were completed with phase I or phase I & II data for 161 patients, 141 adult and 20 pediatric, who completed

treatments with AdV OVT. A total of 972 adverse events were documented in the 7 clinical trials with available data, 808 occurred in adults and 164 occurred in children.
CONCLUSIONS: AdV OVTs have been used in adult and pediatric populations as a novel treatment for primary brain tumors. Insufficient data exists to determine improvement of survival outcomes when compared to standard-of-care regimens, particularly in pediatric populations. Ongoing research and understanding of immunomodulation provide optimism for future drug development and possible treatment success.
KEYWORDS: Neuro-oncology, Neuroimmunology

297. Alternating hemispheric slowing on EEG in three pediatric patients with suspected stoke-like migraine attacks after radiation therapy (SMART) syndrome

Kata K (St. Louis, MO), DeKorver N W, Hoke T, Lee M, Wright-Jin E, Dang M, Guerriero R

OBJECTIVE: SMART syndrome or stroke-like migraine attacks after radiation is a rare consequence of CNS tumor irradiation. It is often a diagnostic challenge with concern for tumor recurrence, infection, stroke, or seizure with monophasic or recurrent encephalopathy, focal neurologic deficits, or headache. Although seizures are described in SMART syndrome, the specific EEG features are not well characterized. We present a case series of three pediatric patients with suspected SMART syndrome with alternating hemispheric slowing during symptomatic phase.
METHODS: Case series with demographic, treatment, radiologic, neuro-diagnostic, and outcome data.
RESULTS: Each patient presented with lateralized paresis with concern for acute stroke. The initial MRI findings showed variable degrees of diffusion restriction, FLAIR changes, and suspicion for focal areas of decreased vascularity, but were without evidence of acute stroke. Initial EEG showed hemispheric slowing corresponding to the contralateral hemisphere to their deficits. Two patients had seizures on EEG shortly after presentation. In all patients, symptoms started to improve, and seizures resolved. However, each later developed new deficits on the contralateral side associated with hemispheric slowing without preceding seizure. All patients received treatment with improvement in function, and one had recurrence of symptoms at a later time point.
CONCLUSIONS: We identify a unique feature in suspected SMART syndrome, with alternating hemispheric slowing on EEG during symptomatic phase and in absence of preceding seizure. This is suggestive of independent focal cerebral dysfunction rather than post-ictal slowing and post-ictal paresis. We speculate possible prolonged lateralized spreading depression akin to aura in migraine resulting in focal neurologic deficits.
KEYWORDS: Neuro-oncology, Epilepsy

298. A presentation of Anti-NMDA encephalitis in a pediatric patient with history of posterior fossa ependymoma

Gupta D (Orange, CA), Fernandez A, Arellano J L

OBJECTIVE: Paraneoplastic anti-NMDAR encephalitis has previously been linked to ovarian tumors and rarely other tumors. Patients with ependymomas have not previously been linked to autoimmune/paraneoplastic encephalitis. Here, we present a case of a child that had total resection of a posterior fossa ependymoma six months prior to his presentation with intractable epilepsy.
METHODS: Patient is a 5-year-old male with a history of posterior fossa ependymoma with resection and radiotherapy who presented six months later with subtle personality changes, new onset seizure-like episodes and persistent oxygen desaturation. The patient was noted to have persistent seizures associated with oxygen desaturation requiring multiple anti-seizure medications.
RESULTS: Combined polysomnography and electroencephalogram(EEG) were performed to evaluate oxygen desaturation which showed focal seizures and central sleep apnea. EEG demonstrated right temporal and left temporal lobe seizures. Central sleep apnea was initially thought to be related to his history of posterior fossa resection. Magnetic resonance imaging was performed without recurrence of ependymoma. Given intractable epilepsy, work up for paraneoplastic and autoimmune processes were performed. He was found to have NMDAR antibodies in the cerebrospinal fluid, titer 1: 8. He was treated with intravenous immunoglobulin G and high dose corticosteroids. With treatment, the patient's seizure burden and central sleep apnea improved during his stay in the ICU.
CONCLUSIONS: This is one of the first cases described in the pediatric population of ependymoma and associated ANTI NMDAR encephalitis six months after resection, highlighting the importance of a broad differential.
KEYWORDS: Neuro-oncology, Neuroimmunology, Epilepsy

PEDIATRIC DEMYELINATING DISEASE

299. Racial, ethnic, and socioeconomic disparities in pediatric aquaporin-4 positive neuromyelitis optica spectrum disorder: A multicenter retrospective study

Poisson K E (Columbus, OH), Nguyen L, Horn P S, Wu H, Beck A, Wesselkamper K, Wheeler Y

OBJECTIVE: Only 5% of aquaporin-4 positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD) cases emerge during childhood. Poorer outcomes have been suggested in Black/African American (AA) adults with NMOSD, but limited data exist for children. We sought to evaluate the impact of health inequities on pediatric NMOSD outcomes.
METHODS: We retrospectively analyzed 38 patients (29 non-Hispanic Black/AA, 5 Hispanic White, and 4 non-Hispanic White) with pediatric AQP4+ NMOSD from three centers between 2009-2021. Patient addresses were connected to social determinants of health (SDOH) measures from the US Census. Pertinent outcomes were developed from clinical presentation/outcomes and healthcare utilization

in 2 years following diagnosis. Analyses used 2-sided t-test and Pearson/polyserial correlations.

RESULTS: Two years after diagnosis, compared to non-Hispanic Whites, Black/AA children had a significantly higher expanded disability status scale (EDSS) (2.46 vs. 0.33, p=0.003), 2.36 more inpatient admissions (p=0.002), and 28.4 more in-hospital days (p=0.002). Children of Hispanic ethnicity trended towards having fewer neurology appointments than non-Hispanic Whites (6.6 vs. 11.0, p=0.078). Children with public insurance had higher relapse rates (p=0.046). At 2 years and most recent follow-up, a significantly higher EDSS was found for children living in census tracts with a lower median income, higher deprivation index, and higher proportion of population on assisted income, in poverty, and with vacant housing.

CONCLUSIONS: We identified racial, ethnic, and socioeconomic disparities in clinical outcomes and healthcare utilization in pediatric AQP4+ NMOSD. Further prospective and household-level data is needed to dissect the interplay of genetics, SDOH, and racism so that interventions to optimize care may be developed.

KEYWORDS: Pediatric Demyelinating Disease, Diversity, Equity, Inclusion, Early Stage Investigator

300. Construct validity of the 10-meter walk/run test to assess motor impairment in patients with Alexander disease

Yarlas A (Carlsbad, CA), Harrington A, Kornafel T, Ballance E, Kopin K, Pierce S, Joung J, Gallison K, Liu G, Faig W, Collins A, Waldman A

OBJECTIVE: To evaluate construct validity of the 10-meter walk/run test (10MWRT) to capture motor impairments in patients with Alexander disease (AxD), a rare progressive astrocytopathy.

METHODS: A natural history study enrolled patients with clinical and radiographic features of AxD confirmed by genetic testing of GFAP. Clinical outcome assessments included 10MWRT, Gross Motor Function Measure-88 (GMFM-88), Peabody Developmental Motor Scales – 2nd Edition (PDMS-2), Pediatric Evaluation of Disability Inventory – Computer Adaptive Test (PEDI-CAT), Berg Balance Scale (BBS) or Pediatric Balance Scale (PBS), Gross Motor Function Classification System – Expanded and Revised (GMFCS-E&R), and Manual Ability Classification System (MACS). For 10MWRT, patients were instructed to walk or run as fast as possible from start to finish line; orthoses or assistive devices were allowed. Strength of associations between the fastest of three 10MWRT trials and concurrent assessments at first visit were evaluated by Pearson correlations (convergent validity) and numeric mean differences (known-groups validity).

RESULTS: Thirty patients (13 females; mean [standard deviation] age, 16.5 [15.3] years; range, 2.2–54.8 years) completed 10MWRT. Fastest 10MWRT time correlated strongly with GMFM-88 (domain E, r=0.82; total, r=0.79), PDMS-2 (<6 years, n=5; gross motor quotient, r=0.88), PEDI-CAT (n=14; mobility domain, r=0.86; activities domain, r=0.73), BBS (≥13 years, n=14; r=0.80), and PBS (<13 years, n=12; r=0.79). Stepwise numeric decreases in mean 10MWRT speed were observed with greater impairments on GMFCS-E&R and MACS. Sensitivity analyses using different approaches for assessing 10MWRT speed supported primary analyses.

CONCLUSIONS: Data support 10MWRT as a construct valid measure to capture motor function in patients with AxD.

KEYWORDS: Pediatric Demyelinating Disease, Movement Disorders

301. Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease Presenting as Pseudotumor Cerebri in 9 year old patient: a case report

York A (Valhalla, NY), Overby P, Wolf S, McGoldrick P, Nuoman R, Hirschberger R

OBJECTIVE: In the pediatric population, myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) shows a range of manifestations. It most commonly presents as acute disseminated encephalomeningitis (ADEM), optic neuritis, and/or transverse myelitis, but varying phenotypes continue to emerge. We present a case that began with Idiopathic Intracranial Hypertension followed by inflammatory myelitis.

METHODS: In this case study, we present a single patient with a unique presentation of MOGAD.

RESULTS: A nine year old presented to the emergency room with a four day history of persistent frontal headache and associated vomiting. Upon admission, lumbar puncture showed CSF elevated opening pressure with CSF pleocytosis and lymphocytic predominance. Initial brain MRI showed narrowing of the transverse sinuses without parenchymal signal change. Her headaches worsened despite treatment with Acetazolamide and a MOGAD syndrome was suspected. Anti MOG antibody testing was sent. Six days following admittance the patient developed confusion, urinary retention, and new lower extensor weakness with sensory loss. Steroids and IVIG were initiated. MRI revealed signal abnormalities within the gray and white matter of both the cervical and thoracic spinal cord consistent with an inflammatory myelitis. Anti MOG serum titers were positive. Following immunotherapy she was discharged with a normal neurological exam.

CONCLUSIONS: Pseudotumor cerebri-like presentation is an emerging manifestation of MOGAD. Pseudotumor combined with idiopathic elevated white blood cell count in a pediatric patient should raise suspicion for MOGAD and prompt anti MOG antibody testing.

KEYWORDS: Pediatric Demyelinating Disease

302. Neurofilament light chain as a predictor of post-transplant neurocognitive outcomes in childhood cerebral adrenoleukodystrophy

Pierpont E I (Minneapolis, MN), Gupta A O, Eisengart J B, Shanley R, Dobyns W, Nascene D, Orchard P, Lund T

OBJECTIVE: Cerebral adrenoleukodystrophy (C-ALD) is a neuroinflammatory disease that emerges unpredictably in some males with ALD, typically between 3 and 12 years of

age. Prior research has established that higher blood neurofilament light chain (NfL) levels in patients with C-ALD are associated with greater white matter lesion severity (Loes MRI scores) and that NfL levels reduce after treatment with hematopoietic stem cell transplantation (HSCT). The relationship of NfL to neurocognitive status in C-ALD patients has not yet been reported. This study investigated associations between pre-transplant NfL levels and neurocognitive test scores at 1-year following HSCT.

METHODS: Plasma NfL protein levels were measured by Simoa Assay in 24 patients with C-ALD (mean age: 8.1±2.8 years) at a median of 0.3 months pre-HSCT. White matter lesions were characterized by Loes MRI severity scores. Post-HSCT neurocognitive outcomes across six domains were measured at a median of 1.0 years post-HSCT using the Wechsler intelligence quotient (IQ) scales, the Beery-Buktenica Test of Visual-Motor Integration, and the Purdue Pegboard test.

RESULTS: Pre-HSCT NfL values in C-ALD patients ranged from 5.0-911.0 (median: 35.9). Higher NfL was associated with lower post-HSCT scores across all neurocognitive domains ($p<.01$). Large effect sizes were seen for visual reasoning, processing speed, fine motor dexterity, and visual-motor integration (Pearson correlations: $r=-0.77$ to -0.82).

CONCLUSIONS: NfL may serve not only as a useful biomarker to characterize emerging cerebral ALD, but it can also aid the prediction of key clinical outcomes after treatment. NfL may enhance prognostic counseling for patients undergoing stem cell therapies.

KEYWORDS: Pediatric Demyelinating Disease

303. Prevalence of corticospinal tract and cerebellar lesions in children and adults with X-linked adrenoleukodystrophy

Winter E (Boston, MA), Nagy A, Li Y, Rapalino O, Becker C, Locascio J, Eichler F

OBJECTIVE: Cerebral adrenoleukodystrophy (CALD), characterized by inflammatory cerebral demyelination, is a severe manifestation of ALD, a rare single-gene disorder. CALD onset can occur in childhood or adulthood. Isolated corticospinal tract (CST) lesions, where demyelination is confined to the CST, are a common feature of adrenomyeloneuropathy (AMN) but are not typically reported in childhood-onset CALD. Cerebellar lesions are uncommon but more prevalent with CST involvement. We aim to analyze MRIs for CST and cerebellar involvement in male ALD patients.

METHODS: 1219 MRIs were reviewed across 224 male ALD patients. Images were reviewed for T2 signal hyperintensities in the CST (corticospinal tracts, internal capsules, cerebellar peduncles, and brainstem) and cerebellum. Chi-squared tests were conducted to determine significance.

RESULTS: The average age at first MRI documenting an isolated CST lesion was 20.75 ± 14.77 years, with the youngest case being 6.19 years old. Isolated CST lesions were present in 9.0% of pediatric patients, which was not significantly different from the adult cohort (13.5%, $p=0.3848$). The prevalence of cerebellar lesions was not significantly different between pediatric (5.2%) and adult (9.0%) patients ($p=0.3713$). All patients with cerebellar lesions (except for one adult) also had CST lesions.

CONCLUSIONS: The similar prevalence of isolated CST involvement in pediatric and adult ALD patients suggests a potential overlap between long-tract axonopathy in AMN and childhood-onset CALD. Therefore, clinicians must monitor for isolated CST hyperintensities during CALD screening as a potential form of childhood-onset CALD.

KEYWORDS: Pediatric Demyelinating Disease, Neuroimaging, Neurogenetics

304. Demographics and healthcare use in Alexander Disease characterized from US national administrative data

Bonkowsky J L (Salt Lake City, UT), Edwards M R, Baker M, Householder K, Kymes S

OBJECTIVE: Alexander disease (AxD) is an ultra-rare genetic, progressive astrocytopathy that often presents as a leukodystrophy in children and as a neurodegenerative disease in adults. Prior to 2023, the lack of a specific ICD code for AxD prevented population-based research. Our objective was to improve understanding of the demographics and healthcare use in AxD using a newly developed ICD10-CM code for AxD.

METHODS: We performed a retrospective analysis of individuals with at least one claim for AxD (G31.86) between October 2023 and March 2024. Data was obtained from Compile Open Claims, a consolidator of claims from health care providers covering 300 million individuals in the United States. We analyzed the demographic characteristics, inpatient hospitalization and emergency room visits. Claims information was available for up to 7 years. Utilization measures were annualized for reporting.

RESULTS: 99 individuals were identified (age range 1-88). 44 were <20 years of age (mean age=10.8), 55 were ≥ 20 (mean age=48.6 years). 53% were female. Among those older than 20 years old, 58% were female, as were 45% of those 20 years old or younger. During the seven-year period, 63% were hospitalized at least once for an average of 2.4 inpatient visits/year. 64% of all patients visited the emergency room at least once per year on average.

CONCLUSIONS: This is the first population-based characterization of AxD demographics and healthcare usage and suggests a significant burden of disease. Enhanced understanding of people living with AxD will develop as the new ICD-10-CM code is broadly utilized.

KEYWORDS: Pediatric Demyelinating Disease, Lifespan Manifestations of Childhood Onset Conditions, Neurodevelopmental Disorders

305. Use of Rituximab as First-Line Therapy in Pediatric Multiple Sclerosis

Willis E (Little Rock, AR), Lewis H E, Haire J, Kiss A

OBJECTIVE: Pediatric multiple sclerosis (MS) presents significant therapeutic challenges due to the limited availability

of disease-modifying therapies (DMTs) specifically approved for children. Rituximab, a monoclonal antibody targeting CD20-positive B cells, has shown promise in adult MS populations but lacks extensive validation in pediatric cases. This retrospective case series aims to explore the efficacy and safety of Rituximab as first-line therapy in pediatric MS.

METHODS: We performed a retrospective chart review of pediatric onset MS patients who received Rituximab as first-line therapy from 2006 to 2023 at Arkansas Chidren's Hospital. We included patients under 18 years of age diagnosed with MS. Patients were excluded if they had received any other DMT prior to Rituximab.

RESULTS: 17 patients received Rituximab as first-line therapy. Median age of the group was 15. Average duration of Rituximab therapy was 89.18 weeks (range 21-216). 16 patients have had zero clinical relapses since starting Rituximab. 1 patient had a relapse prior to Rituximab becoming therapeutic (1 month after induction). All 10 patients who have been on Rituximab for >52 weeks and with follow up brain MRIs showed no new lesions. No serious adverse events have occurred in these patients.

CONCLUSIONS: We observed promising results that underscore the potential of this treatment approach. Notably, no patient has experienced a clinical relapse after Rituximab became therapeutic. Additionally, the absence of serious adverse events among our cohort suggests that Rituximab is not only effective but also safe for use in the pediatric MS population.

KEYWORDS: Pediatric Demyelinating Disease

306. Genetic autoimmunity and interferonopathies in pediatric patients with neuromyelitis optica spectrum disorder

Levine J M (Houston, TX), Fisher K S, Lotze T E, Lupski J, Calame D

OBJECTIVE: Neuromyelitis optica spectrum disorders (NMOSD) are immune-mediated central nervous system demyelinating disorders. Here we investigate the contribution of monogenic autoimmunity and interferonopathies to pediatric NMOSD.

METHODS: Exome and Sanger sequencing were performed in 5 families of patients with NMOSD. Segregation studies and type 1 interferon signature testing were performed.

RESULTS: Of 5 patients with NMOSD, we identified 2 definitive monogenic interferonopathies and 2 candidate genes. We discovered TNFAIP3 haploinsufficiency in a patient with NMOSD and anti-phospholipid syndrome, and in her mother and aunt with systemic autoimmune diseases (AD). TNFAIP3 haploinsufficiency is reported to cause elevated type 1 interferon activity. TLR7 gain-of-function, a cause of type 1 interferonopathy, was identified in a patient with NMOSD and her mother and aunt with systemic ADs. These patients had elevated type 1 interferon activity, and one was started on a Janus kinase (JAK) inhibitor. A patient with NMOSD and her brother with Crohn's disease were found to have compound heterozygous variants in MAP3K9, which is involved in regulatory T cell differentiation. Another patient with NMOSD has a de novo missense variant in CLEC4A, which is linked to systemic ADs.

CONCLUSIONS: Our study supports the interferonopathy hypothesis of NMOSD, suggesting a need for larger studies to estimate the incidence of monogenic interferonopathies and autoimmunity in NMOSD. We show pathogenic alleles segregate with other ADs within families and confirm elevated type 1 interferon signatures in patients with NMOSD and monogenic interferonopathies. These findings have implications for the treatment of this debilitating disease, such as with JAK inhibitors.

KEYWORDS: Pediatric Demyelinating Disease, Neurogenetics, Neuroimmunology

307. Retrospective Case Series of Pediatric First-Time Optic Neuritis: Demographics, Etiologies, and Follow Up

Chandrasekar A (Houston, TX), Aduru C, Fergason K, Rosen J, Lotze T, Yarimi J, Shukla N, Fisher K, Sandweiss A

OBJECTIVE: Optic neuritis (ON) is an inflammatory disorder of the optic nerve that may be isolated or indicative of underlying CNS demyelination. Pediatric studies are limited to a period prior to the routine workup of MOG antibody disorder (MOGAD), thus we evaluated the etiologies of pediatric first-time ON. Lower socioeconomic status is associated with increased prevalence of pediatric neurological disorders. We therefore examined the impact of social determinants of health (SDOH) on outcomes of patients with first-time ON.

METHODS: This is a single-center, retrospective study of pediatric first-time ON between 2016-2023. We compared demographics, diagnoses, and retinal nerve fiber layer thickness (RNFL). We used the Area Deprivation Index (ADI), which considers income, education, employment, and housing qualities, in ranking neighborhoods by socioeconomic disadvantage. An ADI of 1 indicates the least disadvantage and an ADI of 10 the most.

RESULTS: 63 children presented with first-time ON. 11/63 were immediately diagnosed with MS and 5/63 with NMOSD due to other demyelinating lesions on imaging while 47/63 had isolated ON. 53.2% of isolated ON cases were due to MOGAD. 60.3% were Hispanic, disproportionately more than the institution's home city (about 35% Hispanic). RNFL was measured via OCT in 59 patients at presentation; 58.1% with ADI 1-3, 47.6% with ADI 4-7, and 25.0% with ADI 8-10 returned for follow up measurements.

CONCLUSIONS: We found MOGAD is responsible for considerably more isolated ON than previously thought. We also corroborate reports on predispositions and lost follow-up based on socioeconomic disadvantage. Further research on SDOH in autoimmune neurological diseases is warranted.

KEYWORDS: Pediatric Demyelinating Disease, Diversity, Equity, Inclusion, Neuroimmunology

308. Serum neurofilament light chain as a biomarker in pediatric demyelinating disease with and without myelitis

Levine J M (Houston, TX), Kannan V, Fisher K S

OBJECTIVE: Serum neurofilament light chain (sNfL) is an indicator of neuronal damage and is used as a biomarker of disease activity in neuroinflammatory conditions. The utility

of sNfL in pediatric demyelinating diseases (DD) such as multiple sclerosis (MS), myelin oligodendrocyte glycoprotein antibody disease (MOGAD), and neuromyelitis optica spectrum disease (NMOSD) remains unclear. Here we investigate the correlation between sNfL and pediatric DD with and without myelitis.

METHODS: Pediatric patients with confirmed DD and sNfL levels drawn within 90 days of symptom onset were included in a retrospective analysis.

RESULTS: Of 42 patients with DD, 19 presented with myelitis and had significantly higher sNfLs than 23 patients without myelitis (137.5pg/mL vs 13.93pg/mL, p=0.0145). Of 20 patients with MOGAD, 5 had myelitis (75.56pg/mL) with higher sNfL compared to 5 with acute disseminated encephalomyelitis (ADEM) without myelitis (9.72pg/mL, p=0.0369) and compared to 10 with optic neuritis (ON) alone (10.08pg/mL, p=0.0031). Though patients with MS (n=8) and NMOSD (n=4) with myelitis had higher sNfL levels than those without, it did not reach statistical significance. Of 19 patients with clinical concern for myelitis, 12 (63%) had elevated sNfL with non-enhancing lesions on spine MRI, with the remaining 7 (37%) having enhancing spine lesions.

CONCLUSIONS: Pediatric patients with DD with myelitis have significantly higher sNfL compared to those without myelitis, specifically seen in MOGAD. This and further studies are needed to elucidate how sNfL may be useful as a clinical biomarker. Importantly, sNfL may be a more sensitive marker of active disease than enhancing lesions on spine MRI in myelitis.

KEYWORDS: Pediatric Demyelinating Disease, Neuroimmunology, Neuroimaging

PRACTICE PARAMETERES

309. Bridging the Gap: A Formalized Process for Transitioning Neurology Patients from Pediatric to Adult Care

Wolf D S (Atlanta, GA), Albor L C, Dutt M, Thompson A, Shapiro R, Jackson A

OBJECTIVE: This project aimed to develop a structured process to facilitate the transition from pediatric to adult care for neurology patients 18 and older in a high-volume Neurology practice.

METHODS: We conducted comprehensive research to identify best practices around the process to transition from pediatric to adult care. We reviewed over 20 academic articles as well as leading sources such as GotTransition.org. Additionally, we identified best practices from six national pediatric hospitals and collaborated with over 14 internal departments to gather information on relevant transition guidelines. Our transition guidelines underwent a targeted review by two multidisciplinary teams of operational and clinical leaders across Children's Healthcare of Atlanta. Our process was reviewed by our Legal and Risk teams to ensure compliance and alignment with system policies. Finally, in conjunction with a formal process, we developed several Epic tools to help support providers and patients navigating the transition process.

RESULTS: The outcome is a formal transition process tailored specifically for neurology patients, comprised of policy guidelines, an Epic-Based patient health passport, an Epic Smartphrase, and patient resources.

CONCLUSIONS: By integrating insights from interdisciplinary collaboration, academic research, and evidence-based strategies, we have established a robust framework to support seamless transitions at scale, ultimately enhancing continuity of care.

KEYWORDS: Practice Parameters

310. Should we give intermittent clobazam therapy in children with simple febrile seizure aged 6months to 6 years in developing countries?– A Double-blind Randomized control trial

Saini LS (Jodhpur, India), Samad AS, Singh K S, Goyal J G, Choudhary B C, Charan J C, Sondhi VS

OBJECTIVE: To measure the relative risk of recurrence of Simple Febrile Seizures in intermittent clobazam vs placebo group
Adverse drug reaction of clobazam

METHODS: Sample size was calculated based on 35% prevalence of recurrence rate of febrile seizures with 0.35 RR. Computer-generated block randomization was done. Total 130 children with febrile seizures were enrolled, 65 in the clobazam arm and 65 in placebo arm. All children were given clobazam orally 0.75 mg/kg/day in two divided doses for 72 hours from the onset of fever in intervention group and matching placebo in control group. Both groups were followed up for 6 months. Patients were assessed on the basis of recurrence of seizure in both group and the adverse effect of clobazam.

RESULTS: Mean age of participants was 32.7±17.8 months in clobazam group vs 30.3±18.4 months in the placebo group. There were 43(66.2%) males,22(33.8%) females in clobazam group and 44(67.7%) males, 21(32.3%) females in placebo group. During the six-month follow-up period,125 febrile events were witnessed in the clobazam arm associated with 11 episodes of febrile seizures. Similarly, 98 febrile events were observed in the Placebo group, of which 13 were accompanied by febrile seizures. The incidence of febrile seizures in the Clobazam arm was comparable to that in the Placebo arm (OR = 0.63, 95% CI = 0.26, 1.48, p = 0.3). No adverse events were reported from either arm during the study period.

CONCLUSIONS: Intermittent clobazam therapy is not effective in the prevention of recurrence of febrile seizures. Intermittent clobazam @.75 mg/kg is well tolerated.

KEYWORDS: Practice Parameters, Epilepsy, Education

311. Examining trends in and results of autism spectrum disorder genetic testing in the pediatric neurology clinic: a quality assessment study

Reichner H (Newark, NJ), Grew E, Reddy M, Stomel Z, Elgallab J

OBJECTIVE: This study aims to evaluate trends in diagnosis of, genetic testing for, and Genetics referrals for autism spectrum disorder (ASD) in patients in the pediatric neurology clinic, and trends in patient results and successful completion of referrals.
METHODS: All patients with ASD who presented to the Child Neurology clinic from 9/2022-9/2023, who were under the age of 10 at initial visit, who completed at least two visits, and who were initially diagnosed with ASD by Child Neurology providers were included. Demographic information, clinical history, referral status, and testing results were available from Epic. Chi-square analysis examined trends in diagnosis, referrals, and successful completion of referrals.
RESULTS: Sex, race, primary language, and insurance status were not associated with referral for genetic testing or Genetics visit. Patients with dysmorphism (p=0.001) or neurologic family history (p=0.021) were more likely to have genetic testing ordered. Patients of younger age at first visit (p=0.020), with neurocutaneous findings (p=0.006), dysmorphism (p=0.045), hypertonia (p=0.009), or medical comorbidities (p=0.001) were more likely to be referred to Genetics. Patients of female sex (p=0.020), with hypertonia (p=0.002), gross motor delay (p=0.011), global delay (p=0.004), or a history of ADHD (p=0.001) were more likely to have positive genetic results related to their phenotype.
CONCLUSIONS: There were discrepancies in the demographics, physical exam presentations, family histories and medical histories between patients who were most likely to be referred for genetic testing, referred for Genetics visit and those with positive genetic testing. These results prompt reflection on testing and referral habits in our clinic.
KEYWORDS: Practice Parameters, Neurogenetics

SLEEP

312. The Applicability and Ethics of AI in Sleep Management for Children: A systematic review

Wong A (Bloomington, IL)

OBJECTIVE: This review aims to explore the applicability and ethical considerations of artificial intelligence (AI) technologies in the management of sleep disorders in children, focusing on the potential benefits and risks associated with AI interventions.
METHODS: An exhaustive search was performed across PubMed, IEEE Xplore, and ScienceDirect databases for articles published from 2001 to 2023. The search targeted studies involving AI applications in general pediatrics, such as machine learning algorithms for diagnosing sleep disorders, AI-driven intervention tools, and ethical discussions related to AI in pediatric settings. The quality and relevance of studies were assessed using predefined inclusion criteria and a modified PRISMA checklist.
RESULTS: 34 studies were included. The analysis revealed that AI-based diagnostic tools, such as automated polysomnography analysis and wearable sleep trackers, offer high accuracy and efficiency in identifying sleep disorders. However, ethical concerns were significant, revolving around data privacy, consent issues due to the involvement of minors, and the potential for bias in AI algorithms. Ethical guidelines specific to pediatric AI applications were notably lacking in most studies.
CONCLUSIONS: While AI holds promise for revolutionizing pediatric sleep management through enhanced diagnostic and therapeutic precision, there is a critical need for establishing robust ethical frameworks. Such frameworks should ensure the protection of child-specific vulnerabilities, data security, and mitigate biases inherent in AI models, ensuring equitable health outcomes for all pediatric patients.
KEYWORDS: Sleep, Ethics

313. Sleep disorders among 5-year-old survivors of acute provoked neonatal seizures – a study of the Neonatal Seizure Registry

Shellhaas R A (St. Louis, MO), Pilon B, Wusthoff C J, Massey S, Chu C, Soul J, Lemmon M, Numis A, Sturza J, Thomas C, Benedetti G, Anwar T, Berl M, Franck L, Glass H

OBJECTIVE: Acute provoked neonatal seizures confer risk for abnormal neurodevelopment and behavior. We hypothesized that abnormal sleep is associated with adverse outcomes for both children and parents.
METHODS: This 9-center study prospectively followed newborns with acute provoked seizures. When children reached age 5-years, parents completed the Children's Sleep Habits Questionnaire (CSHQ), the Pediatric Sleep Questionnaire–Sleep Related Breathing Disorders (PSQ-SRBD) subscale, Vineland Adaptive Behavior Scales–2, and the Hospital Anxiety Depression Scale (HADS). Children also underwent the Wechsler Preschool and Primary Scale of Intelligence-IV (WPPSI-IV).
RESULTS: Among 116 children, the mean CSHQ score was 45±7 and 74/115 (64%) scored above the healthy threshold of 41. On the PSQ-SRBD, 32/116 (28%) screened positive for sleep-disordered breathing (SDB). SDB was more common among children with cerebral palsy (42% with CP vs. 23% without, p=0.04) and epilepsy (54% with epilepsy vs. 24% without, p=0.02). Children with lower scores on Vineland-2 (rho=-0.31, p=0.003) and WPPSI-IV (rho=-0.31, p=0.001) at age 5 years were more likely to have symptoms of SDB. Worse CSHQ and PSQ-SRBD scores were both associated with parental symptoms of anxiety (CHSQ rho=0.21, p=0.02, and PSQ-SRBD rho=0.32, p=0.0005) and depression on the HADS (CHSQ rho=0.16, p=0.08, and PSQ-SRBD rho=0.19, p=0.04).
CONCLUSIONS: Over half of early school-aged survivors of acute provoked neonatal seizures had parent-reported sleep abnormalities and one quarter screened positive for sleep-disordered breathing. Childhood sleep disorders may contribute to adverse neurobehavioral outcomes and parental anxiety and depression. Early screening and effective treatment for

sleep disorders may be a novel intervention to improve outcomes after neonatal seizures.

KEYWORDS: Sleep, Neonatal Neurology, Lifespan Manifestations of Childhood Onset Conditions

314. The Effectiveness of Behavioral Interventions for Insomnia in Adolescents: A systematic review

Wong A (Bloomington, IL)

OBJECTIVE: This systematic review evaluates the effectiveness of behavioral interventions for treating insomnia in adolescents. Addressing the increasing prevalence of sleep disorders in this demographic, the study aims to synthesize available evidence and guide future clinical practices.

METHODS: We conducted a comprehensive search across multiple electronic databases including PubMed, PsycINFO, and Cochrane Library, from January 2000 to December 2023. Inclusion criteria were studies that specifically targeted adolescents aged 12-18 years with diagnosed insomnia and utilized any form of behavioral intervention. The quality of the studies was assessed using the PRISMA guidelines.

RESULTS: A total of 24 studies met the inclusion criteria, encompassing a diverse range of behavioral approaches such as Cognitive Behavioral Therapy for Insomnia (CBT-I), mindfulness-based interventions, and sleep hygiene education. Meta-analysis results indicated a significant improvement in sleep onset latency, total sleep time, and sleep efficiency post-intervention. The effects were sustained at follow-up intervals of three to six months. Studies varied significantly in methodological quality, intervention duration, and follow-up periods.

CONCLUSIONS: Behavioral interventions, particularly CBT-I, are effective in improving sleep parameters among adolescents with insomnia. The findings support the integration of these interventions into routine clinical care for adolescents. Future research should focus on long-term outcomes, standardizing intervention protocols, and exploring digital delivery methods to enhance accessibility and adherence.

KEYWORDS: Sleep, Behavioral Neurology

STROKE

315. Pediatric ASPECTS is associated with 3-month outcome in children with acute arterial ischemic stroke

Horn F A (Nashville, TN), Balamurugan C, Milner L, Davis S, Rodeghier M, Jordan L

OBJECTIVE: To determine whether initial stroke severity via the pediatric NIH stroke scale (PedNIHSS) and neuroimaging via the modified pediatric Alberta Stroke Program Early CT Score (modASPECTS) are associated with 3-month outcome in children with acute arterial ischemic stroke (AIS).

METHODS: This retrospective observational single-center study identified children (age 29 days–18 years) with a code stroke which includes rapid neurology evaluation, and confirmed AIS, from 2011-2023 from an institutional quality improvement database. The Pediatric Stroke Outcome Measure (PSOM) was recorded; poor outcome was defined as PSOM >2.

RESULTS: Of 100 children with AIS (mean age 8.2 + 6 years, 48% female), the median PedNIHSS was 6.0 (IQR 4.0–12.0) and median modASPECTS was 2.0 (IQR 1.0–5.0). Seven children died. Twelve children underwent mechanical thrombectomy, and three received tPA (two followed by thrombectomy). Outcome was available for 92 of 93 survivors (99%). In univariate analysis, higher modASPECTS score was significantly associated ($p<0.001$) with poor outcome at 3 months (median modASPECTS 5.0, IQR 3.0–7.0) compared to those with good outcome (median modASPECTS score 2.0, IQR 1.0–3.0). Three-month PSOM was not associated with age, sex, race, stroke location (anterior/posterior circulation) or stroke etiology. PedNIHSS showed a trend for association with 3-month PSOM at $p=0.051$.

In a multivariate model, PedNIHSS was not significantly associated with poor 3-month outcome (OR 1.04, 95% CI 0.97-1.12, $p=0.262$), higher ModASPECTS was associated with poor outcome at 3-months (OR 1.79, 95% CI 1.37-2.33, $p<0.001$) adjusted for age and sex.

CONCLUSIONS: ModASPECTS is associated with 3-month outcome in children with acute arterial ischemic stroke.

KEYWORDS: Stroke, Neuroimaging, Early Stage Investigator

316. Unilateral Posterior Reversible Encephalopathy Syndrome Mimicking Arterial Ischemic Stroke in a Child with Schimke Immuno-osseous Dysplasia

Cheronis C (Palo Alto, CA), Russo Barsh G, Tesi Rocha C, Lee S

OBJECTIVE: Schimke Immuno-osseous Dysplasia (SIOD) is a rare condition that manifests as short stature, spondyloepiphyseal dysplasia, immunodeficiency, and renal failure. Half of patients have neurologic manifestations such as migraine headaches, transient ischemic attacks, and cerebral infarctions, the exact mechanism of which is not understood.

METHODS: A 6-year-old male with SIOD, end stage renal disease requiring dialysis, hypertension, and prior transient ischemic attack presented with acute onset left gaze preference, right sided weakness, and expressive aphasia, with last known normal 15 minutes prior to stroke code activation. National Institutes of Health Stroke Scale was 16. He was hypertensive to 145/102 mmHg (>99th percentile for height and age).

RESULTS: Magnetic resonance imaging and angiography (MRI/MRA) of the brain without contrast showed diffusion restriction in the left middle cerebral artery (MCA) and posterior cerebral artery (PCA) territories and decreased prominence of the left MCA branches without occlusion. Alteplase was not administered due to lack of clear vessel occlusion and large area of injury. EEG showed left-sided attenuation and myoclonic seizures involving the right face and upper extremity. Repeat MRI/MRA with contrast the following day showed a marked improvement in diffusion restriction,

diffuse left cerebral hemispheric hyperperfusion suggestive of seizure sequelae, and normalization of the previously attenuated branches of the left MCA. Clinically, the patient's symptoms improved with near-resolution within two weeks.
CONCLUSIONS: The working diagnosis was asymmetric posterior reversible encephalopathy/reversible cerebral vasoconstriction syndrome secondary to hypertension, leading to impaired cerebral autoregulation causing acute exam change and seizures.
KEYWORDS: Stroke, Neuroimaging

317. Reducing Time to Imaging in Pediatric Stroke Using Quality Methodology

Cavallo M (Atlanta, GA), Torres S, Carter R, Wood E, Palasis S, Philbrook B

OBJECTIVE: Pediatric strokes occur with an incidence of 1.2 to 13 cases/100,000 children with approximately 65% having life-long disability. This quality improvement project was developed to reduce the time from presentation to activating stroke alert and obtaining neuroimaging.
METHODS: We created a stroke imaging guideline and order-set, and educated clinicians on stroke recognition, to hasten neuroimaging (with MRI, the preferred imaging modality) when encountering potential stroke patients. These tools were part of a broader initiative to coordinate evaluations for rapid identification of stroke to facilitate prompt interventions.
RESULTS: After interventions, improvement from arrival at the emergency department (ED) to imaging was 115 minutes at baseline to 40 minutes, and time from activation of stroke alert to imaging from baseline 66 minutes to 31 minutes. The number of stroke alerts called also increased. These improvements were observed across our three-hospital system (2 tertiary care) with an ED at each hospital.
CONCLUSIONS: Identification of pediatric stroke is time-sensitive and sometimes difficult, with vague symptoms, or conditions that mimic stroke. A missed or delayed diagnosis can lead to irreversible neurologic damage and poor outcomes. Failure of pediatric stroke recognition is well known, but essential to reducing morbidity and mortality among children with stroke. Our quality interventions improved stroke awareness and recognition, facilitating earlier stroke alerts and confirmatory neuroimaging. We made significant reductions of response times, but we will reset goals to continue improvements through additional interventions and education.
KEYWORDS: Stroke, Neuroimaging

318. A Novel MRI Approach to Investigate Silent vs. Symptomatic Perinatal Arterial Ischemic Stroke

Kinawi O (Calgary, AB, Canada), Carlson H, Kirton A, Dumanski S, Dunbar M

OBJECTIVE: Perinatal arterial ischemic stroke (PAIS) is the most common cause of hemiparetic cerebral palsy and causes lifelong disability. Timely diagnosis is challenging; they lack sudden deficits that herald stroke in older people, thus there are no acute therapies. In one-third of children, their stroke is silent until movement challenges are appreciated in childhood. This study aims to use MRI to investigate why some newborn strokes are silent, particularly in females.
METHODS: Retrospective cross-sectional study using a unique population-based database of arterial ischemic perinatal stroke. Cases are classified as acute (115; 68% male) or silent (46; 48% male) based on timing of presentation. Size of stroke on MRI will be measured using a novel semiautomated pipeline, adapting a validated method by our group. Linear regression will compare volume by diagnosis timing, stratifying by sex. With our sample of 161 cases, we have 80% power to detect a 15% difference in volume. Location of stroke will be classified according to standard categories and compared by timing of diagnosis with chi-square tests.
RESULTS: Our preliminary results show that males are twice as likely to be diagnosed as newborns, and we anticipate that this is due to larger stroke sizes in males, and different stroke locations compared to females.
CONCLUSIONS: The findings will provide insight into the relationship between stroke characteristics, timing of symptoms, and infant sex. This research will discover how brain injury characteristics and symptoms are shaped by infant sex, which will help advance early diagnosis and treatment strategies.
KEYWORDS: Stroke, Neonatal Neurology, Cerebral Palsy

319. Applying Trauma-Informed Care Principles to Qualitative Interview Methodology after Pediatric Hemorrhagic Stroke

Schneider M (San Francisco, CA), Bonk S, Palacios A, Spina S, Wallis D, Wong J, Fox C, Hess L

OBJECTIVE: Trauma-informed care (TIC) is rooted in knowledge that traumatic experiences, like childhood stroke, profoundly alter physical, emotional, and psychological well-being. As part of a larger project investigating wellness after pediatric stroke, we created interview scripts that integrate TIC principles to sensitively discuss wellness after stroke with adolescents and families affected by pediatric hemorrhagic stroke. This novel approach creates a psychologically safe interview experience and yields rich insights into children's and families' experiences with stroke.
METHODS: The research team first participated in a virtual TIC training course. Then the multidisciplinary team, including a pediatric stroke neurologist, occupational therapist, child neurology resident, and occupational therapy students, collaborated to integrate core principles of TIC into the interview script language. Incorporating normalizing and forecasting statements builds safety and trust. Questions about cultural and spiritual beliefs, and access to social support and community resources related to recovery from stroke are asked nonjudgmentally. Offers of choice and acknowledgements of resilience allow for shared power and control. Questions about challenges are followed by discussions of coping strategies and strengths-based discussions. After conducting mock interviews with teens and adults, the scripts were further revised with interviewee's feedback.

RESULTS: Through interdisciplinary collaboration, we created a novel TIC qualitative interview paradigm to sensitively interview teens and families about their wellness after childhood stroke.
CONCLUSIONS: A multidisciplinary team effectively produced a TIC qualitative interview approach to better understand wellness after pediatric stroke. Applying TIC principles affords a sensitive approach to our research process that involves sharing difficult and vulnerable experiences like childhood stroke.
KEYWORDS: Stroke, Traumatic Brain Injury

320. Genetic Testing for Idiopathic Moya-Moya Disease: More Questions than Answers?

Mithal D S (Chicago, IL), Salazar C, McGinnis E, Ivanisevic J, Barry M

OBJECTIVE: Moyamoya disease (MMD) is a rare, progressive intracranial vasculopathy that may occur in Sickle Cell disease, post chemo-radiation, or Trisomy 21. However, nearly 50% of cases are considered idiopathic (iMMD). Over the past decade multiple genes, including RNF213, have been flagged as risk alleles. In the present study, we demonstrate the complexity of interpreting and using genetic results from our iMMD genetic testing program.
METHODS: Seven patients with a confirmed diagnosis of iMMD based on vascular imaging were included in the study. Electronic medical records containing genetic testing, imaging and other clinical data were reviewed for the patients of interest under an IRB-approved protocol.
RESULTS: Four patients had no identified variant in the tested genes. One patient had a pathogenic RNF213 mutation which was inherited from his iMMD-affected father. He also had a variant-positive unaffected sibling. Another patient had a De Novo VUS in RNF213 but the result was inconclusive and did not prompt additional testing. A third patient had a known variant in CBL, which was identified because her sister had CBL+ Juvenile Myelomonocytic Leukemia (JMML). CBL was not on our standard testing panel but was recently described as a cause of iMMD.
CONCLUSIONS: Genetic testing for iMMD may help identify at-risk family members and improve management. However, a growing number of iMMD genes, complex interpretation of results and familial screening are ongoing challenges. Our case series shows that despite aggressive testing, benefits to patients and families remains limited. Further studies are needed to optimize the use of genetic testing in iMMD.
KEYWORDS: Stroke, Neurogenetics, Neurocritical Care

321. Spinal Stroke Secondary to Methamphetamine Toxicity

Wells D A (Houston, TX), Risen S, Sarpong K

OBJECTIVE: To describe a unique case of a patient presenting with flaccid paralysis secondary to methamphetamine toxicity, likely leading to vasoconstriction inducing a spinal cord stroke.
METHODS: Case report.
RESULTS: A 15-month-old previously healthy male presented with acute flaccid paralysis, brought to the emergency room ~ 36 hours after onset of symptoms. Weakness was maximal at onset, and on exam he had no tone, movement, or reflexes below the neck, and was not able to maintain his airway. Significant laboratory findings included a very elevated procalcitonin (18.63) and a positive urine drug screen for amphetamines. On liquid chromatography/mass spectroscopy, methamphetamine and amphetamine levels were twenty times the normal limit. Initial spinal imaging revealed diffusion restriction in the anterior cord from C2 to T4, with significant edema compressing the cord. Given concern for transverse myelitis with profound spinal-cord related impairments, treatment included plasmapheresis, intravenous immunoglobulins, high dose steroids, and a single dose of intrathecal dexamethasone without any clinical improvement. Repeat imaging seven days and three weeks following presentation showed persistent changes in the spinal cord consistent with spinal cord stroke, mostly in the anterior cord sparing the central and dorsal columns. Considering the critically high elevated levels, the most likely mechanism for this stroke is amphetamine-induced vasoconstriction of the anterior spinal artery.
CONCLUSIONS: This case represents a unique etiology of an already rare occurrence of spinal stroke in children.
KEYWORDS: Stroke, Neurocritical Care, Neuroimaging

322. Sex differences in the epileptogenesis of perinatal arterial ischemic stroke

Zarrouk A (Calgary, AB, Canada), Jacobs-Levan J, Dumanski S, Kirton A, Yeates K, Dunbar M

OBJECTIVE: Perinatal stroke, affecting 1 in 1,100 births, is a leading cause of hemiparetic cerebral palsy. While advancements have significantly improved diagnosis and treatment of stroke in adults, there is a lag with perinatal stroke due to vastly different presentation. Two-thirds of newborns with stroke will present with seizures, while the remaining one-third will have no outward symptoms until months or years later, when they show signs of cerebral palsy. These children with silent stroke are twice as likely to be female. This study aims to utilize electroencephalography (EEG) to examine the role of infant sex in the epileptogenesis of perinatal arterial ischemic stroke (PAIS).
METHODS: The retrospective, cross-sectional study is conducted on a database of infants with PAIS. Brain activity on EEG is examined to determine sex-dependent differences in electrographic patterns after perinatal stroke associated with male-biased early post-stroke manifestations. Standardized data of seizure burden and abnormal EEG background activity will be collected. Maximum median hourly seizure burden and median total seizure minutes during EEG monitoring for males and females will be compared using Wilcoxon rank sum test.
RESULTS: Preliminary results indicate that males are more likely than females to experience newborn stroke symptoms. We predict that this is due to higher rates of seizures and unique electrographic brain activity in males.

CONCLUSIONS: Understanding the impact of sex in PAIS will guide individualized therapies, inform population and public health decision making, and facilitate creation of novel diagnosis and treatment protocols to ease the burden of stroke in newborns.
KEYWORDS: Stroke, Neonatal Neurology, Cerebral Palsy

TRAUMATIC BRAIN INJURY

323. Quality of life after pediatric acquired brain injury (ABI): a prospective, longitudinal study in a pediatric neurology program

Johnson-Kerner B L (San Francisco, CA), Vayngortin B, Williams K, Vassar R

OBJECTIVE: Implement quality of life (QL) data collection in a pediatric neurology program to examine reproducibility with previous studies and establish a baseline for future program evaluation.
METHODS: Patients and parents seen outpatient in a neurology ABI clinic were asked to complete the Pediatric Quality of Life (PedsQL 4.0, chronic) questionnaire between 2021 to 2024. Raw scores were converted to scores out of 100 (highest score). Chart review was used to obtain additional information.
RESULTS: 97 unique patients (and 125 questionnaires) were included in this study; 19 patients completed multiple surveys. Participants included 69 males, 28 females. 31 participants had private insurance and 66 had public insurance. 5 participants had ischemic stroke, 5 had hemorrhagic stroke, 85 had TBI, and 2 had PHACE syndrome. The average age at the time of injury was 11.4y. The average time between the injury and the questionnaire was 20 months, with a range 1-116 months. GCS was recorded for 62 cases (average 11.7, range 3-15). Average parent score for PedsQL was 65.2, with physical and psychosocial scores not significantly different. There was no significant correlation between GCS, age that injury occurred, gender, or insurance type. Comparison of parent-child scores had a Pearson's Correlation Coefficient of 0.64. Both parent and child scores significantly improved over time as measured by the Mann Kendall test.
CONCLUSIONS: Parent and child QL scores were strongly correlated, and both showed improvement over time. Change over time may be more meaningful than inter-patient comparison given heterogeneity in baseline characteristics.
KEYWORDS: Traumatic Brain Injury, Stroke, Early Stage Investigator

324. Recovery from adolescent sports concussion during the school year compared to summer

Rose S C (Columbus, OH), Benedict J, Pommering T L, Young J

OBJECTIVE: Adolescents with acute concussion often report increased symptoms with participation in school. Our objective was to compare time to recovery during the school year and summer break.
METHODS: We conducted a cross-sectional retrospective chart review of patients aged 13-18 years presenting to concussion clinic within 14 days of injury. Symptom burden was assessed at each visit. The primary outcome was days to concussion resolution. Secondary outcomes included somatic, cognitive, sleep, and emotional symptom category scores on the day of injury and first clinic visit. Participants were categorized into "school" or "summer" groups based on the timing of their concussion in relation to local school calendars.
RESULTS: A total of 2500 patients (42% female) were included: 2371 with school concussion and 129 with summer concussion. By the first clinic visit (median 5-6 days), median symptom score in the school group was twice that of the summer group (16 vs 8). Median days to resolution differed ($p<0.001$) between the school group (15 days, 95% CI: 15-16) and the summer group (12 days, 95% CI: 11-14). Earlier concussion resolution was associated with injury during the summer (HR 1.51, 95% CI: 1.25-1.82, $p<0.001$, when controlling for other variables). Somatic, cognitive, and sleep symptoms were higher in the school group (all $p<0.05$), while emotional symptoms did not differ.
CONCLUSIONS: Adolescents recover from concussion slower during the school year compared to the summer. Earlier management and treatments targeting somatic, sleep, and emotional symptoms should be offered to patients recovering from concussion during the school year.
KEYWORDS: Traumatic Brain Injury, Behavioral Neurology

325. Increased perivascular space burden is associated with TBI and cognitive outcomes in children

Khambadkone S G (Portland, OR), Dennis E L, Barisano G, Dennis L, Elliott J, Lim M, Iliff J, Giza C, Asarnow R, Piantino J

OBJECTIVE: The glymphatic system, a perivascular space (PVS) network facilitating cerebrospinal and interstitial fluid exchange, is critical for cerebral waste clearance. Enlarged PVS, thought to reflect glymphatic dysfunction, are seen in adults after traumatic brain injury (TBI). In adults, glymphatic dysfunction is implicated in functional outcomes and neurodegeneration. However, it is unclear whether the pediatric brain has similar vulnerability. We investigated the relationship between TBI, PVS volumes, and cognitive performance in children.
METHODS: Children 1-6 months after moderate-severe TBI (ages 8-19, $n=36$) and age/sex-matched controls ($n=47$) underwent cognitive testing and brain MRI. Cognitive outcomes were aggregated into a multidomain cognitive index (CI). T1-weighted images were parcellated to obtain masks for MRI-visible PVS and lobar subregions. Linear regressions were performed for summed total and mean individual PVS volumes adjusted for regional volumes.
RESULTS: Total white matter (WM)-PVS volumes were similar between TBI and controls. Children with TBI had higher mean WM-PVS volumes versus controls ($p=0.014$ adjusted for age and sex). In turn, mean WM-PVS volumes were negatively associated with CI score ($p=0.031$ adjusted for age, sex, and TBI status). To query effects of structural

WM injury, we compared lobar mean PVS volumes among TBI participants with MRI-visible frontal lobe injury (TBI-frontal, n=19), without MRI-visible injury (TBI-negative, n=16), and controls. Frontal PVS volumes were increased to controls in TBI-frontal (p=0.002), with intermediate volumes in TBI-negative. Temporal, parietal, and occipital PVS volumes were similar across groups.

CONCLUSIONS: These data associate pediatric TBI with post-acute, injury-localizing PVS enlargement and suggest a role for this relationship in neurocognitive outcomes.

KEYWORDS: Traumatic Brain Injury, Neuroimaging

326. Quantitative Pupillometry Have a Role in Diagnosing Pediatric Concussion and Predicting Recovery in the Acute Setting?

Pearson R (Orange, CA), Knudsen-Robbins C, Schomberg J, Hayakawa J, Lara B, Bacon K, Valdez B, Shelton S, Romain J, Wallace E, Taraman S, Loudon W, Heyming T

OBJECTIVE: While prior studies have demonstrated the potential utility of pupillometry in concussion assessment, none have evaluated the use of pupillometry in children in the acute post-injury period, which is when immediate diagnosis is arguably most important. We aimed to determine if pupillary metrics are associated with concussion in the acute setting in the pediatric population and if they could predict those at increased risk for persistent post-concussive symptoms.

METHODS: Prospective case-control study of concussed patients presenting to the emergency department within 72 hours post-injury. Pupillary measurements were collected using NeurOptics' PLR 3000 along with a post-concussion symptom checklist and the ImPACT for neurocognitive assessment. Data were analyzed using descriptive statistics and regression models.

RESULTS: 125 patients were enrolled. Significant differences were seen between concussed and control participants for left minimum pupil diameter (P=0.02) and average dilatation velocity (P=0.02) in 12-18-year-olds and time to 75% recovery (T75) of the left pupil in 5-11-year-olds (P=0.03). Models predicting symptom improvement demonstrated one significant association: percent change in the right pupil in 5-11-year-olds (P=0.02). Models predicting neurocognitive improvement demonstrated a significant association between T75 in the left pupil and visual memory, visual motor speed, and reaction time (P=0.002, P=0.04, P=0.04) in 12-18-year-olds.

CONCLUSIONS: There were limited statistically significant associations between acute post-injury pupillary metrics and concussed versus non-concussed status, as well as recovery trajectory. These findings suggest that pupillometry may not be useful in pediatrics in the acute post-injury setting for diagnosis of concussion or in stratifying risk of prolonged recovery.

KEYWORDS: Traumatic Brain Injury

327. Post-Traumatic Hypertrophic Olivary Degeneration with Palatal Myoclonus – A Case Report

Bailey K (East Lansing, MI), Khalil S

OBJECTIVE: To report a unique case of hypertrophic olivary degeneration resulting from traumatic injury in a child, which has not been reported in the literature in the pediatric population previously.

METHODS: This is a case report of a 7-year-old boy with a past medical history of a MVA with resultant structural epilepsy and right sided spastic hemiplegia with developmental delays. Two years later, he developed quivering and twitching of right side of his lip, palate, and neck, initially thought to be epilepsia partialis continua given his history. Multiple anti-seizure medication attempted with no effect including clobazam, lacosamide and levetiracetam. Subsequently, the patient was started on carbamazepine with marked improvement of the palatal myoclonus.

RESULTS: The most recent brain MRI showed significant atrophy of cerebellar hemispheres and subtle T2 hyperintensity signal noted in the inferior olivary nucleus suggestive of hypertrophic olivary degeneration. The patient had a long-term video EEG that captured the abnormal facial twitching with audible palatal clicking that was not associated with any corresponding electrographic changes.

CONCLUSIONS: This case demonstrates the anatomic importance of Guillain-Mollaret triangle, as traumatic disruption of this pathway resulted in palatal myoclonus in this patient. Hypertrophic olivary degeneration (HOD) occurring due to trauma is an incredibly rare etiology with only one other case reported in the literature in a 27-year-old male (Zhou et al, 2021,) with no previous reports of post-traumatic HOD occurring in an individual under 18.

KEYWORDS: Traumatic Brain Injury, Movement Disorders

328. The Pediatric Brain Injury Prognosis Team: A Quality Improvement Study

Berry M (Madison, WI), Hsu D, Seaborg K

OBJECTIVE: We have initiated a new Pediatric Brain Injury Prognosis (PBIP) team to ensure children admitted to our pediatric intensive care unit (PICU) with any type of acute brain injury have appropriate neurologic care. This team was created following a retrospective study of 398 children admitted to our PICU from 2011-2017 with a diagnosis of traumatic brain injury, which demonstrated several risk factors associated with worse neurologic outcomes. With those findings, we created a template for the inpatient pediatric neurology team's use in prognostication for children with any type of brain injury.

METHODS: In order to assess provider responses, we created surveys for distribution to the pediatric neurology team and the other providers caring for acute brain injury patients in the PICU. Surveys were created with the assistance of a quality improvement supervisor.

RESULTS: 61% of non-neurology providers were aware of the PBIP consult during the patient's admission. Of those who were aware, 100% felt the consult provided useful information to the patient's family and to other providers caring for the patient. 100% of pediatric neurology providers found the new consult format helpful, with several suggestions for streamlining documentation.

CONCLUSIONS: Our preliminary review of the Pediatric Brain Injury Prognosis team was favorable. Providers caring for children with acute brain injury felt more informed about the child's prognosis. The note template allowed pediatric neurology providers to standardize the information that is

documented about these patients. The team's effectiveness was limited by provider awareness of the new team's existence.

KEYWORDS: Traumatic Brain Injury, Neurocritical Care

329. Demographics and recruitment of early-middle adolescents with concussions to identify biomarkers of persisting symptoms: the Concussion Assessment Research Education for Kids (CARE4Kids) study

Choe M C (Los Angeles, CA), Cook L J, Gioia G A, Rivara F, Giza C, Study Investigators C4K

OBJECTIVE: To recruit a broad sample of early-middle adolescents with concussions for collection of objective biomarker data predictive of persisting post-concussion symptoms (PPCS).

METHODS: CARE4Kids is a six-site prospective, observational study of adolescents. Inclusion criteria: age 11-<18 years, diagnosed concussion by health care provider, English-speaking patient, and continuing to experience post-concussion symptoms at enrollment. Exclusion criteria: severe autism or developmental delay, other significant neurological or psychiatric diagnosis, acutely suicidal, moderate-severe TBI, inability to start data collection ≤35 days post-injury (timepoint 1 [T1]), but not excluding migraine. Subjects undergo a multimodal battery of objective testing, including neuropsychological, neurological, autonomic, brain imaging and blood biomarker collection.

RESULTS: Since May 2022, 945 subjects were screened, with 701 (74%) meeting inclusion criteria. After applying exclusion criteria, 674 (96%) were approached. Of those approached, 338 (50%) subjects were consented; with 303 completing data collection to date. Small numbers of those consented did not proceed to data collection due to study withdrawal 13 (4%), later found ineligible 7 (2%) or recovered before T1 11 (3%). There are 172 (57.5%) female, 127 (42.3%) male; 22.4% were of Hispanic/Latino ethnicity. Racial breakdown was 1 (<1%) Native American, 12 (4.3%) Asian, 45 (16.3%) Black/African American, 188 (68%) White, 30 (10.8%) Multiracial (Out of total 276 with racial data, 62 not reported).

CONCLUSIONS: Recruiting adolescent patients from multidisciplinary concussion clinics/programs is challenging. More females than males have been recruited. While mostly white, adolescents of different racial and ethnic backgrounds with concussion are able to be recruited to complete a comprehensive data collection protocol.

KEYWORDS: Traumatic Brain Injury, Neuroimaging
(Association of Child Neurology Nurses - 330, 331, 332)

LATE BREAKING ABSTRACTS

333. Knowledge and Attitude of Teachers Towards Students With Epilepsy in Addis Ababa, Ethiopia

Shifatu O Z (Washington, DC), Serawit Negussie A, Zelleke T

OBJECTIVE: Several studies have shown that children with epilepsy attend school at lower rates compared to their counterpart without epilepsy. In an earlier study in Addis Ababa, nearly half of school aged children with epilepsy were not attending school. This study aims to evaluate barriers to school attendance for children with epilepsy by assessing the knowledge, belief and attitude of teachers regarding epilepsy.

METHODS: Four primary schools across Addis Ababa were chosen and a total of 40 teachers were invited to participate. For the quantitative portion, participants were given a structured questionnaire. Following the quantitative portion, teachers and interviewer participated in a focus group discussion. Focus group discussions were continued until it reached the point of saturation.

RESULTS: There were significant misconceptions regarding the cause of epilepsy with 87% of participants believing epilepsy is a curse from God and 60% believing it is caused by spiritual possession. The majority of teachers had a favorable attitude towards students with epilepsy with 55% stating they would be comfortable having a child with epilepsy in their classroom. Only 15% of teachers received training on how to care for a student during a seizure.

CONCLUSIONS: Despite the misconceptions regarding the cause of epilepsy, majority of teachers generally have favorable attitudes towards students with epilepsy and are eager to advocate for and support students with epilepsy. Teachers would benefit from targeted epilepsy education in order to engage them as powerful stakeholders in keeping children at school and also help changing societal misconceptions regarding those with epilepsy.

KEYWORDS: Global Neurology, Epilepsy

334. The Developmental and Neuropsychiatric Profile of Succinic Semialdehyde Dehydrogenase Deficiency

Tokatly Latzer I (Boston, MA), Hanson E, Bertoldi M, García-Cazorla A, Juliá-Palacios N, Opladen T, Jeltsch K, Rotenberg A, Roullet J-B, Pearl P

OBJECTIVE: To provide the most comprehensive description, to date, of the developmental and neuropsychiatric profile of individuals with succinic semialdehyde dehydrogenase deficiency (SSADHD) and assess whether neuroimaging, neurophysiologic, and biochemical indices of cortical inhibition correlate with those of standardized developmental and behavioral tests.

METHODS: Participants enrolled in the SSADHD Natural History Study underwent medical and neurological examinations, MRI, MRS, plasma GABA, TMS, and gene expression quantification, as well as a complete neuropsychiatric assessment including standardized measures for cognition, adaptive skills, motor function, receptive and expressive language, autism spectrum disorder, and behavior problems.

RESULTS: The study's 62 enrollees [53% females, median (IQR) age 9.6 (5.4-14.5)] were universally characterized by intellectual disability and language (expressive>receptive) deficits. Autism was noted in ∼50%, and behavioral problems in ∼70%, predominated by obsessive-compulsive behaviors and attention problems but also including affective problems, anxiety, and, rarely, aggression and possible psychosis. Correlation analyses showed that increased internalizing, externalizing, and overall psychiatric morbidity significantly correlated with increasing age ($R = 0.391$, $p = 0.033$), as well as age-

independent indices representing decreased cortical inhibition such as lower MRS-derived GABA (R = -0.530, p = 0.029) and TMS-derived resting motor threshold (R = -0.418, p = 0.053).

CONCLUSIONS: The description of the developmental and neuropsychiatric profile of SSADHD provided by this study is based on the largest SSADHD cohort ever studied. Its findings linking increased psychiatric morbidity in SSADHD with age-independent decreased cortical inhibition may serve as the basis for establishing disorder-specific biomarkers for behavior and psychiatric outcomes in SSADHD and other non-syndromic psychiatric disorders.

KEYWORDS: Neurometabolic, Neurodevelopmental Disorders, Behavioral Neurology

335. Headaches in pediatric patients during the past decade: Comparative analysis by age group from multicenter study

Han JY H (Daejeon, Republic of Korea)

OBJECTIVE: Establishing an accurate diagnosis of headaches in pediatric patients can be particularly challenging. It is important to be well aware of the characteristics of pediatric headaches to make a precise and timely diagnosis. We aimed to investigate the clinical characteristics of pediatric headaches according to underlying etiology and age groups.

METHODS: We retrospectively reviewed the medical records of 3,374 pediatric patients presenting with headaches between January 2012 and November 2023.

RESULTS: The proportion of primary headaches (PH) was significantly higher in adolescents (40.1% vs. 22.9%), whereas that of secondary headaches (SH) was considerably higher in preschoolers (37.5% vs. 16.3%) ($p < 0.001$). The preschool and school-aged children experienced a significantly higher prevalence of headaches attributed to infection (90.8% vs. 80.2%, $p < 0.001$), while the adolescents exhibited significantly higher frequencies of cranial and/or cervical vascular disorders (3.7% vs. 1.3%, $p = 0.044$) and psychiatric disorders (5.6% vs. 0.6%, $p < 0.001$). Statistically significant differences were observed between preschool/school-aged children and adolescents in terms of headache characteristics, as well as in the prevalence of headache-associated symptoms (60.4% vs. 74.1%, $p < 0.001$ in PH), neurologic abnormalities (10.2% vs. 23.6%, $p < 0.001$ in PH; 2.4% vs. 11.7%, $p < 0.001$ in SH), and headache triggers (19.9% vs. 24.2%, $p = 0.008$ in PH; 2.0% vs. 8.0%, $p < 0.001$ in SH).

CONCLUSIONS: Recognizing both the etiology and age-specific differences in the clinical characteristics of headaches is crucial for an accurate and timely diagnosis.

KEYWORDS: Headache

336. Multicenter study of KCNQ2-Related Epilepsy in Korea : Comorbidities and Functional Impairments

Kim EA (Seoul, Republic of Korea), Yum M-S, Lee S B, Cho J S, Lee JH, Lim B C

OBJECTIVE: This study aimed to investigate the phenotype of KCNQ2-related epilepsy in Korea, particularly focusing on the comorbidities and the functional status.

METHODS: A multicenter observational study was conducted across three tertiary hospitals in Korea, starting from November 2023. We assessed the clinical features, genetic findings, and functional status scales of 20 patients diagnosed with KCNQ2 related epilepsy confirmed by genetic test.

RESULTS: The study enrolled 20 patients, 45% of whom were male. The mean age of first seizure onset was 484 days (1 day to 12 years old), with mean follow-up period of 4 years and 1 months (2 months to 12 years). Five of them can be categorized as Self-limited neonatal-infantile epilepsy, and others as Neonatal-onset developmental and epileptic encephalopathy or Early-infantile developmental and epileptic encephalopathy. The types of seizures varied, including focal, generalized, and epileptic spasms. Background EEG was normal in most cases (80%) and 75% exhibited epileptiform discharges. Fifteen patients (75%) could achieve one year seizure-freedom. Nine patients (45%) had comorbid conditions including 4 patients with autism spectrum disorder, 3 with intellectual disability, and 1 had both ASD and ID. The average Functional Status Scale score among the 20 patients was 7.1 (12 patients with normal FSS score of 6), indicating a range from normal to mild impairment.

CONCLUSIONS: The seizures of KCNQ2-related epilepsy can be controlled in most of them and they exhibited normal to mild impairment on the Functional Status Scale. However, ASD/ID is highly prevalent in this population suggesting the need for a multidisciplinary approach to management.

KEYWORDS: Epilepsy, Neurogenetics

337. Characterization of iron sequestration response in microglia/macrophages in a model of neonatal hypoxic ischemic brain injury.

Vithayathil J (Philadelphia, PA), Jensen F, Talos D, Dunaief J

OBJECTIVE: Iron accumulation and its toxic effects on lipid peroxidation have been identified to play a role in the pathophysiology of neonatal hypoxic-ischemic (HI) brain injury. However, the timing and cell specific changes to iron and lipid peroxidation continue to be important questions that will provide insight into the development of targeted therapies and treatment windows that disrupt this toxic response.

METHODS: A mouse model of HI in post-natal day 9 C57BL6 mouse pups was used to evaluate changes in labile iron and cell specific responses using flow cytometry, quantitative PCR and immunofluorescence.

RESULTS: Dissociated cells from HI hippocampi had increased intracellular labile iron at 24h (2.3 fold increase compared to sham, $p<0.001$) that decreased at 72h (1.8 fold increase compared to sham, $p<0.001$). Lipid peroxidation was then assessed by measuring isoprostanes and neuroprostanes in hippocampal tissue. F4-neuroprostanes were elevated at 24h (97% increase compared to sham, $p<0.001$), but then decreased below sham levels by 72h (62% decrease compared to sham, $p<0.001$). To assess which cells accumulate iron, L-ferritin immunoreactivity in HI tissue peaked at 72h post-injury and co-localized with Iba1+ cells (microglia/macrophages). Isolated CD11b+ cells (microglia/macrophage enriched) from HI hippocampi showed gene expression changes in L-ferritin (38% increase,

p<0.05), transferrin receptor (78% decrease, p<0.05) and Ferroportin1 (44% decrease, p<0.05) when compared to microglia/macrophages from sham hippocampus, which is consistent with a cellular iron sequestration response (CISR) in microglia/macrophages.
CONCLUSIONS: In conclusion, Iba1+ microglia/macrophages activate a CISR response that peaks at 72h post-HI and correlates with a decrease in labile iron and lipid peroxidation.
KEYWORDS: Cerebral Palsy, Neonatal Neurology, Stroke

338. Resting-state functional connectivity in children and adults with spinal muscular atrophy.

Groulx-Boivin E (Montreal, QC, Canada), Carlson H, Oliveira-Carneiro A, Floer A, Kirton A, Mah J, Saint-Martin C, La Piana R, Oskoui M

OBJECTIVE: Despite the use of disease-modifying therapies, many individuals with spinal muscular atrophy (SMA) have chronic motor impairments. Although neuromodulator therapies have optimized outcomes in other neurological disorders, the effects of early motor unit dysfunction on brain connectivity in SMA remain unclear. This study aimed to investigate differences in resting-state functional connectivity between individuals with SMA and neurotypical peers.
METHODS: We conducted a multicenter cross-sectional case control study of individuals with 5q SMA and peer controls matched by age and sex. Blood oxygen level dependent fluctuations at rest were acquired on 3T magnetic resonance imaging (MRI) scanners. Seed-based functional connectivity analyses were performed using CONN in SPM12, with site as a covariate. Connectivity between regions of interest identified on primary analysis, expressed as Fisher-transformed correlation coefficients, were then assessed for correlation with motor function scores and SMN2 copy number.
RESULTS: A total of 42 participants completed the study (mean age 17.4, range 7-40; 67% male). Compared to their peer controls, individuals with SMA demonstrated lower functional connectivity within the cerebellum and within salience network regions, alongside higher functional connectivity between the precentral gyri and the default mode network (corrected p<0.05). No association between the connectivity values and motor function or SMN2 copy number was observed in individuals with SMA when controlling for age at MRI and site.
CONCLUSIONS: Differences in resting-state functional connectivity in individuals with SMA encompass various brain regions, extending beyond motor areas. Insights into the reorganization of brain networks in SMA may open new pathways for adjunctive therapies to optimize outcomes.
KEYWORDS: Neuromuscular, Neuroimaging

339. Core Outcome Set for Pediatric Spinal Muscular Atrophy

Iraqi I (Montreal, QC, Canada), Ng P, Desautels C, Clegg J, Cushen N, Fiscaletti M, Gonorazky H, Haldenby R, Hodgkinson V, Jaworski M, Mackenzie A, McMillan H, Mortenson P, Osman HJ, Potter B, Round J, Séguin O, Selby K, Sheriko J, Smith M, Oskoui M,

OBJECTIVE: To establish a core outcome set (COS) for children with spinal muscular atrophy (SMA) to facilitate robust evidence generation and enhance synthesis of data across studies.
METHODS: We conducted two rounds of a Delphi consensus survey of health care providers, individuals with SMA, caregivers, policy advisors, and industry representatives across Canada. A list of candidate outcomes was generated from those used in SMA pivotal trials and TREAT-NMD registries. Participants rated the importance of these on a nine-point scale (1–3: not important, 4–6: important but not critical, 7–9: critical). This was followed by a consensus workshop using an adapted nominal technique, open discussion, and voting. Outcome measurement tools were selected for each outcome.
RESULTS: The review identified 33 candidate outcomes and an additional 12 outcomes were suggested by participants. Over the course of the Delphi survey, 47 (round 1) and 38 (round 2) participants narrowed the list to 19 candidate outcomes. After the consensus workshop, we finalized 8 core outcomes: event-free survival, ventilatory support, feeding & growth, musculoskeletal, function in activities of daily living, motor function, use of disease-modifying therapies, and healthcare utilization, spanning 4 core areas, each with recommended measurement tools.
CONCLUSIONS: We established a COS for children with SMA. Its implementation will facilitate the synthesis of evidence across studies and optimize the use of limited data generated in this rare disease, ensuring they are meaningful to all stakeholders.
KEYWORDS: Neuromuscular

340. CNS INVOLVEMENT IN INFANTILE-ONSET POMPE DISEASE: UNVEILING RISKS THROUGH NEURORADIOLOGICAL SURVEILLANCE

Regmi N (DURHAM, NC), Malinzak M, Jung D, Jung S-H, Nitching G, Spiridigliozzi G, Kishnani P

OBJECTIVE: FDA approval of alglucosidase alfa has improved survival in Infantile-Onset Pompe Disease (IOPD). As patients live longer, neurological complications like gait disturbances, dysarthria, white matter hyperintensities (WMHI) on brain MRI, and seizures have become apparent. This study aims to evaluate CNS involvement in IOPD using the Modified Fazekas Score (MFS), an MRI-based visual grading system, and identify predictors of neurological risk.
METHODS: 13 patients from a natural history study underwent brain MRI from ages 5, with follow-ups every 2-3 years. The MFS quantified WMHI across 9 brain regions, scoring each from 0-5, with total scores of 0 to 45. Patients were categorized into two cohorts: those with neurological phenotypes (seizures and/or encephalopathy, n=6) and clinically stable long-term survivors (age >18 years, n=7). Clinical and MRI data from 48 scans were analyzed.
RESULTS: Patients with neurological phenotype had higher baseline scores (>20) between ages 5-7, preceding neurological decline and seizures (ages 8-13). Clinically stable survivors had consistently low baseline scores (0-19) from ages 2-7,

which remained stable through ages 18 to 22. A score of 20 was identified as a predictor of CNS risk.

CONCLUSIONS: Modified Fazekas Scoring System effectively quantifies WMHI in IOPD and may serve as a neurological predictor. Cutoff score of 20 was identified as a potential predictor for the development of neurological phenotype. As CNS-targeted therapies are developed, this scoring system could be instrumental in patient selection for clinical trials and in evaluating treatment responses. Baseline MRI starting at age 5 is recommended for neurological monitoring of patients with IOPD.

KEYWORDS: Neurogenetics, Neuroimaging, Neurometabolic

341. Prognosis in Infantile Epileptic Spasms Syndrome (IESS) with Normal Brain magnetic resonance imaging: A Multicenter Retrospective Study

Kim H B (Seoul, Republic of Korea), Yoo B, Lee JH, Lim B C, Yum M-S, Kim HM, Kim J S, Lee JW, Choi SA, Kim M-J, Kim WJ, Woo HY, Han JY, Kim MH, Kim HJ

OBJECTIVE: This multicenter cohort retrospectively evaluated the treatment and development outcome of the patients with infantile epileptic spasms syndrome (IESS) with normal brain magnetic resonance imaging (MRI).

METHODS: Data were collected from five hospitals in South Korea from 2010 to 2022, including 387 patients with IESS and over two years of follow-up. This study focused on 136 patients (35.1%) with normal brain MRI, analyzing demographics, treatments, etiologies, seizure outcome, and developmental outcome.

RESULTS: The mean age at diagnosis was 6.99 $\pm$ 4.47 months. Spasms were the first seizure in 122 patients (89.7%). Before onset, development was normal in 61 patients (44.8%) and delayed in 48 (35.3%). One year after the onset, 22 patients (16.2%) maintained normal development. Genetic testing was done in 77 patients and identified pathogenic variants or copy number variants in 22 patients. Initial treatments were vigabatrin monotherapy in 80 patients (58.8%) and vigabatrin with corticosteroids in 47 (34.6%). Patients achieving spasm control within 6 months had better seizure and cognitive outcomes (p= 5.01e-10, 0.031). Those treated with vigabatrin and corticosteroids showed significantly better seizure outcomes than those treated with vigabatrin monotherapy. (p= 0.011).

CONCLUSIONS: In patients with IESS with normal brain MRI, co-treatment with corticosteroid showed better seizure outcome than vigabatrin monotherapy. Early spasm control within 6 months affected the better cognitive or developmental outcome. Genetic testing helped to predict the clinical outcomes of IESS.

KEYWORDS: Epilepsy

342. Clinical and genetic characteristics of GRIN-related neurodevelopmental disorders

Cha J H (Seoul, Republic of Korea), Kim J, Yun H-Y, Jang S, Kim H J, Kim W J, Kim SK, Lim BL, Kim KJ, Lee SL, Chae J-C

OBJECTIVE: The GRIN family of genes is associated with neurological disorders. We aim to demonstrate the neurological phenotypes of GRIN-related disorders and describe clinical characteristics based on variant types.

METHODS: We reviewed the clinical phenotypes of 26 patients with genetically confirmed GRIN-related neurological disorders from a single tertiary center. Variants were categorized into GRIN1 (7 patients), GRIN2A (4 patients), GRIN2B (14 patients), and GRIN2D (1 patient). Reviewed clinical phenotypes included neurodevelopmental status, and the presence of seizures and movement disorders. GRIN variants were classified into truncating and missense variants, with missense variants divided into those located in the M3-M4 helices, and those were not. We pooled 606 previously reported GRIN variants to compare phenotypic differences according to variant types.

RESULTS: GRIN variants were comprised of 21 missense, 1 nonsense, 1 in-frame deletion, 3 large deletion mutations. Trio analysis confirmed 19 de novo variants, and 13 variants had not been previously reported. All patients manifested severe neurodevelopmental delay, with 18 patients (69.2%) could not walk independently and 22 patients (84.6%) could not speak meaningful words. Variants located in the M3-M4 helices were significantly associated with severe neurodevelopmental delay across the GRIN family. Variants in GRIN2A and GRIN2B had significant higher risk of movement disorders and cortical visual impairment.

CONCLUSIONS: Children with GRIN mutations presented with a wide spectrum of neurological features, with a greater severity and diversity for variants located in the M3-M4 helices. We highlight the structure-function relationship of the N-methyl-D-aspartate receptor, emphasizing the detailed GRIN variant information could inform personalized treatment approaches.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

343. Catecholamine Modulation Using the Tyrosine Hydroxylase Inhibitor L1-79 For the Treatment of Socialization Impairments in Adolescents and Young Adults with Autism Spectrum Disorders.

Megerian J T (Orange, CA), Fischer T, Nguyen U, Beversdorf D

OBJECTIVE: Determine efficacy, safety and tolerability of d,l-alpha-methyl-para-tyrosine (L1-79) for treatment of core symptoms of social impairment in autism spectrum disorder (ASD).

METHODS: Male and female subjects 12-21 years of age with ASD meeting inclusion criteria (See https://clinicaltrials.gov/study/NCT05067582) were randomized in a double-blind, placebo-controlled crossover study. Subjects were assigned to active (L1-79 200mg or 300mg BID) or placebo for 12 weeks, with 6-week washout, then the alternate treatment for 12 weeks. The primary outcome assessment was the Vineland-3 Socialization Domain. Clinical global impression of severity/change (CGI-S/CGI-C) and caregiver global impression of change of 3 most bothersome symptoms of ASD (CGI-3P) were key secondary measures. Analysis for crossover (N= 41, study completers) and parallel design (N=44, period 1 completers, 23 active treatment, 21 placebo)

were prespecified using a mixed repeated measures model with least square means comparisons.
RESULTS: There was carryover and sequence effect observed in the crossover, so the parallel group period 1 completers were analyzed as the primary efficacy target. There were statistically significant and clinically meaningful improvements in the Vineland-3 Socialization Standard Score with L1-79 versus placebo (difference: 7.94, p=0.0115). Similar findings were seen for CGI-S and CGI-3P (CGI-S difference: -0.62, p=0.0155; CGI-3P Symptom 1: -0.6, p=0.0293, Symptom 2: -0.48, p=0.0399; Symptom 3: -0.61, p=0.0469). The Vineland-3 responder analysis did not show significant separation between active and placebo. L1-79 was well-tolerated.
CONCLUSIONS: Modulation of catecholaminergic tone with L1-79 demonstrated statistically significant and clinically meaningful improvements in socialization as measured on the Vineland-3, and socialization focused clinician and parent rating scales.
KEYWORDS: Neurodevelopmental Disorders, Experimental Therapeutics, Behavioral Neurology

344. Clinical Features and Outcome of Pediatric Probable Antibody-negative Autoimmune Encephalitis

Kim H J (Seoul, Republic of Korea), Jang SY, Kim J M, Cha J H, Kim WJ, Kim S Y, Cho A, Kim HM, Chae J-H, Kim KJ, Kim BC

OBJECTIVE: This study aims to evaluate clinical features and outcome of pediatric patients with probable antibody-negative autoimmune encephalitis (Ab-negative AE).
METHODS: Patients who satisfied proposed criteria for probable Ab-negative pediatric AE were recruited from a single center between 2012 and 2024. Clinical outcome was assessed using modified Rankin Scale (mRS) score, with good outcome defined as mRS ≤2. Seizure outcome was evaluated based on development of postencephalitc epilepsy, defined as persistent seizures six months after onset.
RESULTS: Sixty-five patients with median onset age of 11 years (interquartile range [IQR] 6-13) were included. The median follow-up duration was 25 months (IQR 9.5-52.25). Altered mentality was the most frequent neurologic symptom (92.3%) followed by seizures in 84.6%. Among patients with seizures, status epilepticus, and refractory status epilepticus occurred in 47.7%, and 40.0% respectively. Most patients (89.2%) received immunotherapy (IT) with first-line IT (methylprednisolone and/or intravenous immunoglobulins) in all and second-line IT (rituximab or in combination with tocilizumab) in 32.3%. The overall prognosis was favorable, 94.6% of patients achieved good outcome at 12 months; 96.7% with first-line IT alone, and 87.5% with additional second-line IT. Postencephalitic epilepsy was observed in 49.1%, and status epilepticus and persistent seizure after one month were identified as risk factors (odds ratio 4.99 and 6.54; 95% confidence interval, 1.26-20.45 and 1.37-32.25).
CONCLUSIONS: Our study suggested that pediatric Ab-negative pediatric AE treated with immunotherapy seemed to show a favorable clinical outcome in most patients. However, second-line immunotherapy did not show additional benefit regarding clinical outcome and postencephalitic epilepsy.
KEYWORDS: Epilepsy, Neuroimmunology

345. Subgroup analysis of pediatric patients in a phase III, randomized, placebo-controlled crossover trial with Levacetylleucine (IB1001) for Niemann-Pick disease type C

Schafer J (Austin, TX), Zanrucha B, Grosso M, Fields T, Bremova-Ertl T, Strupp M

OBJECTIVE: Niemann-Pick disease type C (NPC) is a rare, autosomal recessive neurodegenerative disorder. IB1001-301 was a Phase III, double-blind, randomized, placebo-controlled, crossover trial comparing levacetylleucine with placebo for the treatment of neurological signs and symptoms in NPC after 12 weeks. In a cohort of 60 NPC patients aged 5 to 67 years, the primary Scale for the Assessment and Rating of Ataxia (SARA) endpoint was reduced -1.97 points with levacetylleucine and -0.60 for placebo (p<0.001).
METHODS: Subgroup analysis was conducted to evaluate the effects of levacetylleucine in pediatric patients (aged <18 years). The primary Scale for the Assessment and Rating of Ataxia (SARA) and secondary Clinical Global Impression of Improvement (CGI-I), Spinocerebellar Ataxia Functional Index (SCAFI), and Modified Disability Rating Scale (mDRS) were assessed.
RESULTS: 23 pediatric patients aged 5 to 17 years with genetically confirmed NPC were randomized at 8 multinational sites. The improvement on the SARA scale with levacetylleucine in pediatric patients was superior to Placebo [mean change -1.80 (2.35); 95% CI -0.79, -2.82, p=0.001]. Secondary endpoints were also improved with levacetylleucine compared to placebo. The frequency of adverse events was comparable between pediatric patients while on levacetylleucine and placebo, and no treatment-related serious adverse events occurred.
CONCLUSIONS: Levacetylleucine demonstrated a statistically significant improvement over placebo in pediatric patients with NPC and a clinically meaningful improvement in symptoms (motor and cognitive) consistent with investigator and caregiver-reported outcome measures regarding functioning. Levacetylleucine was safe and well-tolerated, providing a favorable benefit-risk profile for the treatment of pediatric patients with NPC.
KEYWORDS: Neurodevelopmental Disorders, Global Neurology, Movement Disorders

346. NGN-401, A Novel Regulated Gene Therapy for Rett Syndrome: Preliminary Results from the First-in-Human Study

Suter B (Houston, TX), Lieberman D, Benke T, Neul J, Jaggumantri S, Feng C, Albanis E, Cobb S, Jordan J

OBJECTIVE: Rett syndrome (RTT) is a severe X-linked neurodevelopmental disorder caused by MECP2 gene mutations that lead to deficiency of methyl-CpG binding protein 2 (MeCP2). NGN-401 is an AAV9 gene therapy designed to express controlled levels of full-length MeCP2 using the EXACT™ transgene regulation technology and has potential to be disease-modifying. The ongoing Phase 1/2 clinical trial

is evaluating safety, tolerability, and preliminary efficacy of NGN-401 in subjects with RTT.

METHODS: The Phase 1/2 open-label trial is enrolling 16 female subjects ages 4-10 years with classic RTT (NCT05898620). NGN-401 is delivered as a one-time intracerebroventricular (ICV) administration in two dose cohorts (low dose 1E15 vg; high dose 3E15 vg) with prophylactic immunosuppression. ICV was chosen as the optimal route of administration to target key areas of the nervous system underlying RTT pathophysiology.

RESULTS: The first three low-dose subjects were ages 7, 4 and 6 years and the first high-dose subject was age 5 years at baseline. Follow-up at abstract submission was ∼12, 9, 6 and 3 months, respectively. NGN-401 has shown a favorable safety profile, and no signs or symptoms indicative of MeCP2 overexpression have been reported, including in a subject with a mild variant predicted to result in residual MeCP2 expression. There have been no treatment-emergent or procedure-related serious adverse events.

CONCLUSIONS: NGN-401 has a favorable safety profile, and no clinical evidence indicative of MeCP2 overexpression has been reported. Preliminary efficacy results for the first three subjects and additional safety data from both cohorts will be presented.

KEYWORDS: Neurodevelopmental Disorders, Neurogenetics

347. Clinical Significance of Myelin Oligodendrocyte Glycoprotein Antibodies in Cerebrospinal Fluid in Pediatric Inflammatory CNS Disorders

Jang S (Seoul, Republic of Korea), Kim H-J, Kim J, Kim W, Kim S-Y, Chae J, Kim K-J, Lim B-C

OBJECTIVE: To assess the clinical significance of myelin oligodendrocyte glycoprotein antibodies (MOG-Abs) in cerebrospinal fluid (CSF) in pediatric patients with inflammatory CNS disorders.

METHODS: Paired serum and CSF samples were collected from patients under 18 years old with suspected inflammatory demyelinating disease (IDD) during a retrospective chart review from 2000 to 2020. MOG-Abs were detected using live cell-based assays, and patients were classified as having MOG antibody-associated disease (MOGAD) if MOG-Abs were present in either serum or CSF.

RESULTS: A total of 62 patients were included, with 42 female (67.7%) and 20 male (32.3%) participants. MOG-Abs were found in both serum and CSF in 44 patients (71.0%), only in serum in 16 patients (25.8%), and only in CSF in 2 patients (3.2%). CSF WBC counts were significantly higher in CSF-positive patients compared to CSF-negative patients, particularly in the MOG-Abs seronegative but CSF-positive group ($p = 0.019$). The seropositive but CSF-negative group had higher disability at last follow-up ($p = 0.002$) and experienced more relapses ($p = 0.021$) than the CSF-positive groups. Ophthalmologic findings did not significantly differ between CSF-negative and CSF-positive groups.

CONCLUSIONS: MOG antibodies in both serum and CSF are essential for diagnosis, with some patients showing restricted antibodies in CSF. Testing for MOG-IgG in the CSF is particularly important in seronegative IDD cases where MOGAD is strongly suspected, which might aid in diagnosis and management.

KEYWORDS: Pediatric Demyelinating Disease, Neuroimmunology

348. Trio-Based Rapid Whole-Genome Sequencing of Pediatric Patients

Kim S Y (Seoul, Republic of Korea), Lee S, Koh J, Kim J M, Jang S, Kim H J, Lim BC, Chae JH

OBJECTIVE: The development of next-generation sequencing has significantly impacted clinical practice, and rapid whole-genome sequencing (rWGS) offers potential benefits for urgent medical decision-making, particularly in neonatal and pediatric intensive care units (NICU/PICU). This study aimed to implement rWGS in critically ill pediatric patients in a real-world healthcare system.

METHODS: Between March 2023 and June 2024, 20 patients aged <36 months admitted to the NICU/PICU or those with suspected rapidly progressive genetic disorders were enrolled. Trio-based genome sequencing was performed and analyzed using a customized rapid processing pipeline.

RESULTS: Among 20 enrolled patients, 11 were from NICU. The median time between symptom onset and study enrollment was 73 days for 18 patients referred from other hospitals and less than a week for 2 in-hospital patients. The median turnaround time (TAT) for rWGS was 10 days, with the shortest being 5 days. A definite or presumed genetic diagnosis was achieved in 11 patients (55%) and two additional patients were found to have non-genetic etiologies after rWGS. Management plans were altered for eight of the 11 patients (72.7%), including medication changes, diet modifications, and preimplantation genetic testing for future pregnancies.

CONCLUSIONS: This study highlights the feasibility and clinical utility of rWGS in critically ill pediatric patients in Korea, with a high diagnostic yield and significant impact on patient management. Establishing a nationwide fast-track system and providing detailed testing indications are required for effective implementation. Further automation and resource optimization may reduce the TAT and improve the efficacy of rWGS in critical care settings.

KEYWORDS: Neurogenetics, Neonatal Neurology, Fetal Neurology

349. Neurocognitive outcomes after gene therapy with elivaldogene autotemcel (eli-cel) to treat cerebral adrenoleukodystrophy (CALD): pooled analyses from ALD-102 and ALD-104 trials

Pierpont E I (Minneapolis, MN), King K, Duncan C, Eichler F, Sevin C, Thrasher A, Shah A, Kühl J-S, De Oliveira S, Amartino H, Raymond G, Van Haren K, Smith N, Dalle J-H,

Downey G, Dietz A, Prasad V, Thakar H, Williams D, Orchard P

OBJECTIVE: Eli-cel is a lentiviral-based gene therapy for CALD. Herein we report neurocognitive outcomes from participants treated with eli-cel in ALD-102 (NCT01896102) and ALD-104 (NCT03852498).

METHODS: Boys aged ≤17 years with active CALD received eli-cel after myeloablation. MRI severity at baseline was quantified using the Loes score. Longitudinal assessments of intellectual functioning (Wechsler scales) at baseline, year 2 (Y2), and year 4 (Y4) measured posttreatment outcomes across four domains.

RESULTS: As of April 25, 2024, 67 participants had received eli-cel (median [range] age at treatment: 6 [4-14] years; baseline Loes score: 2.0 [1.0-9.0]; follow-up, 55.5 [13.4-124.6] months). Across the full cohort, the proportion of boys with neurocognitive scores within normal limits (ie, score ≥85) were: visual-spatial reasoning (baseline, 87% [54/62]; Y2, 79% [45/57]; Y4, 68% [25/37]), verbal reasoning (baseline, 81% [48/59]; Y2, 79% [38/48]; Y4, 86% [25/29]), working memory (baseline, 77% [34/44]; Y2, 75% [33/44]; Y4, 67% [20/30]), and processing speed (baseline, 76% [44/58]; Y2, 59% [32/54]; Y4, 70% [26/37]). Participants with higher Loes scores tended to have lower cognitive scores at follow-up. The safety profile of eli-cel remained consistent with prior reports; hematologic malignancy is a known risk.

CONCLUSIONS: In this first report of neurocognitive outcomes for the combined ALD-102 and ALD-104 gene therapy studies, eli-cel was effective in preserving neurocognitive status within normal limits over time in the majority of participants. Changes among participants with higher Loes scores underscore the need for early treatment of CALD. Additional follow-up is needed to confirm the maintenance of neurocognitive stability.

KEYWORDS: Pediatric Demyelinating Disease, Neurometabolic

350. A practice survey of prenatally identified supratentorial midline brain malformations

Chirigos A (Cincinatti, OH), Agarwal S, Ostrander B, Young M, Smego A, Natarajan N, Vawter-Lee M, Gano D, Venkatesan C, Keene J

OBJECTIVE: Supratentorial midline brain malformations (MBMs), a common category of prenatally-diagnosed central nervous system malformation, comprise approximately one third of fetal neurology consults. Outcomes associated with MBMs are broad and include a high risk for endocrine and ophthalmologic complications, epilepsy, cerebral palsy, intellectual disability, autism, behavioral disorders. Our study aims to characterize the care of infants with prenatally-identified MBMs to support development of multidisciplinary care guidelines.

METHODS: We distributed a Redcap survey regarding management of infants with MBMs to U.S.-based pediatric neurologists. Respondents were asked about their practice context and recommendations regarding care pre-delivery, postnatal imaging, endocrine and ophthalmologic evaluation, and developmental monitoring. Data analysis was descriptive.

RESULTS: Twenty surveys were completed from 15 institutions across the U.S. Most (19/20, 95%) respondents perform fetal neurology consultations in a multidisciplinary setting. MBM complexity affected delivery location (11/20, 55%) and postnatal imaging recommendations (15/20, 75%). All respondents pursue endocrine evaluation for infants with certain MBMs, and 14/20 (70%) recommend unequivocal endocrine evaluation. Most (19/20, 95%) recommend ophthalmologic evaluation for certain infants (86% refer for holoprosencephaly, 71% for complex MBMs, 57% for isolated absent septum pellucidum or isolated absence of the corpus callosum in female infants), and 12/20 (60%) recommend universal ophthalmology referral. Developmental monitoring through pediatric neurology clinic (18/20, 90%) and Early Intervention (13/20, 65%) was recommended.

CONCLUSIONS: Patients with prenatally-identified MBMs require a multidisciplinary approach, including endocrine and ophthalmologic evaluations and developmental monitoring, to optimize neurodevelopmental outcomes and facilitate early diagnosis of medical complications. Results of this survey may inform a standardized approach to care.

KEYWORDS: Fetal Neurology, Neonatal Neurology, Neurodevelopmental Disorders

351. Clinical and genetic characteristics of Japanese patients with CDKL5 deficiency disorder; from the results of nationwide survey

Kitami Y (Tokyo, Japan), Itoh M

OBJECTIVE: Patients with pathogenic mutations in cyclin-dependent kinase-like-5 gene (CDKL5) are designated CDKL5 deficiency disorder (CDD). This study aimed to delineate the clinical and genetic characteristics, including the treatment for epilepsy and sleep disorder.

METHODS: To investigate the number of patients with CDD and clarify the clinical characteristics of Japanese patients with CDD, we launched the nationwide survey. We recruited patients who underwent genetic analysis and were confirmed CDKL5 pathogenic variants. We retrospectively reviewed clinical feature, genetic information, and focused on the treatment for epilepsy and sleep disorder.

RESULTS: We identified 26 patients (23 females and 3 males) with CDKL5 pathologic mutations. Among of 26, 20 patients were confirmed mutation patterns. All patients had an early onset seizure, severe developmental delay, abnormality of muscle tone, stereotyped movement and night terror. Antiepileptic drugs achieving 50% reduction in seizure frequency were sodium valproate, vigabatrin and lamotrigine in each one patient. Ketogenic diet in three patient and vagus nerve stimulation in two patients were achieved 50% reduction in seizure frequency. In sleep disorder, all patients had sleep terror (100%, 26/26). We also found difficulty falling asleep (35%, 9/26), excessive daytime sleepiness (31%, 8/26), circadian rhythm sleep-wake disorder (19%, 5/26),

nocturnal awakenings (19%, 5/26), sleep-wake disorder (8%, 2/26), sleep breath disorder (4%, 1/26) and hypersomnia (4%, 1/25). Risperidone and Ramelteon were effective in one patient and triclofos sodium in another patient.
CONCLUSIONS: This study revealed the nature and magnitude of sleep disturbances on patients with CDD and their families.
KEYWORDS: Epilepsy, Neurogenetics, Sleep

352. Congenital myopathies: revising and revisiting the definition and nomenclature

Hayes L H (Boston, MA), Raga S, Villar Quiles N, Bonnemann C, Dowling J, Ferreiro A, Oates E

OBJECTIVE: To establish a definition and updated nomenclature for congenital myopathies.
METHODS: Twenty-six individuals including clinical/research experts, curation specialists, and patient advocates with global representation convened in June 2024 for the 277th European Neuromuscular Centre (ENMC) workshop.
RESULTS: The group reached consensus on (1) a concise definition of congenital myopathies and (2) a nomenclature and related, but distinct, classification scheme.
CONCLUSIONS: "Congenital myopathy" (CMYO) is an umbrella term used to describe a heterogeneous group of genetic muscle disorders that typically present at birth (even prenatally) or during infancy with hypotonia and muscle weakness. They are typically nonprogressive or only slowly progressive. The initially defining histopathological findings are distinctive structural abnormalities in skeletal muscle fibers without overt dystrophic features. CMYOs should be conceptualized around three axes: (1) Gene +molecular mechanism, (2) Clinical "class" or syndrome with biopsy findings if available, (3) Disease impact on function. From these, features can be incorporated into nomenclature depending on what clinical, genetic, and histopathological knowledge is available for each affected individual. An illustrative example would be: "autosomal recessive RYR1-congenital myopathy with cores". In cases where the gene is unknown and/or the biopsy is unavailable or nonspecific, the diagnosis of congenital myopathy alone may be used, though by definition the term congenital myopathy should be applied only to individuals who either have a confirmed genetic basis (i.e. pathogenic variant(s) in a known CMYO gene) or consistent muscle features.
KEYWORDS: Neuromuscular, Neurogenetics, Education

353. Striking Brain fMRI Differences Between Dysregulated and Resilient Children with Neurodevelopmental and Sensory Processing Dysfunction

Marco E (San Rafael, CA), Choi H, Powers R, Lazerwitz M, Cai L, Brandes-Aitken A, Trimarchi K, Garcia R, Chu R, Mukherjee P

OBJECTIVE: Functional connectivity (FC) in children with sensory over-responsivity (SOR) has not been explored. We hypothesize SOR children will show FC differences in brain networks and FC in these networks will segregate Neurodevelopmental Disorder (NDD) children, with and without SOR, who are behaviorally dysregulated from those who are resilient.
METHODS: NDD children, 8-12 years (n=123), were assigned to SOR and non-SOR cohorts using the Sensory Processing 3-Dimensions Assessment and scanned using multiband echo-planar fMRI at 3T. There were 83 non-autistic children with adequate fMRI (mean age: 10.47 $\pm$ 1.59; 30 females; 39 SOR). Fractional amplitude of low-frequency fluctuations (fALFF), a measure of local FC, was computed for 7 exogenous (cerebellar; 3 somatomotor; 3 visual) and 7 endogenous (central executive, default mode, dorsal attention, left/right frontoparietal, salience, and ventral attention) networks. Dysregulated and resilient clusters were derived using latent profile analysis of the Behavior Assessment System for Children-3 (n=71; 25 females; 31 SOR; 48 resilient).
RESULTS: NDD-SOR children displayed elevated endogenous and reduced exogenous fALFF versus those without SOR. Furthermore, behaviorally dysregulated NDD children show relatively matched, intermediate endogenous and exogenous fALFF while resilient NDD-SOR children show marked elevation of their endogenous FC and lower exogenous FC. The non-SOR resilient NDD children show a diametrically opposing pattern.
CONCLUSIONS: These findings indicate that SOR children show different resting state FC patterns relative to non-SOR children. While, FC patterns are similar in dysregulated NDD children, resilience is associated with dramatic differences in endogenous and exogenous processing in SOR versus non-SOR children suggesting a sensory-based approach to treatment.
KEYWORDS: Neurodevelopmental Disorders, Neuroimaging, Behavioral Neurology

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