Child Neurology Society

Presented at
The Vancouver Convention Center
Vancouver, BC, Canada
October 4 – October 7, 2023
CME Joint Sponsorship Provided
by Minnesota Medical Association
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Annals of NEUROLOGY

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Annals of Neurology

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

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October 4-7, 2023

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Donald Gilbert 2017-2019
Michael Shevell 2017-2019
Lori Jordan 2018-2020
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Audrey Brumback 2020-2022
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

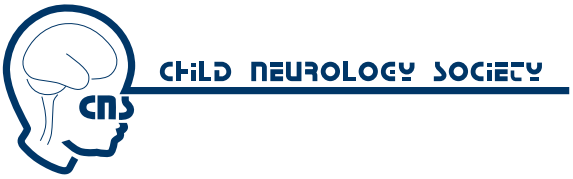
1976
Monterey, California

1975
Hamilton, Ontario, Canada

1974
Madison, Wisconsin

1973
Nashville, Tennessee

1972
Ann Arbor, Michigan



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2023
Phillip L. Pearl
Boston, MA

2022
Leon G. Epstein
Chicago, IL

2021
Jonathan W. Mink
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

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2023
Amy R. Brooks-Kayal
Sacramento, CA

2022
Steven Paul Miller
Vancouver, BC, Canada

2021
Jerry Mendell
Columbus, OH

2020
Joseph Gleeson
San Diego, CA

2019
Scott Pomeroy
Boston, MA

2018
William B. Dobyns
Seattle, WA

2017
Solomon Moshé
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
Montreal, QC, Canada

2006
Donna Ferriero
San Francisco, CA

2005
O. Carter Snead III
Toronto, ON, Canada

2004
Karin Nelson
Bethesda, MD

2003
Darryl C. De Vivo
New York, NY

2002
Francis Collins
Bethesda, MD

2001
Huda Zoghbi
Houston, TX

2000
Joseph Volpe
Boston, MA

1999
Carla Shatz
Berkeley, CA

1998
Andrew Engel
Rochester, NY

1997
Martha Bridge Denckla
Baltimore, MD

1996
Verne S. Caviness
Boston, MA

1995
Gerald D. Fischbach
Boston, MA

1994
David Prince
Stanford, CA

1993
C. Thomas Caskey
Houston, TX

1992
Louis M. Kunkel
Boston, MA

1991
Marcus E. Raichle
St. Louis, MI

1990
Roscoe O. Brady
Bethesda, MD

1989
Salvatore DiMauro
New York, NY

1988
Victor Dubowitz
London

1987
Hugo Moser
Baltimore, MD

1986
Louis Sokoloff
Bethesda, MD

1985
Patricia Goldman-Rakic
New Haven, CT

1984
William L. Nyhan
La Jolla, CA

1983
Roger N. Rosenberg
Dallas, TX

1982
John O'Brien
La Jolla, CA

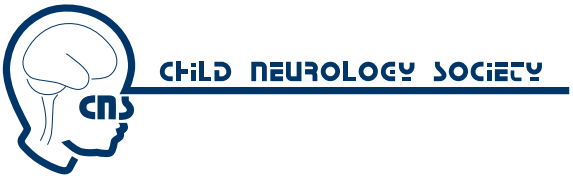
1981
Pasko Rakic
New Haven, CT

1980
Dominick Purpura
New York, NY

1979
Fred Plum
New York, NY

1978
W. Maxwell Cowan
St. Louis, MO

1977
George Cahill
Boston, MA



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2023
Siddharth Srivastava
Boston, MA

2022
Bhooma Aravamuthan
St. Louis, MO

2021
Monica Lemmon
Durham, NC

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

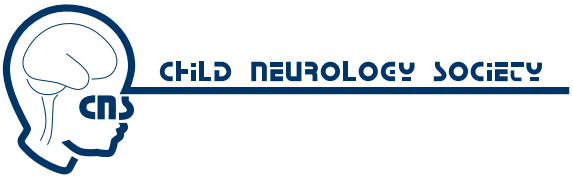
1988
Huda Zoghbi
Houston, TX

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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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

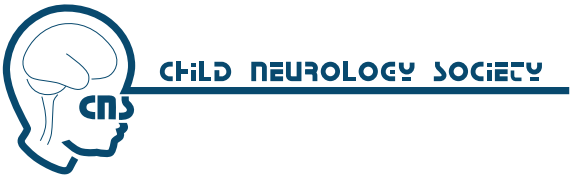
2006
Raymond Chun
Madison, WI

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

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

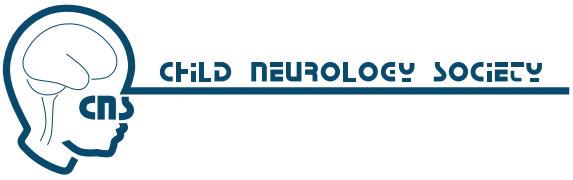
2014
Kenton Holden
Mt. Pleasant, SC

2013
Douglas Postels
East Lansing, MI

2012
Marvin Fishman
Houston, TX

2011
Shaul Harel
Tel Aviv, Israel

2010
Ruth Ness
New York, NY



Martha Bridge Denckla Award Recipients

2023
William Davis Gaillard
Washington, DC

2022
Michael Shevell
Montreal, QC, Canada

2021
Elizabeth Berry-Kravis
Chicago, IL

Bernard D'Souza International Fellowship Award

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

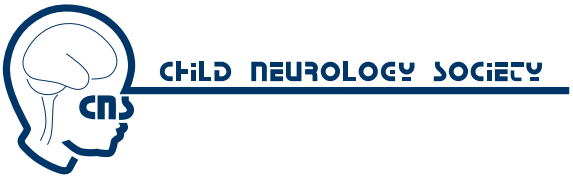
1993
Anu Soot
Tartu, Estonia

1992
Qin Jiong
Beijing, China

1991
Sergi A. Antoniuk
Curitiba, Brazil

1990
Najoua Miladi
Tunis, Tunisia

1989
Meral Ozmen
Istanbul, Turkey



Tauen Chang Junior Member Award Recipients

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

Tauen Chang Junior Member Award Recipients | 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

Tauen Chang Junior Member Award Recipients | 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

Outstanding Junior Member Post Graduate Award Recipients

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 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.

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

AAP Section on Neurology Trainee Travel Award Repients

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

CNS/PECN Training Director Award Recipient

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

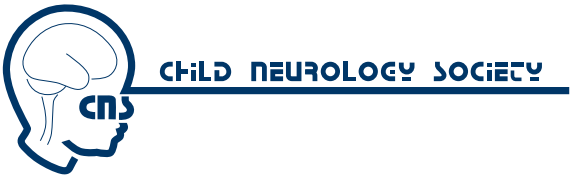
2017
Sidney M. Gospe Jr.
Seattle, WA

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 Prize Recipients

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

ASSOCIATION OF CHILD NEUROLOGY NURSES

Claire Chee Award for Excellence

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 Excellence Award

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

52nd Annual Meeting of the Child Neurology Society Scientific Program

Vancouver, BC, Canada

October 4 – October 7, 2023

Bruce H. Cohen, MD, FAAN, President, CNS
Yasmin Khakoo, MD, FAAN, FAAP; Chair & Bhooma Aravamuthan, MD, DPhil; Co-Chair,
CNS Scientific Selection and Program Planning Committee

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Minnesota Medical Association and Child Neurology Society. The Minnesota Medical Association (MMA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Minnesota Medical Association designates this live activity for a maximum of *22.5 AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

NOTE: Program book went to press in July. Session times may have been revised. For most recent and reliable schedule information, consult the 52nd CNS Annual Meeting Program and CNS Annual Meeting Website.

PROGRAM

Wednesday, October 4

8:00 AM-11:00 AM **SYMPOSIUM I: CNF SYMPOSIUM: *Clinical Trials in Pediatric Neurology: Dilemmas After the Trial***
Supported by the Child Neurology Foundation

Organizers:
Erika Fullwood Augustine, MD, MS
Kennedy Krieger Institute, Baltimore, MD
Anup Patel, MD, FAAN, FAES
Nationwide Children's Hospital, The Ohio State University, Columbus, OH

Welcome
Anup D. Patel, MD, FAAN, FAES; Nationwide Children's Hospital, The Ohio State University, Columbus, OH

The Family's Perspective
Betsy Pilon

The PI's Perspective
M. Scott Perry, MD; Jane and John Justin Institute for Mind Health, Cook Children's Medical Center, Fort Worth, TX

After FDA Approval
Michael Storey, PharmD, MS; Nationwide Children's Hospital, Columbus, OH

Winding Down
Erika Fullwood Augustine, MD, MS; Kennedy Krieger Institute, Baltimore, MD

11:30 AM – 1:30 PM **KENNETH F. SWAIMAN CNS LEGACY LUNCHEON**

Welcome and Introduction:
Bruce H. Cohen, MD, FAAN; President, Child Neurology Society

Presentation of 2023 Bhuwan Garg High School Student Neuroscience Award

- Rania Sophia Lateef; Manassas, VA

Presentation of 2023 CNS/PECN Training Director Award

- Rana R. Said, MD; UT Southwestern Medical Center, Dallas, TX

Presentation of 2023 D'Souza Award Recipients

- Prem Chand, MBBS, FCPS; Aga Khan University, Karachi, Sindh, Pakistan
- Priyanka Madaan, MD; Amrita Institute of Medical Sciences and Research Centre, Faridabad, Haryana

Presentation of 2023 Arnold P. Gold Foundation Humanism in Medicine Award

- Yasmin Khakoo, MD, FAAN, FAAP; Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY

Presentation of 2023 Roger & Mary Brumback Lifetime Achievement Awards

- Radha Giridharan, MD; SUNY Downstate Medical Center, Brooklyn NY
- Robert S. Greenwood, MD; UNC School of Medicine, Chapel Hill, NC
- James John Riviello, Jr., MD; Texas Children's Hospital, Houston, TX

2:00 PM – 4:30 PM

Navigating the Landscape of Publication and Leadership in Child Neurology
Organizers:
Alexander Cohen, MD, PhD; Boston Children's Hospital, Harvard Medical School, Boston, MA
Ariel Maia Lyons-Warren, MD, PhD; Texas Children's Hospital, Baylor College of Medicine, Houston, TX
Rujuta Wilson, MD, MS; UCLA David Geffen School of Medicine, UCLA Center for Autism Research and Treatment, Los Angeles, CA

2:00 PM – 5:30 PM

Professors and Educators of Child Neurology (PECN)
PECN Business Meeting
(2:00 PM - 3:30 PM)
Organizer: Soe Mar, MD; Washington University School of Medicine, St. Louis, MO

Introduction and Agenda
Soe Mar, MD; Washington University School of Medicine, St. Louis, MO

Match report, Preference Signaling, and the Interview Season Prep
Margie Ream, MD, Ph.D.; Nationwide Children's Hospital, Columbus, OH

Subcommittees of PECN and Education Reform
Kathryn Xixis, MD; University of Virginia, Charlottesville, VA
Adam Wallace, MD; University of Wisconsin, Madison, WI

Genomics Education for Child Neurology Trainees - Needs Assessment and Curriculum Development
Kuntal Sen, MD; The George Washington University, Washington DC

CNCDP-K12 Report
Bradley L. Schlaggar MD, PhD; Kennedy Krieger Institute, Baltimore, MD

Minority Research Scholars Program
Erika Fullwood Augustine, MD, MS; Kennedy Krieger Institute, Baltimore, MD

Updates AAP Section of Pediatric Neurology
Tim Lotze, MD; Baylor College of Medicine, Houston, TX

Updates AAN Section of Child Neurology
Donald Gilbert, MD; University of Cincinnati, Cincinnati, OH

Future of NDD
Miya Asato, MD; Kennedy Krieger Institute, Baltimore, MD

The ACGME, the RC and Child Neurology Training
Louise Castile, ACGME, Chicago, IL
Howard Goodkin MD PhD. U of Virginia

Future of Child Neurology Training requirement: Balancing "push" and "pull"
Soe Mar, MD; Washington University School of Medicine, St. Louis, MO
Nancy Bass, MD; Medical College of Wisconsin, Milwaukee, WI
Donald Gilbert, MD; University of Cincinnati, Cincinnati, OH

Merger between PECN and CNS: What to expect
Donald Gilbert, MD; University of Cincinnati, Cincinnati, OH
Nancy Bass, MD; Medical College of Wisconsin, Milwaukee, Wisconsin
Soe Mar, MD; Washington University School of Medicine, St. Louis, MO

2:00 PM – 7:30 PM **EXHIBIT HALL**

3:30 PM – 5:30 PM **Professors and Educators of Child Neurology (PECN) Meeting (CME): Artificial Intelligence: What's Coming for Child Neurology Education**

Faculty:
Jessica Goldstein, MD; Associate Professor of Neurology, University of Minnesota
Rachel Gottlieb-Smith, MD, MHPE; Assistant Professor of Pediatrics, University of Michigan
Andrew Knox, MD, MS; Assistant Professor of Neurology, University of Wisconsin
Jacyln Martindale, DO; Assistant Professor of Neurology, Atrium Health Wake Forest Baptist
Justin Rosati, MD; Senior Instructor of Neurology, University of Rochester
Kathryn Xixis, MD; Assistant Professor of Neurology, University of Virginia

You Can Run, But You Can't Hide: Artificial Intelligence Is Here
Andrew Knox, MD, MS; University of Wisconsin School of Medicine, Madison, WI

AI in Recruitment
Rachel Gottlieb-Smith, MD; University of Michigan, Ann Arbor, MI
Kathryn Xixis, MD; University of Virginia, Charlottesville, VA
Justin Rosati, MD; University of Rochester, Rochester, NY

AI in Medical Education
Jaclyn Martindale, DO; Wake Forest Baptist Medical Center, Winston-Salem, NC
Jessica Goldstein, MD; University of Minnesota, Minneapolis, MN

Open Discussion

6:00 PM-7:30 PM **WELCOME RECEPTION**

8:00 PM-10:00 PM **MOVEMENT DISORDERS VIDEO ROUNDS**

Thursday, October 5

8:00AM – 10:15 AM **SYMPOSIUM II: PRESIDENTIAL SYMPOSIUM: *Mitochondrial Disease: 10 Years of Advances & Progress***

Organizer: Sumit Parikh, MD; Mitochondrial Medicine Center, Cleveland Clinic, Cleveland, OH

Mitochondrial Disease Basics (nDNA/mtDNA, Review of Red Flag Symptoms, Approach to Testing, Improvement in Genomics, Limitations of Muscle Biopsies)
Mary Kay Koenig, MD; University of Texas, Houston, Houston, TX

Development of National and International Consensus Guidelines for Diagnosis, Care and the US Mitochondrial Care Network
Sumit Parikh, MD; Mitochondrial Medicine Center, Cleveland Clinic, Cleveland, OH

Advances in Mitochondrial Disease Clinical Trials
Amel Karaa, MD; Massachusetts General Hospital, Boston, MA

Secondary Mitochondrial Dysfunction in Other Genetic Disorders
Amy Goldstein, MD; Children's Hospital of Philadelphia, Philadelphia, PA

Epilepsy in Mitochondrial Disease
Russ Saneto, MD, PhD; Seattle Children's Hospital, Seattle, WA

The Ketogenic Diet and Mitochondrial Function
Jong Rho, MD; University of California, San Diego, San Diego, CA

Autism and Mitochondrial Dysfunction
Robert Naviaux, MD, PhD; University of California, San Diego School of Medicine, San Diego, CA

Oncology and Mitochondrial Dysfunction
Bruce Cohen, MD, FAAN; Northeast Ohio Medical University, Akron Children's Hospital, Akron, OH

Q&A
Bruce H. Cohen, MD, FAAN; Northeast Ohio Medical University, Akron Children's Hospital, Akron, OH

10:45 AM – 12:00 PM **SEMINAR 1: *Neuromodulation in the Clinic: Current and Emerging Applications***

Organizer: Angela Hewitt, MD, PhD; University of Rochester Medical Center, Rochester, NY

Moderator: Angela Hewitt, MD, PhD; University of Rochester Medical Center, Rochester, NY
Moderator: Steve Wu, MD; Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Neuromodulation for Headache: Zap the Pain Away
Daniel N. Lax, MD; Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY

Stopping Seizures with Stimulation
Keith Starnes, MD; Mayo Clinic, Rochester, MN

Zap the Wiggles Away
Amy Robichaux Viehoever, MD, PhD; Washington University in St. Louis, St. Louis, MO

10:45 AM – 12:00 PM **SEMINAR 2: *Biomarkers & Endpoints for Trials in Neurodevelopmental Disorders***

Organizer: Rujuta Wilson, MD, MS; Semel Institute for Neuroscience and Human Behavior, UCLA Center for Autism Research and Treatment, Los Angeles, CA

Current State and Future Directions of Clinical Trials and Biomarker Development in NDDs Across a Lifespan
Evdokia Anagnostou, MD; Bloorview Research Institute, University of Toronto, Toronto, ON, CAN

Measures of Motor Function as Biomarkers in Neurodevelopmental Disorders
Rujuta Wilson, MD, MS; Semel Institute for Neuroscience and Human Behavior, UCLA Center for Autism Research and Treatment, Los Angeles, CA

The National Institutes of Health (NIH) Toolbox Cognition Battery as an Outcome Measure for Neurodevelopmental Disorders
David Randal Hessl, PhD; University of California-Davis, Division of Clinical Psychiatry, Sacramento, CA

Electrophysiological Biomarkers for Clinical Trials in Genetic Neurodevelopmental Disorders
Shafali Jeste, MD; Division of Neurology, Neurological Institute, Children's Hospital, Los Angeles, Los Angeles, CA

10:45 AM – 12:00 PM **SEMINAR 3: *Sleep in Children with Neurodevelopmental Disorders***

Organizer: Amy Licis, MD, MSCI, FAASM; Washington University Department of Neurology, St. Louis, MO

Sleep in Normal and Abnormal Development: Insights from Pre-clinical Models
Marcos Frank, PhD; Elson S. Floyd College of Medicine, Washington State University, Spokane, WA

Insomnia in Children with Neurodevelopmental Disorders: Considering the Causes and Optimizing Treatment
Amy Licis, MD, MSCI, FAASM; Washington University Department of Neurology, St. Louis, MO

Nocturnal Spells in Children with Neurodevelopmental Disorders: Is It a Seizure, a Parasomnia, or Something Else?
Robert Rudock, MD, MBA; Washington University School of Medicine in St. Louis, St. Louis, MO

Providing Patient-Centered Care: Addressing Sleep Issues Comprehensively in Children with Neurodevelopmental Disorders
Anne Morse, DO, FAASM; Geisinger Commonwealth School of Medicine, Geisinger Medical Center, Janet Weis Children's Hospital, Scranton, PA

11:30 AM – 7:00 PM **EXHIBIT AND POSTER REVIEW**

12:30 PM – 2:00 PM **POSTER REVIEW & GUIDED POSTER TOUR #1**

2:30 PM – 3:00 PM **Martha Bridge Denckla Award Lecture:** ***Imaging insights into cognitive system development and plasticity***
William Davis Gaillard, MD

3:00 PM – 5:15 PM **SYMPOSIUM III:** ***Sexual and Gender Minority Healthcare in Child Neurology***

Organizer: Jaclyn Martindale, DO; Wake Forest University School of Medicine, Winston Salem, NC

Moderator: Jaclyn Martindale, DO; Wake Forest University School of Medicine, Winston Salem, NC
Moderator: Alison Christy, MD, PhD; Providence Health and Services, Portland, OR

Practicing the Basics: Inclusive Neurology Care for Sex, Sexuality, and Gender Diverse People
Casey Orozco-Poore, MD; University of California - Los Angeles, Los Angeles, CA

Functional Neurological Disorder and Cerebrovascular Disease in LGBTQ+ Pediatric Patients
Z Mackenzie L'Erario, MD; Fordham Graduate School of Social Service, New York, NY

Headache in Transgender Patients
Jennifer Hranilovich, MD; Children's Hospital of Colorado, Aurora, CO

5:30 PM – 7:00 PM **POSTER REVIEW (WINE & CHEESE) & GUIDED POSTER TOUR #2**

Friday, October 6

8:00 AM – 8:15 AM **CNS/CNF/ACNN Awards**

Taeun Chang Outstanding Junior Member Awards

- Claudia Gambrah-Lyles, MD; Children's Hospital of Philadelphia, PA
- Mary Rolfes, MD; University of California, San Francisco, San Francisco, CA
- Alexander Sandweiss, MD, PhD; Baylor College of Medicine, Texas Children's Hospital, Houston, TX
- Alexandra Santana Almansa, MD; Boston Children's Hospital, Boston, MA

Taeun Chang Outstanding Junior Member Award—Post Graduate

- Milena Andzelm, MD; PhD Boston Children's Hospital, Boston, MA
- Jennifer Harmon, MD, PhD; Atrium Health Wake Forest Baptist Medical Center, Winston-Salem, NC

M. Richard Koenigsberger Scholarship Award

- Hui Li, MD, PhD; University of Wisconsin Hospitals and Clinics, Madison, WI

AAP Section of Neurology Travel Grant

- Miranda Creasey, MD; Virginia Commonwealth University, Richmond, VA

ACNN Award Announcements

8:15 AM – 8:45 AM **Philip R. Dodge Young Investigator Award Lecture:** ***Cerebral Palsy in the Modern Genomics Era***
Siddharth Srivastava, MD

8:45 AM – 9:30 AM **Bernard Sachs Award Lecture:** ***Molecules, Medicines & Mentorship: Seeking Precision Therapy for Epilepsy***
Amy R. Brooks-Kayal, MD

10:00 AM – 11:15 AM **SEMINAR 4:** ***Mitochondrial Biomarkers: State of the Art, Future of the Science***

Organizer:
Melissa A. Walker, MD, PhD; Child Neurology Division, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Diagnostic and Prognostic Biomarkers in Primary Mitochondrial Disease
Amy Goldstein, MD; Mitochondrial Medicine Frontier Program, Children's Hospital of Philadelphia, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA

Metabolic Crisis: Using Biomarkers in the Critical Care Setting
Divakar S. Mithal, MD; Section of Neurology, Ann and Robert H. Lurie Children's Hospital of Chicago, Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL

From Full Scan Metabolomics to Single Cell (Dual) Genomics: New Horizons in Mito Biomarkers
Melissa A. Walker, MD, PhD; Child Neurology Division, Massachusetts General Hospital, Harvard Medical School, Boston, MA

10:00 AM – 11:15 AM **SEMINAR 5: *Carpe Noctem! Unraveling the Epilepsy - Sleep Interface***

Organizer: Robert C. Stowe, MD; Boston Children's Hospital, Harvard Medical School, Boston, MA

Interconnections Between Sleep and Epilepsy
Temitayo Oyegbile-Chidi, MD, PhD, FAAN; University of California, Davis, Sacramento, CA

Dissecting the Effects of Sleep Versus Circadian Rhythms on Seizure Risk
Vishnu Cuddapah, MD, PhD; Children's Hospital of Philadelphia, Philadelphia, PA

Developmental/Epileptic Encephalopathy with Spike-Wave Activation in Sleep: New Name, Same Problems
Robert C. Stowe, MD; Boston Children's Hospital, Harvard Medical School, Boston, MA

10:00 AM – 11:15 AM **SEMINAR 6: *From Lorenzo's Oil to Gene Therapy - Changing X-ALD Therapeutics***

Organizer: Martha Carlson, MD, PhD; University of Michigan, Ann Arbor, MI

X-ALD Clinical Diversity and Neuroimaging
Martha Carlson, MD, PhD; University of Michigan, Ann Arbor, MI

The Evolving Landscape of Newborn Screening: X-ALD and More
Kuntal Sen, MD, FACMG; Center for Neuroscience and Behavioral Medicine, Children's National Hospital, GWU School of Medicine and Health Sciences, Washington DC

How to Implement HSCT Versus Gene Therapy for X-ALD
Florian Eichler, MD; Massachusetts General Hospital, Harvard Medical School, Boston, MA

ALD in Adults: What Child Neurologists Should Know
Fuki Marie Hisama, MD, FACMG, FAAN; University of Washington School of Medicine, Seattle, WA

11:45 PM – 1:45 PM **INDUSTRY SPONSORED SATELLITE SYMPOSIUM**

12:00 PM – 1:30 PM **LUNCH**

12:30 PM – 1:45 PM **SEMINAR 7: *Early Life Epilepsy: Closing the Gaps with Collaborative Research***

Organizer: Renée A. Shellhaas; Washington University School of Medicine, St. Louis, MO
Organizer: M. Scott Perry, MD; Jane and John Justin Institute for Mind Health, Cook Children's Medical Center, Fort Worth, TX

Introduction
M. Scott Perry, MD; Jane and John Justin Institute for Mind Health, Cook Children's Medical Center, Fort Worth, TX

Lessons Learned from Collaboration on Neonates with Seizures
Renée A. Shellhaas; Washington University School of Medicine, St. Louis, MO

Care Inequities for Children with Epilepsy, What We Learned, and Can We Fix It?
Zachary Grinspan, MD, MS; Weill Cornell Medicine, New York, NY

How Quickly Should We Move to Epilepsy Surgery?
Nathan Cohen, MD; The George Washington University School of Medicine, Children's National Hospital, Washington DC

Measuring Inch Stones of Success for Those with Profound Intellectual and Multiple Disabilities: From FDA Guidances to Community Initiatives
Anne T. Berg, PhD; Decoding Developmental Epilepsies, Washington, DC

12:30 PM – 1:45 PM **SEMINAR 8: *Heads Up: What's Next for Pediatric Migraine Treatment***

Organizer: Marielle Kabbouche Samaha, MD, FAHS, FAAN; Cincinatti Children's Hospital, Cincinatti, OH

Neuromodulators: "It's Electric!"
Joanne Kacperski, MD, FAHS; Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH

Proceeding with Procedures: The When, The Why and The How
Rachel Gottlieb-Smith, MD, MHPE; University of Michigan, Ann Arbor, MI

CGRP Therapies for Children and Adolescents?
Daniel N. Lax, MD; Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY

Behavioral Therapies for Migraine: Applications, Impact and Future
Shalonda Slater, PhD; Cincinnati Children's Hospital Medical Center, Cincinnati, OH

12:30 PM – 1:45 PM **SEMINAR 9: *Prognostic Dilemmas in Fetal Neurology: What Would You Do?***

Organizer: Sonika Agarwal, MBBS, MD; Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA

Introduction: Sonika Agarwal, MBBS, MD; Associate Professor, Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA

Panelists: Dawn Gano, Vann Chau, Sarah Mulkey, Sonika Agarwal, Mark Scher

Case 1: Sarah Mulkey
Sarah Mulkey, MD, PhD; Associate Professor, Prenatal Pediatrics Institute, Children's National Hospital, Washington, DC

Case 2: Vann Chau
Vann Chau, MD, FRCPC; Associate Professor, The Hospital for Sick Children, University of Toronto, Toronto, Canada

Case 3: Dawn Gano
Dawn Gano, MD, MAS; Associate Professor, Neurology, UCSF Weill Institute for Neurosciences, San Francisco, CA

Mark Scher (panelist)
Mark Scher, MD; Emeritus Professor, University Hospitals of Cleveland, Rainbow Babies and Children, Cleveland, OH

2:15 PM – 4:00 PM **PLATFORM I, II & III**

PLATFORM I

2:15 PM – 2:30 PM PL1-1 Anderson et al.
Drug resistant epilepsy in a mouse model of TSC: in vivo and ex vivo analysis

2:30 PM – 2:45 PM PL1-2 Knowles et al.
Myelin Plasticity Promotes Thalamocortical Hypersynchrony and Generalized Epilepsy Progression

2:45 PM – 3:00 PM PL1-3 McWalter et al.
Exome-based testing for patients with seizures identifies genetic diagnoses missed by panel-based testing

3:00 PM – 3:15 PM PL1-4 Santana Almansa et al.
Retrospective, multicenter study of lacosamide to treat neonatal seizures

3:15 PM – 3:30 PM PL1-5 Li et al.
Neurocognitive outcomes of neonates with HIE and normal MRIs

3:30 PM – 3:45 PM PL1-6 Martindale et al.
Past, Present, and Future of the Child Neurology Society: The Time to Change is Now

3:45 PM – 4:00 PM PL1-7 Zakharova et al.
Hyperkinetic dystonia in dyskinetic cerebral palsy responds to combined DBS stimulation in thalamus and pallidum.

PLATFORM II

2:15 PM – 2:30 PM PL2-1 Rolfes et al.
Host transcriptomics identifies unique host gene expression patterns in childhood arterial ischemic stroke

2:30 PM – 2:45 PM PL2-2 Gambrah-Lyles et al.
Assessing needs and perceptions of research participation in pediatric onset multiple sclerosis: a multi-stakeholder survey

2:45 PM – 3:00 PM PL2-3 Sandweiss et al.
Infectious profiling reveals potential triggers of pediatric NMDAR encephalitis: a large case-control study

3:00 PM – 3:15 PM PL2-4 Andzelm et al.
Human Genetic Modulation of the Neuronal Response to Interferons

3:15 PM – 3:30 PM PL2-5 Gulati et al.
Sleep related breathing disorder in 5-18 years children with dystrophinopathy: a cross sectional study

3:30 PM – 3:45 PM PL2-6 Hasan et al.
Interim Analysis of EVOLVE: A Long-term Observational Study Evaluating Eteplirsen, Golodirsen, or Casimersen in Routine Clinical Practice

3:45 PM – 4:00 PM PL2-7 Creasey et al.
Representation of Non-White Participants in Interventional Duchenne Muscular Dystrophy (DMD) Clinical Trial Publications

PLATFORM III

2:15 PM – 2:30 PM PL3-1 Santoro et al.
Immunotherapy Responsiveness and Risk of Relapse in Down Syndrome Regression Disorder

2:30 PM – 2:45 PM PL3-2 Gelineau-Morel et al.
Investigation of the biotransformation of trihexyphenidyl and application to dystonic cerebral palsy

2:45 PM – 3:00 PM PL3-3 Musolino et al.
Interim Results from the NEXUS Open-Label Phase 2 Study on the Safety and Efficacy of Leriglitazone in the Treatment of Childhood Cerebral Adrenoleukodystrophy

3:00 PM – 3:15 PM PL3-4 Amanat et al.
A Comprehensive Approach for Designing Effective Antisense Oligonucleotides in the Treatment of Inherited White Matter Disorders

3:15 PM – 3:30 PM PL3-5 Bonkowsky et al.
Astrocyte-targeted gene therapy demonstrates safety and efficacy in two murine models of Vanishing White Matter disease

3:30 PM – 3:45 PM PL3-6 Harmon et al.
Development of a Clinical-Translational Model of Leukoencephalopathy with Calcifications and Cysts

3:45 PM – 4:00 PM PL3-7 Patterson et al.
Evaluation of the Long-Term Effect of Arimoclomol in NPC - 48 Months Data from CT-ORZY-NPC-002

4:30 PM – 5:00 PM **CNS BUSINESS MEETING**

4:30 PM – 6:00 PM **JUNIOR MEMBER FORUM AND BREAKOUT SESSIONS**

5:30 PM – 7:00 PM **INDUSTRY SPONSORED SATELLITE SYMPOSIUM**

5:30 PM – 7:00 PM **BOD MEET AND GREET**

5:30 PM – 7:00 PM **SCIENTIFIC PROGRAM & PLANNING COMMITTEE MEETING**

7:00 PM – 9:00 PM **CLOSING GALA**

Saturday, October 15

8:00 AM – 8:45AM **Hower Award Lecture: *The Neurology of Creativity***
Phillip L. Pearl, MD

9:00 AM – 11:45 AM

SYMPOSIUM IV: Year in Review

Organizer: Grace Gombolay, MD; Emory University/Children's Healthcare of Atlanta, Atlanta, GA

Organizer: Dave Clarke, MD; University of Texas Dell Medical School, Austin, Texas

SPEAKERS:

Neonatal neurology
Dawn Gano, MD, MAS; UCSF Weill Institute for Neurosciences, San Francisco, CA

Genetic epilepsies
Annapurna Poduri, MD; Boston Children's Hospital, Boston, MA

General Epilepsy
Sucheta Joshi, MD; C.S. Mott Children's Hospital, University of Michigan, Ann Arbor, MI

Diversity, Equity and Inclusion
Diana Cejas, MD, MPH; Carolina Institute for Developmental Disabilities (CIDD) University of North Carolina at Chapel Hill, Chapel Hill, NC

Neuroimmunology
Manuscripts to Mentorship: Navigating the Landscape of Publication and Leadership in Child Neurology
Jennifer Yang, MD; UC San Diego and Rady Children's Hospital San Diego, San Diego, CA

Neuromuscular
Michael Lopez, MD, PhD; University of Alabama at Birmingham, School of Medicine, Birmingham, AL

Movement Disorders
Michael Kruer, MD; University of Arizona College of Medicine – Phoenix, Phoenix, AZ

Pediatric Stroke and Neurocritical Care
Lisa Sun, MD; The Johns Hopkins Hospital, Baltimore, MD

Neuro-oncology
Fatema Malbari, MD; Neurology Brain Tumor Program Epilepsy Center Neurofibromatosis Clinic, Texas Medical Center, Houston, TX

Headache
Lori Billinghurst, MD, MSc, FRCPC; McMaster Children's Hospital, Hamilton, ON, Canada

Neurogenetics
Andrea Gropman, MD; George Washington School of Medicine and Health Sciences, Children's National Hospital, Washington DC

12:15 PM – 4:15 PM

CNS Clinical Research Annual Workshop: 2023 - Pediatric Neurology Clinical Trials-Outcome Measures

Organizer: Ariel Maia Lyons-Warren, MD, PhD; Texas Children's Hospital, Baylor College of Medicine, Houston, TX

Co-Organizer: Rose Gelineau-Morel, MD; Children's Mercy Hospital, Kansas City, KS
Josh Bonkowsky, MD, PhD; University of Utah School of Medicine, Primary Children's Hospital, Salt Lake City, UT
Janet Soul, MDCM, FRCPC; Boston Children's Hospital, Harvard Medical School, Boston, MA
Angela Hewitt, MD, PhD; University of Rochester Medical Center, Rochester, NY
Daniel Calame, MD, PhD; Baylor College of Medicine, Houston, TX
Mustafa Sahin, MD PhD; Boston Children's Hospital, Harvard Medical School, Boston, MA

Welcome
Ariel Maia Lyons-Warren, MD, PhD; Texas Children's Hospital, Baylor College of Medicine, Houston, TX

Introduction to Outcomes Measures
Kristi Hardy, PhD; National Institute of Health, Bethesda, MD

Coffee break and networking

Case report forms and database management
Janet Soul, MD; Boston Children's Hospital, Boston, MA

Breakout sessions

Finding and Adapting Fit-for-purpose Clinical Outcome Measures: FDA-Patient-Focused Drug Development Guidance
Anne T. Berg, PhD; Northwestern University, Chicago, IL

Panel Discussion

12:15 PM – 4:15 PM **Biomedical Writing Workshop**

Organizer: E. Steve Roach, MD
Editor-in-Chief of the *Annals of the Child Neurology Society*
University of Texas Dell Medical School, Austin, TX

PRESENTERS:
Grace Gombolay, MD; Associate Editor of the *Annals of the Child Neurology Society*
Emory University/Children's Healthcare of Atlanta, Atlanta, GA

Yasmin Khakoo, MD; Editor-in-Chief, *Pediatric Neurology*
Sloan-Kettering Cancer Institute, New York, NY

Dave Clarke, MD; Associate Editor, *ACNS*
University of Texas Dell Medical School, Austin, TX

ASSOCIATION OF CHILD NEUROLOGY NURSES

2023 ACNN Conference

Vancouver, BC, Canada

October 4 – October 6, 2023

PROGRAM

Wednesday, October 4

8:00 AM - 9:00 AM — ***Janet Brucker Keynote Address: Part 1; Advances in Child Neurology***
Elizabeth Rende, DNP, APRN, CPNP-PC, PMHS-BC, FAANP; CentraCare Clinic, St. Cloud, MN
Rebecca Schultz PhD, APRN, CPNP-PC, FAES; Texas Woman's University, Houston, Texas

9:00 AM - 9:45 AM — ***The Changing Landscape of Behavioral Comorbidities***
Deanna Duggan DNP, APRN, CPNP-PC, PMHS, AQH; Texas Children's Hospital, Houston, TX

9:45 AM - 10:15 AM — ***Pediatric Migraines Management and the Newest CGRP Migraine Treatments***
Tara Pezzuto DNP, CPNP; Nemours Alfred I duPont Hospital for Children, Wilmington, DE

10:15 AM - 10:30 AM — **Break**

10:30 AM - 11:00 AM — ***Nurse Practitioner-Lead Diagnostic/Therapeutic Lumbar Puncture Clinic and Standardization of Cerebral Spinal Fluid Collection and Reconciliation***
Sara Del Vecchio FNP; Boston Children's Hospital, Boston, MA

11:00 AM - 11:45 AM — **Panel Discussion 1**

1:45 AM - 12:45 PM — **Lunch**

12:45 PM - 1:30 PM — ***Therapeutic Plasma Exchange in Pediatric Neurology: a Clinical Review and Development of a Proposed "TPE Initiation Tool"***
Joley Johnstone, NP; The Hospital for Sick Children Toronto, Toronto- Ontario, Canada

1:30 PM - 2:15 PM — ***Seeing Isn't Believing: Caring for Patients with Cortical Vision Impairment***
Tristen Dinkel MSPC, BSN, CNRN, CPN; Colorado Children's Hospital, Aurora, CO

Thursday, October 5

8:00 AM - 9:00 AM — ***Janet Brucker Keynote Address: Part 2; Present and Future of Child Neurology / ACNN***
Scott Turner, DNP, RN, FNP-BC; Children's of Alabama and University of Alabama Hospital, Birmingham, AL
Mona Jacobson MSN, CPNP; Children's Hospital of Colorado, Aurora, CO

9:00 AM - 9:45 AM — ***Genetic Testing in Childhood Epilepsies***
Daniel Crawford DNP, ARNP, CPNP-PC, CNE; University of Iowa, Iowa City, IA

9:45 AM - 10:00 AM **Break**

10:00 AM - 10:45 AM ***To Treat or Not to Treat: Suspected Psychogenic Non-Epileptic Seizures***
Heather Kennedy MSN, RN, PCNS-BC, CCRN, CWOCN; Boston Children's Hospital. Boston, MA
Sara Houston BSN, RN, CPN, CNRN; Boston Children's Hospital, Boston, MA

10:45 AM - 11:30 AM ***Staring Spells in Children, a Clinical Dilemma***
Nina Robinson, NP; Children's Hospital Colorado, Aurora, CO

11:30 AM - 12:15 PM **Panel Discussion**

12:15 PM - 1:15 PM **Lunch Break / SIG Groups**

1:15 PM - 1:45 PM ***Childhood-onset Movement Disorders***
Rasha Srouji DNP, CPNP, CNRN; Boston Children's Hospital, Boston, MA

1:45 PM - 2:15 PM ***Understanding Immune Dysfunction in Mitochondrial Disease- Implications for Practice***
Shannon Kruk; BsC RN; National Human Research Institute, Bethesda, MA
Eliza Gordon-Lipkin, MD; National Human Research Institute, Bethesda, MA

2:15 PM - 2:45 PM **Award Ceremony**

Friday, October 6

8:30 AM - 9:30 AM **Business Meeting**

9:30 AM - 10:15 AM ***Neurofibromatosis: An Overview with Discussion of Genetics and Related Conditions.***
Carolyn Dickinson PNP; University of Rochester Medical Center, Rochester, NY

10:15 AM - 10:30 AM **Break**

10:30 AM - 11:00 AM ***Tuberous Sclerosis Complex***
Sara Houston BSN, RN, CPN, CNRN; Boston Children's Hospital, Boston, MA

11:00 AM - 11:45 AM ***Batten Disease: A Complex Neurological Diagnosis***
Amy Vierhile, NP; University of Rochester Medical Center, Rochester, NY

Poster Presentations
Racheal Bingham, DNP, CPNP-PC, CPON; Texas M.D. Anderson Cancer Center, Houston, TX
Maria DeMeo, NP; Boston Children's Hospital, Boston, MA
Carolyn Hickman, PhD-CPNP-PC; Phoenix Children's, Phoenix, AZ
Meena Kadiwal, MN, NP; Hospital for Sick Children, Toronto, Ontario, Canada
Iris Marku, MSN, RN, AC-PNP; Phoenix Children's, Phoenix, AZ
Sarah Emily Wignall, CRNP; Children's of Alabama, Birmingham, AL

PLATFORM PRESENTATIONS

PLATFORM SESSION 1: Friday, October 6 (2:15 PM – 4:00 PM)

PL1-1. Drug resistant epilepsy in a mouse model of TSC: in vivo and ex vivo analysis

Anderson A (Houston, TX), Martinez L, Lee W, Susheer V, Ma Q, Jiang X

OBJECTIVE: Tuberous Sclerosis Complex (TSC), caused by mutations in TSC1 or 2, is associated with drug resistant epilepsy. mTOR inhibitors may reduce seizure burden and be disease modifying. We treated TSC mice exhibiting early-onset seizures with the mTOR inhibitor RAD001 or the antiseizure drug phenobarbital (PHB) and evaluated in vivo and ex vivo physiology and mTOR activation.

METHODS: Mice with deletion of Tsc2 in excitatory neurons (KO) and wild type (WT) littermates were treated with vehicle or 6mg/kg RAD001 every other day starting on postnatal day 8 (P8). Video-EEG (vEEG) was recorded starting on P10. phospho-S6 (pS6) level were used as a marker of mTOR activation. Mice were tested for response to 50 mg/kg PHB using 30 mg/kg pentylenetetrazole (PTZ) for seizure stimulation. Whole-cell patch clamp recordings were obtained from separate cohorts.

RESULTS: vEEG revealed that RAD001 significantly delayed seizure onset in KO mice from P12 to P50. RAD001 significantly reduced pS6 levels in KO mice between P8 and P35 levels were significantly increased at P45 ($p<0.05$) in KO compared to WT when epileptiform activity emerged in KO mice. PHB suppressed PTZ seizures in WT but not KO mice. Whole cell patch clamp recordings revealed that both excitatory and inhibitory neurons in KO slices exhibited significantly higher firing frequencies relative to WT neurons.

CONCLUSIONS: Our results support drug resistant epilepsy in the TSC rodent model and that mTOR inhibition does not render a long-lasting disease modifying effect. Studies are ongoing to further characterize circuit properties and mechanisms of drug resistance in this TSC model.

KEYWORDS: Epilepsy, Neurogenetics, Experimental Therapeutics

PL1-2. Myelin Plasticity Promotes Thalamocortical Hypersynchrony and Generalized Epilepsy Progression

Knowles J (Stanford, CA), Chau G., Saucedo T, Xu H, Alonso V, Batra A, Talmi S, McNab J, Huguenard J, Monje M

OBJECTIVE: In the healthy brain, neuronal activity-induced myelination is adaptive, increasing network synchrony to support neurological function. We demonstrated (Knowles et al, Nature Neuroscience 2022) that myelin plasticity can also become dysregulated by absence seizures. We hypothesized that seizure-induced myelination occurs in large white matter territories that overlap with absence seizure activity, contributing to pathological hyper-synchrony between cortical regions.

METHODS: Studies were performed in Scn8a+/mut mice, exhibiting spontaneous, progressive, bilateral frontoparietal absence seizures. To visualize brain-wide myelination, we mapped g-ratios (myelin sheath thickness per axon diameter) with qMTI (quantitative magnetization transfer in conjunction with diffusion MRI). We measured EEG coherence between inter-hemispheric electrode pairs. Brain Derived Neurotrophic Factor signaling through oligodendrocyte precursor cell (OPC) TrkB receptors is required for activity-dependent myelination; to determine the specific role of myelin plasticity, we induced OPC-specific TrkB receptor deletion during seizure progression in Scn8a+/mut;TrkBfl/fl; PDGFRa::Cre mice.

RESULTS: G-ratios were decreased (indicating increased myelin sheath thickness) across the longitudinal extent of anterior corpus callosum, connecting frontal and parietal regions of the bilateral hemispheres. By contrast, there were no differences in posterior corpus callosum and hippocampal commissures, connecting brain regions where absence seizures are not prominent. qMTI findings were validated by gold standard histology. Myelin plasticity blockade in Scn8a +/mut mice markedly decreased seizure progression and ictal EEG coherence in brain regions connected by anterior corpus callosum.

CONCLUSIONS: Aberrant activity-dependent myelination in Scn8a+/mut mice mirrors the anatomical distribution of absence seizures, and promotes hyper-synchrony and seizure progression. Maladaptive myelination is a newly recognized pathogenic mechanism which can predispose brain networks toward seizures.

KEYWORDS: Epilepsy, Early Stage Investigator

PL1-3. Exome-based testing for patients with seizures identifies genetic diagnoses missed by panel-based testing

McWalter K (Gaithersburg, MD), Morrow M, Butler E, Havens L, Napier M, Wain K, Kruszka P

OBJECTIVE: Characterize the diagnostic rate of exome-based testing for a patient cohort with clinical indications including seizures

METHODS: We reviewed the diagnostic outcomes of exome-based testing from a large commercial laboratory (GeneDx) database under IRB approval for 22,500 individuals with a clinical history of seizures or suspected seizures. We compared the genes with likely pathogenic or pathogenic (L/PATH) findings to lists of genes included on commercially available epilepsy gene panels to identify diagnoses potentially missed by panel testing.

RESULTS: Exome-based testing identified L/PATH variants in 725 seizure-related genes for 24% of individuals with seizures. Common commercially available epilepsy panels included just 210 (29%) of these genes. Clinically relevant results unlikely to be identified via panel included diagnostic cases with variants in genes not on the epilepsy panels

(39%), variants in genes associated with neurological concerns that potentially explain the seizures (2%), findings related to clinical indications other than seizures (5%) and nondiagnostic cases with findings in candidate genes having potential for future reclassification to disease-associated (26%).

CONCLUSIONS: Nearly 25% of patients with seizures received a genetic diagnosis through exome-based sequencing, compared to a previously reported 19% diagnostic yield for multi-gene panels (PMID: 34893972). Seventy-one percent of genes with L/PATH variants would not have been identified on epilepsy panels. Additionally, exome-based testing produced clinically relevant findings unrelated to seizures, and otherwise nondiagnostic cases included potentially contributory and candidate gene findings that may lead to future diagnoses. These data further support the use of exome sequencing as a first-tier test for patients with unexplained seizures.

KEYWORDS: Epilepsy, Neurogenetics

PL1-4. Retrospective, multicenter study of lacosamide to treat neonatal seizures

Santana Almansa A (Boston, MA), Landers J, Abend N, Chu C, Knox A, Massey S, Moen S, Pardo A, Shellhaas R, Tsuchida T, Thomas C, Wang S, Sansevere A, Soul J

OBJECTIVE: Anti-seizure medications (ASMs) for neonatal seizures are off-label except for phenobarbital. We hypothesized that lacosamide may be safe and effective for neonatal seizures. We aimed to evaluate lacosamide safety and efficacy for neonatal seizures.

METHODS: We conducted a 10-center, retrospective study of lacosamide for neonatal seizures. Neonates born between 2008-2020, with seizure onset <44 weeks postmenstrual age (PMA) and lacosamide treatment initiated by ≤48 weeks PMA were included. Clinical data were collected from medical records.

RESULTS: We identified 62 eligible neonates. Lacosamide was the 4th line ASM or later in 93%. Adverse events (AEs) were reported in 53%, none of which were attributed to lacosamide. The most common AEs were cytopenias (15%) and cardiac disorders (8%), including atrial arrhythmia (2%), bradycardia (8%) and cardiac arrest (3%). No deaths (16) were attributed to lacosamide. Seizure cessation occurred in 21% of neonates treated with lacosamide without addition of another ASM; these neonates had lower seizure burden 4 hours after first lacosamide dose ($p = 0.029$), 24 hours after first lacosamide dose ($p = 0.01$), and on the first day of highest daily lacosamide maintenance ($p < 0.001$) than neonates without seizure cessation. Lacosamide was continued at hospital discharge in 72% of neonates.

CONCLUSIONS: Despite high rates of intractable seizures in this neonatal cohort, AEs were not attributed to lacosamide, some neonates experienced seizure cessation after lacosamide administration, and most neonates continued on lacosamide at hospital discharge. These results suggest potential benefit without adverse events and a rationale for future prospective studies.

KEYWORDS: Neonatal Neurology, Epilepsy

PL1-5. Neurocognitive outcomes of neonates with HIE and normal MRIs

Li H (Madison, WI), Mietchen J, Showers T, Chladek SS, Almane D, Jones JJ, Kessler-Jones AM, Ikonomidou C

OBJECTIVE: Neonates with hypoxic ischemic encephalopathy (HIE) are at significant risk for neurodevelopmental disability. Biomarkers have been used to predict neurological outcomes, including severity of neonatal encephalopathy, Apgar scores, cord gases, EEG background pattern, neonatal seizure burden, and evidence of brain injury on neuroimaging. This study aims to determine whether normal brain MRIs at 4-6 days of life predict normal neuromotor and neurocognitive development in infants with HIE.

METHODS: This is a prospective study of neonates with HIE, born at >37 weeks of gestation and admitted to our NICU between 5/2009 and 12/2020. Eligible subjects are children with a history of HIE and normal brain MRIs at 4-6 days of life. Starting in 1/2022, these children underwent standardized exams by pediatric neurologists. Additionally, a battery of neuropsychological tests was administered and included the KBIT-2 as well as several cognitive and emotion scales of the NIH Toolbox.

RESULTS: Seventy-six neonates with HIE had normal brain MRIs. Twenty patients have been recruited for our study so far. They all demonstrated normal neurological exam findings. Their mean KBIT-2 verbal and nonverbal scores and mean IQ composite scores were at or above the 50th percentile for age for typically developing children. Similarly, using the NIH toolbox these children tested at or above the 50th percentile in most cognitive domains compared to typically developing children.

CONCLUSIONS: These data suggest that a normal brain MRI in the first week of life in infants with HIE predicts a normal neurocognitive outcome.

KEYWORDS: Neonatal Neurology, Neuroimaging, Neurodevelopmental Disorders

PL1-6. Gender Representation in Leadership Roles and Awards in the Child Neurology Society

Martindale J (Winston Salem, NC), Gombolay G, Christy A, Aravamuthan B, Joshi S, Tilton A, Khakoo Y

OBJECTIVE: Studies demonstrate the underrepresentation of women physicians in award recognition and leadership across multiple medical specialty societies. The objective was to evaluate gender representation among leadership and award recipients in the Child Neurology Society (CNS).

METHODS: We reviewed lists of awardees and board members of the CNS from 1972-2022. The primary outcome measures were total available awards or board positions for each year and then the proportions of gender for each award or position.

RESULTS: Between 1972-2022, we identified 150 board of director positions and 190 recognition awards presented by the CNS. The proportions of women in the CNS were estimated by previously published or publicly available data

- 31.4% (2002), 35.3% (2014), and 41.2% (2023). Women represented 28.2% (n = 42) of the board of directors and 20% (n= 38) of the award recipients. Women held more supportive positions, such as secretary-treasurer (35.7%) or councilor (31.7%) than presidential positions (12.5%). Between 2003-2022, the percentage of women holding supportive positions increased compared to the president, which decreased to 0% since 2018. Award gender distribution slightly increased, from 23.89% of women awardees in the past twenty years to 26.5% in the past five years.

CONCLUSIONS: Even in child neurology, women remain underrepresented at the highest levels of recognition. Awards and leadership positions tend to show gender parity emphasize youth, or are classically supportive leadership roles. These results demonstrate gender gaps and suggest possible gender biases in selecting leaders and award recipients within CNS.

KEYWORDS: Diversity, Equity, Inclusion, Ethics

PL1-7. Hyperkinetic dystonia in dyskinetic cerebral palsy responds to combined DBS stimulation in thalamus and pallidum.

Zakharova A (Irvine, CA), Sanger T, MacLean J

OBJECTIVE: To describe the response of hyperkinetic dystonia in eight pediatric patients with dyskinetic CP to combined DBS stimulation in thalamus and pallidum.

METHODS: Retrospective chart review and video analysis was performed on eight pediatric cases of dyskinetic CP and significant hyperkinetic dystonia who underwent DBS surgery. Videos from pre-operative and six-month follow-up visits were rated on the Burke-Fahn-Marsden dystonia rating scale (BFMDRS) which is sensitive to both hyperkinetic and hypertonic dystonia, as well as the Unified Dystonia Rating Scale (UDRS) which is sensitive for the hyperkinetic dystonia. Additionally, we used UDRS scale to rate improvement in hyperkinetic dystonia at the initial thalamic programming visit.

RESULTS: All patients had DBS implanted in bilateral GPi, as well as varying subnuclei of the thalamus, Vo, VA, or Vim according to preoperative depth electrode evaluation of efficacy. The average reduction in dystonic symptoms was 24% on the BFMDRS. Reduction in the upper extremity component of the UDRS at 6 months was on average 43% across all subjects, which is significant for this test. Furthermore, three subjects with proximal leg dystonia showed reduction in hyperkinetic movements.

Additionally, initial thalamic programming showed improvement of the hyperkinetic component within minutes of initiating thalamic stimulation (in the absence of GPi stimulation) in all patients with an important reduction in the UDRS scale (31% on average).

CONCLUSIONS: Combined GPi and thalamic DBS stimulation may have better efficacy in reducing hyperkinetic components of dystonia compared to GPi alone. Controlled studies with a larger cohort of patients will be required to confirm this hypothesis.

KEYWORDS: Movement Disorders, Cerebral Palsy

PLATFORM SESSION 2: Friday, October 6 (2:15 PM – 4:00 PM)

PL2-1. Host transcriptomics identifies unique host gene expression patterns in childhood arterial ischemic stroke

Rolfes M (San Francisco, CA), Ramachandran P, Dandekar R, Zia M, Colao K, Hills N, Wilson M, Fullerton H, VIPSII Investigators V

OBJECTIVE: Pediatric arterial ischemic stroke (AIS) is a major cause of childhood disability. Animal models suggest injury is ongoing days after the initial insult. Understanding the host response to pediatric AIS might inform post-stroke therapeutic targets to improve recovery.

METHODS: From 12/2016-1/2022, 22 North American centers enrolled AIS cases (28 days – 18 years) and stroke-free controls. Bulk RNA sequencing was performed on peripheral blood collected within 72 hours of AIS and compared to healthy controls. Differential gene expression analysis and unsupervised hierarchical clustering identified unique gene expression patterns between cases and controls (adjusted p-value <0.05). Ingenuity Pathway Analysis assessed for upregulated and downregulated molecular pathways.

RESULTS: Cases (n=194) were a median age of 11.9 years (IQR 5.5, 15.6) and 55% male and controls (n=95) a median age of 11.8 years (IQR 6.7, 15.3) and 48% male. 2310 genes were differentially expressed between cases and controls. Unsupervised hierarchical clustering demonstrated clustering of cases. 13 genes had a fold change > |2|. Significantly upregulated signaling pathways correlated with proinflammatory immune responses, including toll-like receptor and TREM-1 signaling. Additional immune-related signaling pathways, natural killer cell and IL-12 in macrophages, were the most downregulated.

CONCLUSIONS: This is the first study to investigate the host response of pediatric AIS using host transcriptomics. Our findings are consistent with evidence of proinflammatory immune dysregulation in adults with AIS and provide new insight into the underlying pathogenesis of pediatric AIS. Upregulated pathways may serve as future therapeutic targets with the potential to improve patient outcomes.

KEYWORDS: Stroke, Neuroimmunology

PL2-2. Assessing needs and perceptions of research participation in pediatric onset multiple sclerosis: a multi-stakeholder survey

Gambrah-Lyles C (Philadelphia, PA), Loud S, Chitnis T, Charles Casper T, Harris Y, Mar S, Pediatric MS Centers US

OBJECTIVE: Patient-powered research networks (PPRNs) for autoimmune disease are widely used in the adult population, but few have expanded to include pediatric patients [1, 2]. This study describes the needs and perceptions of research participation among patients with pediatric-onset multiple sclerosis (POMS) and their care teams via an online survey.

METHODS: In collaboration with the US Network of Pediatric MS Centers, the Accelerated Cure Project via its iConquerMS research network, launched an electronic survey to evaluate viewpoints regarding POMS research. Three questionnaires were disseminated: 1) to patients with POMS (PwPOMS), 2) to caretakers of PwPOMS (C-PwPOMS), and 3) to health care providers and researchers in POMS (HR-POMS).
RESULTS: 70 participants completed the survey. 33% were PwPOMS, 53% were C-PwPOMS and 14% were HR-POMS. 65% of PwPOMS reported interest in participating in research, with 43% interested in testing treatments, completing surveys, and designing studies. 76% of C-PwPOMS reported interest in having their child participate in research. 57% of both groups reported interest in supporting research that seeks to find a cure for MS. HR-POMS reported difficulty finding funding sources (100%) and obtaining biological samples and recruiting participants (57%).
CONCLUSIONS: The POMS population is a growing cohort of patients interested in participating in research. This online survey circulated via a PPRN is the first to specifically provide insight on research priorities identified by PwPOMS and C-PwPOMS, as well as difficulties that HR-POMS encounter in POMS research. PPRNs are an essential tool for recruiting POMS and can guide design and implementation of future research efforts in POMS.
KEYWORDS: Pediatric Demyelinating Disease, Neuroimmunology

PL2-3. Infectious profiling reveals potential triggers of pediatric NMDAR encephalitis: a large case-control study

Sandweiss A (Houston, TX), Erickson T, Jiang Y, Kannan V, Yarimi J, Levine J, Fisher K, Muscal E, Demmler-Harrison G, Murray K, Ronca S

OBJECTIVE: Anti-NMDA receptor encephalitis is an antibody-mediated disorder characterized by seizures, psychosis, movement disorder, focal neurological deficits, and autonomic dysfunction. Post-herpes simplex virus-1 meningoencephalitis (HSV ME) and ovarian teratoma are two well-known triggers, but most pediatric cases are idiopathic. We evaluated if other infections precede pediatric NMDAR AE.
METHODS: This is a single-center, retrospective, case-control study of 86 pediatric NMDAR AE cases presenting to Texas Children's Hospital between 2006-2022 and sex-matched controls diagnosed with idiopathic intracranial hypertension who received a lumbar puncture as part of workup for comparison to compare the incidence of infections between the two populations.
RESULTS: Active or recent HSV ME was significantly more common in NMDAR AE patients than control patients (15.3% vs 0%, $p<0.005$), while there was no difference in HSV infection between the two groups (40% vs 25%, $p=0.600$). Active or recent Epstein Barr virus (EBV) infection was detected in the NMDAR AE group but was not statistically significant due to sample size (19% vs 4%, $p=0.07$). Our power analysis revealed 100 additional control subjects are necessary for a sufficiently powered study. Other Herpesviridae viruses, common respiratory (including influenza, parainfluenza, rhinovirus, human metapneumovirus, respiratory syncytial virus, adenovirus, and COVID-19), gastrointestinal viruses, common bacterial causes of pneumonia, and arboviruses were not different among the two groups.
CONCLUSIONS: In addition to HSV, EBV may have a role as an infectious trigger of NMDAR AE. Our data highlight the need for multi-institutional studies with a sufficiently powered control group to study the underlying infectious precursors of autoimmune encephalitis.
KEYWORDS: Neuroimmunology, Neuroinfectious Disease

PL2-4. Human Genetic Modulation of the Neuronal Response to Interferons

Andzelm M (Boston, MA), Meyer D, Tegtmeyer M, Nehme R, McCarroll S

OBJECTIVE: Interferons (IFNs) are critical in a robust host defense against infection but also contribute to central nervous system pathology in pediatric neuroinflammatory disease such as Aicardi-Goutières Syndrome or Rasmussen's Encephalitis. These diseases can have significant variability in disease course, suggesting that identifying genetic modifiers of the neuronal IFN response can provide valuable insight on disease pathophysiology.
METHODS: One significant limitation to assessing how natural human genetic variation affects the neuronal IFN response has been the ability to analyze many genetically diverse human cells under identical growth conditions to limit technical variation and correlate genotype variation with cellular phenotypes. To address this, our lab developed a "cell villages" model which we applied to a neuroinflammatory context. We cultured induced pluripotent stem cell-derived excitatory neurons from many individuals together, stimulated with IFNs, and performed single-cell RNA sequencing. Donor cell identification was performed concurrent with transcriptomic readout. We then correlated allele states of common single nucleotide polymorphisms to gene expression to define expression quantitative trait loci and their associated genes (eGenes).
RESULTS: We characterized the distinct but overlapping neuronal transcriptional responses to IFN-alpha and IFN-gamma, as well as identified hundreds of eGenes, many of which emerged specifically upon IFN treatment. As proof-of-concept, we examined interindividual variation in the IFN-gamma dependent induction of one eGene, Caspase 7, an executioner caspase in apoptosis.
CONCLUSIONS: The eGenes identified provide testable hypotheses for how interindividual variation yields differential biology in response to inflammatory stimuli in neurons, which may provide insight into why some children are more susceptible to neuroinflammatory disease.
KEYWORDS: Neuroimmunology, Neurogenetics

PL2-5. Sleep related breathing disorder in 5-18 years children with dystrophinopathy: a cross sectional study

Gulati S (New Delhi, India), Parashar A, Meena AK, Yoganathan S, Kamila G, Sikka K, Jauhari P, Chakrabarty B, Kabra M, Kabra SK, Pandey RM, Bisoi S

OBJECTIVE: Respiratory impairment is a significant cause of morbidity and mortality in Duchenne Muscular Dystrophy(DMD). Young patients are at risk of obstructive apnoea because of weight gain, secondary to progressive physical inactivity and prolonged corticosteroid therapy. We studied the prevalence of SRBD in patients with dystrophinopathies and correlated its severity with clinical and laboratory parameters.
METHODS: Children diagnosed with DMD(diagnosed by Multiplex PCR/MLPA/NGS/muscle biopsy) aged 5-18 years, and on oral steroids for atleast 6 months were enrolled. Clinical data(6-min-walk test, Brook-Vignos scale) and responses of the Childhood & Adolescent Sleep Evaluation Questionnaire(CASEQ) were recorded. Overnight polysomnography(for Apnoea-Hypopnoea Index(AHI)) was done.
RESULTS: Fifty patients were enrolled with a mean age of 10+2 years. Among them, 29(58%) patients were ambulatory. Based on the AASM and ICSD-3 guidelines, one or more primary sleep disorder was observed in 36/50 patients-prevalence of 72%(95% CI: 57.7 – 82.9), and SRBD in 34/50 patients-prevalence of 68%(95% CI: 53 – 80.5). Patients with SRBD had a lower FVC(66.7%) and higher FEV1/FVC ratio(109%) as compared to children without SRBD(FVC: 78.1%; FEV1/FVC: 105.8%)[p-value<0.01 in both parameters]. CASEQ was found to have high sensitivity(85.7%) and specificity(78.6%) for detecting any sleep related disorder, with positive predictive value of 90.9% and negative predictive value of 68.8%.
CONCLUSIONS: SRBD is a common comorbidity in dystrophinopathy and its early identification helps in early intervention and improved life expectancy and quality of life in these patients. CASEQ can be used as an easy tool for screening of sleep related problems in dystrophinopathy.
KEYWORDS: Neuromuscular, Sleep

PL2-6. Interim Analysis of EVOLVE: A Long-term Observational Study Evaluating Eteplirsen, Golodirsen, or Casimersen in Routine Clinical Practice

Ricchetti-Masterson K (Cambridge, MA), Santra S, Hornibrook S, Byrne B, Kumar A, Mathews K, Ramos-Platt L, Waldrop M, Zaidman C, Sehinovych I, Miller D, Hasan N, McDonald C

OBJECTIVE: Eteplirsen, golodirsen, and casimersen are exon-skipping therapies approved for patients with Duchenne muscular dystrophy (DMD) with mutations amenable to 51, 53, and 45 exon skipping, respectively. Here, we assess the safety, usage, and clinical outcomes of their long-term use in routine clinical practice from EVOLVE, an ongoing 5-year, phase 4, multicenter, observational study.
METHODS: This interim analysis includes data on serious adverse events (SAEs) and adverse events of special interest, as well as loss of ambulation (LOA).
RESULTS: As of December 2021, 144 patients were enrolled. Mean (SD) age (years) was: eteplirsen (n=123), 13.7 (5.50); golodirsen (n=17), 13.5 (4.27); and casimersen (n=4), 16.3 (11.67). Mean (SD) duration of treatment (years) was: eteplirsen, 4.7 (1.88); golodirsen, 1.3 (0.45); and casimersen, 0.3 (0.22). Mean time (years) from DMD diagnosis to treatment initiation was: eteplirsen, 6.0 (4.74); golodirsen, 8.2 (3.76); and casimersen 13.5 (14.04). At treatment initiation, 82/123 (66.7%) eteplirsen-treated, 7/17 (41.2%) golodirsen-treated, and 2/4 (50%) casimersen-treated patients were ambulatory. To date, favorable safety profiles have been observed for all 3 therapies. SAEs occurred in 14 (11.4%) eteplirsen-treated patients, none were treatment related; none were reported for golodirsen or casimersen. Median age at LOA for eteplirsen-treated patients was 15.3 years, consistent with prior clinical trial post hoc results; small sample size to date precludes analysis of age at LOA for golodirsen or casimersen.
CONCLUSIONS: These real-world data from the EVOLVE interim analysis support the safety profiles and continue to describe long-term clinical outcomes of eteplirsen, golodirsen, and casimersen.
KEYWORDS: Neuromuscular

PL2-7. Representation of Non-White Participants in Interventional Duchenne Muscular Dystrophy (DMD) Clinical Trial Publications

Creasey M (Richmond, VA), Thangarajh M

OBJECTIVE: Inequitable racial and ethnicity representation with disproportionate over-representation of white participants in Duchenne Muscular Dystrophy (DMD) observational and natural history studies have been previously reported (Barnard et al., 2020). We were interested in investigating racial and ethnic distribution in Phase II and III DMD clinical trials.
METHODS: Publicly available data between 2005 to 2018 was accessed using the Clinical Trials database (clinicaltrials.gov) to establish the demographic representation in Phase II and III DMD interventional clinical trials. We also stratified the data based on geographic location (United States only versus international) and funding sources (academic versus industry).
RESULTS: A total of 36 DMD Phase II and III trials were evaluated for racial and ethnic composition. The representation of white participants accounted for 72% of subjects enrolled in interventional DMD clinical trials over the past two decades. Among these 36 trials, 50% (18/36) did not report ethnicity and 17% (6/36) did not report racial information. In trials conducted within continental United States, white participants were overwhelmingly represented (74%). Most studies (89%) were funded by industry, 3% of which were also funded by the National Institutes of Health (NIH), and only 3% were funded exclusively by the NIH. Eight percent of studies were funded by other sources.
CONCLUSIONS: There is significant lack of representation of non-white study participants in DMD interventional trials. In addition, the reporting of race and ethnicity in Phase II and III clinical trials are insufficient. These data warrant further investigation regarding approaches to diversify and include equitable representation in DMD clinical trials.
KEYWORDS: Neuromuscular, Diversity, Equity, Inclusion

PLATFORM SESSION 3: Friday, October 6 (2:15 PM – 4:00 PM)

PL3-1. Immunotherapy Responsiveness and Risk of Relapse in Down Syndrome Regression Disorder

Santoro J D (Los Angeles, CA), Spinazzi N A, Filipink R A, Hayati-Rezvan P, Kammeyer R, Patel L, Khoshnood M, Jafarpour S, Partridge R, Gombolay G Y, Christy A L, Quinn E, Rafii M

OBJECTIVE: Down syndrome regression disorder (DSRD) is a clinical symptom cluster consisting of neuropsychiatric regression without an identifiable cause. This study evaluated the clinical effectiveness of IVIg and evaluated clinical characteristics associated with relapse after therapy discontinuation.

METHODS: A prospective, multi-center, non-randomized, observational study was performed. Patients met criteria for DSRD and were treated with IVIg. All patients underwent a standardized wean off therapy after 9-12 months of treatment. Baseline, on therapy, and relapse scores of the Neuropsychiatric Inventory Total Score (NPITS), Clinical Global Impression-Severity (CGI-S), and the Bush-Francis Catatonia Rating Scale (BFCRS) were used to track clinical symptoms.

RESULTS: Eighty-two individuals were enrolled in this study. Patients had lower BFCRS (MD: -6.68; 95% CI: -8.23, -5.14), CGI-S (MD: -1.27; 95% CI: -1.73, -0.81), and NPITS scores (MD: -6.50; 95% CI: -7.53, -5.47) while they were on therapy compared to baseline. Approximately 46% of the patients ($n = 38$) experienced neurologic relapse with wean of IVIg. Patients with neurologic relapse were more likely to have any abnormal neurodiagnostic study ($\chi2 = 11.82$, $p = 0.001$), abnormal MRI ($\chi2 = 7.78$, $p = 0.005$), and abnormal LP ($\chi2 = 5.45$, $p = 0.02$), and a personal history of autoimmunity (OR: 6.11, $p<0.001$) compared to patients without relapse.

CONCLUSIONS: IVIg was highly effective in the treatment of DSRD. Individuals with a history of personal autoimmunity or neurodiagnostic abnormalities were more likely to relapse following weaning of immunotherapy, indicating the potential for, a chronic autoimmune etiology in some cases of DSRD.

KEYWORDS: Behavioral Neurology, Neurodevelopmental Disorders, Neuroimmunology

PL3-2. Investigation of the biotransformation of trihexyphenidyl and application to dystonic cerebral palsy

Gelineau-Morel R (Kansas City, MO), Toren P, Pearce R, Leeder JS

OBJECTIVE: Trihexyphenidyl (THP) is an anticholinergic drug used to treat dystonia in cerebral palsy. Dystonia pathophysiology involves overexcitation of striatal cholinergic interneurons and rodent models demonstrate normalization of striatal activity after exposure to THP. Yet patients treated with THP demonstrate inconsistent efficacy and adverse effects, potentially due to variable systemic exposure. This project investigated THP biotransformation to inform individualized dosing and equalize systemic exposure.

METHODS: THP and D11-THP were incubated with recombinant CYP2D6, CYP2C9, and CYP3A4 enzymes, and human liver microsomes. Analysis of metabolite formation in vitro and in vivo in 5 urine samples obtained from patients taking THP was conducted by liquid chromatography and tandem mass spectrometry.

RESULTS: Incubation of THP with recombinant enzymes produced two hydroxylated metabolites: one associated with CYP2D6 (M1) and one with CYP3A4 (M2). Incubation of THP with human liver microsomes revealed predominant M1 formation at lower THP concentrations (0.2 μg/ml), which transitioned to predominant M2 at higher (supra-physiologic) concentrations (6 μg/ml). Patient urine samples revealed both M1 and M2, with predominance of M2. Incubation of D11-THP confirmed hydroxylation of the cyclohexane ring by both CYP2D6 and CYP3A4.

CONCLUSIONS: CYP2D6 and CYP3A4 hydroxylate the cyclohexane ring of THP and produce distinct metabolites that are present in the urine of patients taking THP. Future genotype-stratified pharmacokinetic analysis of THP will examine concentration-time profiles for individual patients. This will inform individualized dosing recommendations to equalize systemic exposure, improve treatment efficacy, and reduce adverse effects.

KEYWORDS: Experimental Therapeutics, Cerebral Palsy, Movement Disorders

PL3-3. Interim Results from the NEXUS Open-Label Phase 2 Study on the Safety and Efficacy of Leriglitazone in the Treatment of Childhood Cerebral Adrenoleukodystrophy

Musolino P L (Boston, MA) Mallack E, García-Cazorla A, Ribeiro J, Sevin C, Yazbeck E, Rosewich H, Jimenez S, Chia-Yi Chiang G, Rapalino O, Caruso P, Helmer K, Balentine D, Pascual S

OBJECTIVE: Cerebral adrenoleukodystrophy (cALD) is a rapidly fatal, X-linked neurodegenerative disorder characterized by inflammatory brain demyelination. Allogeneic and autologous hematopoietic stem cell transplantation (HSCT) may halt disease progression, but there is an unmet need for less invasive therapies that can be administered immediately upon lesion identification. Leriglitazone is a peroxisome proliferator-activated receptor γ agonist with potential for treating cALD.

METHODS: NEXUS (NCT04528706) is a 96-week, open-label, multicenter registration study of once-daily oral leriglitazone that has so far enrolled 19 boys (target: 13) aged 2–12 years with cALD with or without gadolinium-enhancing lesions. The primary endpoint is the proportion of patients with clinically and radiologically arrested disease at week 96 (success criteria: one-sided 95% confidence interval [CI] >10%). We present a prespecified 24-week interim analysis, including assessment of study continuation criteria (≥4/13 patients with arrested disease or lesion growth deceleration without clinical progression). Secondary endpoints

include change from baseline in neurological function score (NFS) and Loes score (LS).

RESULTS: Eleven patients were evaluable at week 24. Continuation criteria were met: all patients demonstrated lesion growth deceleration. All remained clinically stable (free of major functional disability and stable NFS). Five patients had arrested disease (45.5%, 95% CI: 13.9–68.4%). Median (range) change from baseline was 0.0 (0.0–1.0) for NFS and 0.0 (0.0–3.0) for LS. There were no severe adverse events, treatment-related serious adverse events or deaths.

CONCLUSIONS: Leriglitazone was well tolerated, and disease arrest or stabilization was demonstrated radiologically and clinically. LS changes are comparable to HSCT-based therapies.

KEYWORDS: Experimental Therapeutics, Neurometabolic, Pediatric Demyelinating Disease

PL3-4. A Comprehensive Approach for Designing Effective Antisense Oligonucleotides in the Treatment of Inherited White Matter Disorders

Amanat M (Baltimore, MD), Nemeth C, Moser A, Ratajczak A, Fine A, Fatemi A

OBJECTIVE: Antisense oligonucleotides (ASOs) are synthetic nucleotides capable of modulating gene expression by targeting RNA molecules. ASO design involves careful consideration of several factors to optimize their therapeutic efficacy. We aimed to outline the process of designing effective ASOs and present our novel therapies for X-linked adrenoleukodystrophy (X-ALD) and leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL).

METHODS: To develop effective ASOs, a deep understanding of the pathogenesis of their target disorders is necessary. The accessibility of target sequences on RNA secondary structures and the stability of the ASO-RNA duplex should be assessed to predict efficacy. Depending on the structure and chemical modifications, ASOs are able to eliminate toxic proteins, enhance the production of functional proteins, or alter the structure of impaired proteins to improve function. We implemented these strategies and developed three ASOs for X-ALD to increase expression of the ALD-related protein gene, ABCD2, in patient-derived fibroblasts, and one ASO for LBSL to enhance exon 3 inclusion within DARS2 mRNA in patient-derived neurons.

RESULTS: ASOs targeting ABCD2 increased gene expression in fibroblasts by up to 7-fold, compared to untreated cells and dose-dependently reduced levels of very long chain fatty acids in fibroblasts. The ASO targeting DARS2 mRNA of LBSL neurons restored gene expression and exhibited over 50% reduction in lactate levels of culture media.

CONCLUSIONS: To develop an effective ASO, several elements including chemical modifications, length, and structure of ASOs should be assessed. Our findings highlight the potential of ASOs as disease-modifying agents in leukodystrophies.

KEYWORDS: Experimental Therapeutics, Neurodevelopmental Disorders, Neurogenetics

PL3-5. Astrocyte-targeted gene therapy demonstrates safety and efficacy in two murine models of Vanishing White Matter disease

Bonkowsky J (Salt Lake City, UT), Herstine J, Chang P-K, Chornyy S, Nokhrina K, Redinger J, Wentz J, Pyne N, Holaway C, Sunshine A, Scholl E, Vetter T, Stevenson T, Flanigan K, Bradbury A

OBJECTIVE: Vanishing White Matter Disease (VWM) is a severe leukodystrophy caused by mutations in subunits of eukaryotic initiation factor 2B (EIF2B), with pathologic variants in EIF2B5 being the most common. Due to VWM's monogenic nature, it is a good candidate for adeno-associated virus (AAV)-mediated gene replacement therapy. VWM pathology suggests that astrocytes are a critical target for therapy, as their differentiation, morphology, and function is impaired.

METHODS: We designed gene replacement constructs to compare astrocyte-specific (AAV9.GFAP, AAV9.gfaABC(1)D) or ubiquitous (AAV9.CAG) expression. AAV vectors were delivered using intracerebroventricular (ICV) injections into mice pups. We tested GFP-containing vectors to assess biodistribution of expression, or EIF2B5-containing to assess safety and efficacy. Following injection, mice were monitored for mortality, and for functional outcomes including rotarod gait analysis.

RESULTS: ICV injection of AAVs expressing GFP into wild-type mice revealed that astrocyte-specific reporter constructs achieved appropriate expression in astrocytes. Because of significant differences in expression between promoters, we generated a novel, tailored promoter: gfaABCD1405. We evaluated our constructs in two murine VWM models, Eif2b5Arg191His and Eif2b5Ile98Met, which display significant gait deficits, myelin loss, and shortened life span, and are monitoring disease progression using traditional and clinically relevant readouts including MRI, immunohistochemistry, and gait analysis.

CONCLUSIONS: Our current data suggests that our astrocyte-targeted gene therapy does not worsen phenotypes in the VWM mouse models. Further, the astrocyte-specific expression is associated with delay of disease progression, partial rescue of body weight, and significantly increased latency to fall on rotarod in both disease models, offering promise for clinical translation.

KEYWORDS: Neurogenetics, Experimental Therapeutics

PL3-6. Development of a Clinical-Translational Model of Leukoencephalopathy with Calcifications and Cysts

Harmon J (Washington, DC), Pierce B, Chau N, Rhee J, Whitehead M, Schroeder J, Tochen L, Fraser J

OBJECTIVE: Leukoencephalopathy with Calcifications and Cysts (LCC, Labrune Syndrome) is an ultra-rare neurodegenerative disorder associated with biallelic mutations in SNORD118, which encodes the box C/D small nucleolar RNA (snoRNA) U8. Our work seeks to deeply phenotype our LCC patient cohort and simultaneously develop an LCC rodent model to better understand the pathogenesis of this disease.

METHODS: Patients were evaluated with serial in-person and virtual assessments, chart review, and neuroradiology review. With Jackson Laboratory, we used CRISPR/Cas9 technology to develop a knock-in (KI) mouse model of a recurrent pathogenic variant (n.8G>C) in Snord118; a knock-out (KO) line with deletion of the first 6 nucleotides of the gene was identified as a byproduct of the gene-editing process. Heterozygotes were used to establish breeding colonies, and litters of each line were followed from birth to establish survival and growth trends.
RESULTS: Fifteen patients from 12 families were recruited. The most common clinical characteristics included preterm birth, epilepsy, movement disorders and neurocognitive dysfunction. Initial MRI showed the classic triad of calcifications, cysts, and white matter changes in 60% of patients, with the remainder demonstrating only calcifications and white matter changes.
Homozygote KI mice are viable at birth and have an observable phenotype, including distal hypopigmentation and decreased weight compared to wild-type littermates. Homozygous KO mice demonstrate early embryonic lethality.
CONCLUSIONS: The simultaneous development of a clinical natural history study along and a rodent model of a pathological gene variant identified in affected patients represents a powerful opportunity to better understand rare disease.
KEYWORDS: Neurogenetics

PL3-7. Evaluation of the Long-Term Effect of Arimoclomol in NPC - 48 Months Data from CT-ORZY-NPC-002

Patterson M (Rochester, MN), Dali C, Mengel E

OBJECTIVE: A statistically significant and clinically meaningful effect of arimoclomol in Niemann-Pick disease type C (NPC) was demonstrated in NPC-002, a 12-month, double-blind, placebo-controlled trial (ClinicalTrials.gov: NCT02612129). Here, we evaluate the long-term effect.
METHODS: Disease progression was assessed with the 5-domain NPC Clinical Severity Scale. Data from clinical trials NPC-001 and NPC-002, and 1 observational cohort (ASIS-01), were included. NPC-001 (observational) included 36 patients assessed at baseline and after 6-14 months. NPC-002 included patients randomized to double-blind arimoclomol (34 patients) or placebo (16 patients) for 12 months, followed by open-label arimoclomol treatment for up to 48 months with biannual assessments. The ASIS-01 cohort included 22 patients observed for 2-7 years, assessed during clinic visits.
Disease progression without arimoclomol was estimated by pooling data from NPC-001 and NPC-002 placebo patients. Annual progression was calculated from a linear regression model and extrapolated up to 48 months. Comparisons were made to corresponding progression rates from the ASIS-01 cohort and literature reports.
Disease progression with arimoclomol treatment was estimated by pooling data for all patients treated with arimoclomol at any timepoint during NPC-002 and presented relative to initiation of arimoclomol. The progression trajectory based on mixed model repeated measures analysis was compared graphically to the progression rate for untreated NPC-001/NPC-002 patients.
RESULTS: Similar cohorts of NPC patients exhibit similar progression rates on the population level. These cohorts are comparable regarding age, standard of care, and disease severity.
CONCLUSIONS: This dataset suggests long-term progression may be reduced in patients treated with arimoclomol for up to 48 months.
KEYWORDS: Neurometabolic

AUTONOMIC DISORDERS

1. Characterizing Sensory Processing Typologies in a Mixed Neurodevelopmental Cohort: Evaluating Associations with Emotion Dysregulation, Anxiety, and ADHD

Aitken A (Brooklyn, NY), Powers R, Wren J, Mukherjee P, Marco E

OBJECTIVE: Children with autism and sensory processing disorder (SPD) demonstrate distinct patterns of sensory processing abilities and frequently show problems with internalizing and externalizing behaviors. Further research is needed to 1) characterize the prevalence of emotional dysregulation in children with SPD and autism, 2) develop data-driven sub-typologies of sensory processing profiles, 3) evaluate differences in emotion dysregulation, anxiety, and ADHD based on sensory typology.
METHODS: The current study included children (ages 8-12) with a confirmed diagnosis of autism and/or SPD. Parent-reported sensory over-responsivity, under-responsivity, and seeking behaviors were collected using the Sensory Processing Scales-Inventory. Additionally, parent-reported emotional dysregulation and anxiety measures were obtained using the BASC-3, and ADHD-scores were collected from the Connors-3.
RESULTS: Results showed an increased prevalence of clinically concerning emotion dysregulation problems (40%) Five sensory profiles were identified using latent profile analysis: Typical Processing, Sensory Seeking (SS), Sensory Under-responsive (SUR), Sensory Over-Responsive (SOR), and Combined. The SOR, SS, and Combined subgroups exhibited higher emotion dysregulation scores than the other groups. The SOR and Combined groups had higher anxiety scores than the other groups, and the SS and Combined groups demonstrated higher ADHD scores.
CONCLUSIONS: This study suggests a higher prevalence of emotional dysregulation among children with autism and SPD. Children with SOR and SS subtypes were uniquely associated with elevated anxiety and ADHD symptoms, respectively, but shared problems with emotion dysregulation in common. These findings suggest that emotion dysregulation may be a shared neurocognitive deficit underlying

internalizing and externalizing symptoms in children with neurodevelopmental differences.
KEYWORDS: Autonomic Disorders

BEHAVIORAL NEUROLOGY

2. The Effects of Medical Cannabis on Behavior, Sleep and Quality of Life for Children with ASD

Nazareno J (Plano, TX), Maqbool M

OBJECTIVE: Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that affects communication, social interaction, and behavior. Recently, medical marijuana has gained attention as a potential treatment option for ASD, as it has been reported to alleviate some associated symptoms. This study investigated the effects of medical marijuana on children with ASD, precisely behavior, sleep, and quality of life.
METHODS: The primary outcome measure is the changes in behavior, sleep, and quality of life assessed by Caregiver Global Impression of Change (CaGI-C), three to twenty-four months into the treatment. Secondary outcome measures include dose-dependent effectiveness, tolerability, and safety during the study period. This study is a retrospective open-label study of children between the ages of 3 and 17 diagnosed with ASD.
RESULTS: 113 participants received medical cannabis at varying doses and ratios of CBD and THC. CaGI-C-based scores were improved for behavior, sleep, and quality of life. The medical cannabis products were tolerated well, with minimal side effects.
CONCLUSIONS: This study provides valuable insights into the potential therapeutic effects of medical cannabis on children with ASD. The results demonstrated that medical marijuana is effective in reducing the symptoms associated with ASD. This study also presents supporting evidence in the ongoing debate around the use of medical cannabis for children with ASD. However, the results are based on the guardians' recollection of symptoms. The treatment period is also short and only implies short-term improvement. The effects of long-term therapy need to be investigated to establish efficacy and safety over time.
KEYWORDS: Behavioral Neurology, Neurodevelopmental Disorders, Sleep

3. Assessment of Anxiety in Children during the COVID-19 Pandemic

Lastra C (New Brunswick, NJ), Abrahams R, Anash G, Prisby K, Goyco-Ortiz L, Melean A, Moreno R, Scott P, John S, Mehrotra N, Schramm A

OBJECTIVE: To assess anxiety levels in children during the COVID-19 pandemic. The study explores how factors related to COVID-19 may have impacted the prevalence of anxiety disorders among the pediatric population.
METHODS: Childhood anxiety symptoms were assessed at various pediatric practices in Central New Jersey between July 2021 and September 2022. The sample comprised 476 children and adolescents aged 8-17 who participated in the Screen for Child Anxiety Related Disorders (SCARED) questionnaire, administered at their annual well-child visits. Participants included both the child and the caregiver. The anxiety prevalence was compared to pre-pandemic standards published by the Centers for Disease Control (CDC).
RESULTS: The prevalence of anxiety for children aged 8-17 (28.3%) was greater than pre-pandemic levels (7.1%; $p < 0.0001$). Among children aged 8-11, anxiety increased from 6.6% to 38.1% ($p < 0.0001$), while for children aged 11-17, anxiety increased from 10.5% to 22.2% ($p < 0.0001$). Previously diagnosed anxiety was a strong predictor of a high anxiety score on the questionnaire (mean = 28.95) compared to children without a history of anxiety (mean = 17.65; $p < 0.001$). Furthermore, a disparity was identified in the responses between the child and the caregivers' questionnaires ($p < 0.0001$).
CONCLUSIONS: This study shows that children's anxiety levels increased during the COVID-19 pandemic. Moreover, an inconsistency was found between children self-reporting anxiety and caregivers underreporting their child's anxiety. These findings underscore the need for targeted support for those affected, especially children with a history of anxiety.
KEYWORDS: Behavioral Neurology

4. Adverse Childhood Experiences and the Development of Down Syndrome Regression Disorder

Santoro J (Los Angeles, CA) Wang S, Patel L, Sannar E, Koshnood M, Boyd N, Mendez L, Spinazzi N, Quinn E, Rafii M

OBJECTIVE: Down syndrome regression disorder (DSRD) is a clinical symptom cluster of acute or subacute neurocognitive regression in otherwise health persons with Down syndrome. The objective of this study was to evaluate if adverse childhood experiences (ACEs) were more prevalent in children with DSRD than those with DS alone.
METHODS: A survey-based, cohort-based study was performed. Caregivers of individuals with DSRD with onset of symptoms between age 10-30 years and DS alone were administered the ACEs questionnaire via an online REDCap survey.
RESULTS: A total of 159 responses were collected after excluding incomplete surveys and those not meeting criteria for DSRD. Individuals with DSRD were not more likely to experience ACEs (p=0.18, 95%CI: 0.43-1.17). In those with ACEs prior to the onset of symptoms, the median time prior was 7 months (IQR: 5-10). Individuals with DSRD were more likely to report three or more ACEs (52, 33%) compared to those with DS alone (39, 22%) (p=0.02, 95%CI: 1.08-2.87). Exposure to ACEs were not predictive of response to particular therapeutic interventions although those with multiple ACEs 3 months prior to the onset of symptoms was associated with lower response rates to benzodiazepines and immunotherapy (p=0.02, 95%CI: -3.64- -1.13).
CONCLUSIONS: This study provides preliminary data that individuals with DSRD experience ACEs at a similar rate to

individuals with only DS alone, although three or more ACEs, often preceding the onset of symptoms, was more prevalent in individuals with DSRD.
KEYWORDS: Behavioral Neurology, Neurodevelopmental Disorders, Neurogenetics

5. Evidence of Neuroinflammation and Immunotherapy Responsiveness in Individuals with Down Syndrome Regression Disorder

Santoro J (Los Angeles, CA), Partridge R, Tanna R, Pagarkar D, Khoshnood M, Kammeyer R, Gombolay G, Fisher K, Christy A, Patel L, Manning M, Van Mater H, Rafii M, Quinn E

OBJECTIVE: Down syndrome regression disorder (DSRD) is a symptom cluster consisting of neuropsychiatric regression without cause. This study evaluated the incidence of neurodiagnostic abnormalities in individuals with DSRD and determined if abnormalities were associated with therapeutic interventions.
METHODS: A retrospective multi-center was performed. Patients were required to have subacute onset and the presence of four of five symptom groups present (cognitive decline, expressive language, sleep derangement, loss of ability to perform activities of daily living, and/or a new movement disorder) and no other explanation for symptoms.
RESULTS: Individuals with DSRD were comparable to a cohort of individuals with only Down syndrome although had higher rates of autoimmune disease ($p = 0.02$, 95%CI 1.04-1.75). Neurodiagnostic abnormalities were found on EEG ($n = 19$, 26%), neuroimaging ($n = 16$, 22%), and CSF ($n = 9$, 17%). Pleocytosis was appreciated in five cases, elevated total protein in nine, elevated IgG index in seven, and oligoclonal bands in two. Testing within 2 years of symptom onset was more likely to have neurodiagnostic abnormalities ($p = 0.01$, 95%CI 1.64-37.06). In individuals with neurodiagnostic abnormalities, immunotherapy was four times more likely to have a therapeutic effect than in those without neurodiagnostic abnormalities (OR 4.11, 95%CI 1.88-9.02). In those with normal neurodiagnostic studies ($n = 43$), IVIg was effective in 14 of 17 (82%) patients as well although other immunotherapies were uniformly ineffective.
CONCLUSIONS: This study reports the novel presence of neurodiagnostic testing abnormalities in individuals with DSRD, providing credence to this symptom cluster potentially being of neurologic and/or neuroimmunologic etiology.
KEYWORDS: Behavioral Neurology, Experimental Therapeutics, Neurodevelopmental Disorders

6. An Open-Label Study of Cranial Electrotherapy Stimulation (CES) on Sleep, Constipation, and Headaches in a Neurodivergent Cohort

Aitken A (Brooklyn, NY), Hattangadi N, Shapiro K, Marco E

OBJECTIVE: Children with neurodevelopmental differences (NDD) often experience comorbid health-related issues such as insomnia, headaches, and constipation. Cranial electrotherapy stimulation (CES) is a non-invasive transcranial current stimulation technique that has shown efficacy in adult populations for headaches and insomnia. This study examined the effects of a 4-week CES intervention on comorbid health concerns in a cohort of children and adolescents with a variety of neurodevelopmental diagnoses including autism, attention-deficit hyperactivity disorder, and sensory processing disorder.
METHODS: A single-arm observational study recruited 263 individuals aged 4-24 receiving care at our clinical centers. Participants were instructed to administer CES treatment at home using an AlphaStim AID device for 20 minutes per day, at least 5 days a week. Parent-reported assessments of sleep, headaches, and constipation were completed before and after the intervention. Multilevel logistic regression models evaluated within-person change in symptoms pre- and post-intervention.
RESULTS: At baseline, 70% of children reported problems with sleep, 15% with headaches, and 38% with constipation. After 4 weeks of CES treatment, the study population showed significant improvements in sleep (17% reduction) and constipation (20% reduction), but not headaches (1% reduction).
CONCLUSIONS: This study highlights the use of cranial electrotherapy stimulation in the context of clinical care for alleviating symptoms of sleep disruption and constipation in individuals with NDDs. These findings support the need for future randomized controlled trials to assess the efficacy of CES in neurodivergent children and adolescents with comorbid health concerns.
KEYWORDS: Behavioral Neurology

CEREBRAL PALSY

7. Prevalence and risk factors for cerebral palsy in children with congenital heart disease based on risk of surgical mortality.

Ghosh S (Brooklyn, NY), Lien I, Martinez K, Lin T, Bleiweis M, Philip J, Jordan L, Pavlakis S

OBJECTIVE: Children with congenital heart disease (CHD) have a higher prevalence of motor impairment secondary to brain injury, resulting in cerebral palsy (CP) The purpose of this study is to determine the prevalence of CP in CHD in a single-center cohort, stratify risk based on surgical mortality using Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery categories (STAT categories) and identify risk factors for developing CP.
METHODS: Retrospective cohort study of pediatric patients in our local Society of Thoracic Surgeons (STS) Congenital Heart Surgery database from 2006-2017 with a diagnosis of CHD who continued prospective follow up for > 2 years who were operated on at the University of Florida.
RESULTS: Of 701 children with CHD meeting criteria for analysis, 54 (7.7%) were identified as having CP. Most children with CHD and CP had spastic hemiplegia. Analysis of surgical and ICU factors between the two groups showed that children with CHD and CP had a longer time from admission to surgery ($p = 0.003$), higher STAT categories 4 and

5 ($p = 0.038$), higher frequency of brain injury and seizures ($p<0.001$). Developmental disabilities and rehabilitation needs were significantly greater for children with CHD and CP when compared to CHD alone ($p<0.001$).

CONCLUSIONS: In our cohort, 1 in 13 children with congenital heart disease develop cerebral palsy. This is significantly higher than the 2010 US population estimate of 1 in 345. Our study suggests higher STAT categories, brain injury and seizures are associated with developing CP in children with CHD.

KEYWORDS: Cerebral Palsy, Neurocritical Care, Neurodevelopmental Disorders

8. Over two years of data from PTC Pinpoint CP Spectrum: A sponsored no-cost 424-gene panel for patients with symptoms suggestive of CP and absence of risk factors for an acquired brain injury

Miller R (Liverpool, NY), Kopesky J, Morales A, McKnight D

OBJECTIVE: Cerebral palsy (CP) is one of the most common neurodevelopmental disorders affecting 2-3/1,000 live births. Studies have found 10-30% of cases have a genetic etiology. Increasing numbers of patients with CP are undergoing genetic testing. Identifying a genetic etiology has a significant impact on clinical management decisions. We report the utilization patterns and molecular diagnostic yield of a targeted, no-cost to patients sponsored gene panel program.

METHODS: Diagnostic yield was calculated from results of tests ordered for 3913 individuals between 9/15/2020 (program inception) and 1/10/2023. Testing was ordered by healthcare providers in the United States and Canada. Program eligibility criteria: (I) symptoms suggestive of CP, (II) absence of risk factors for an acquired brain injury. Gene curation focused on genes associated with clinical phenotypes consistent with cerebral palsy. Physician-reported clinical history was collected.

RESULTS: 491/3913 (12.5%) individuals had a definitive genetic cause of CP identified. There were causative variants identified in 153 different genes, with SPAST and CTNNB1 being the most common cause in 34 patients and 24 patients, respectively. Providers (n=831) from over 18 different specialties have utilized the panel. Age at testing varied greatly (ages 0-74) but the average age at testing was 8 years.

CONCLUSIONS: PTC Pinpoint CP Spectrum panel is a valuable tool utilized by a variety of providers that can identify the underlying genetic cause for patients with CP of unknown etiology. The diagnostic yield has improved with continued gene curation. This no-cost to patients sponsored gene panel program has expanded genetic testing options for patients with CP.

KEYWORDS: Cerebral Palsy, Neurogenetics

9. Clinical utility of a genetic diagnosis by exome sequencing in patients with cerebral palsy

Santana Almansa A (Boston, MA), Gable D, Frazier Z, Sveden A, Chopra M, Poduri A, Srivastava S

OBJECTIVE: The diagnostic yield of exome sequencing (ES) in cerebral palsy (CP) has been increasingly recognized. Nonetheless, evaluation of its clinical utility remains limited. We aimed to characterize the clinical utility of ES in patients with CP.

METHODS: Participants with CP were enrolled to conduct phenotyping and ES. Information regarding changes in diagnostic evaluation, treatment or prognosis as a result of a pathogenic or likely pathogenic variant in a human disease gene identified on ES were gathered retrospectively through chart review.

RESULTS: Of 175 patients who underwent ES, 38 had a pathogenic or likely pathogenic variant, of whom 30 were included in this analysis.

93% of patients had changes in their evaluation, management or prognosis based on identified variant on ES.

Evaluation changes included diagnostic studies to investigate complications of the disorder in 40%, referral to new subspecialists in 30%, continued follow up with established subspecialists to screen for manifestations of the disorder in 17%, referral to experts in the disorder in 33%, clinical genetics referral in 23% for surveillance recommendations, carrier testing in unaffected relatives in 10% and testing of potentially affected relatives in 3% of patients. Treatment changes included changes in mitochondrial cocktail supplementation in 7%, ketogenic diet in 3% and fasting avoidance in 3% of patients. 40% of patients had a change in prognosis, including changes from a static to progressive disorder and early mortality.

CONCLUSIONS: This study highlights the clinical utility of ES as evidenced by changes in investigations, management and prognosis as a result of variants identified on ES.

KEYWORDS: Cerebral Palsy, Neurogenetics, Neurodevelopmental Disorders

10. Disabling perinatal hypoxic-ischemic brain injury commonly occurs without neonatal encephalopathy

Fortin O (Montreal, QC, Canada), Husein N, Oskoui M, Shevell M, Kirton A, Dunbar M

OBJECTIVE: Perinatal hypoxic-ischemic brain injury is a leading cause of cerebral palsy. Diagnosis is commonly made in the neonatal period. However, children without a history of neonatal encephalopathy may present later in childhood with motor disability and neuroimaging findings consistent with perinatal hypoxic-ischemic injury. We sought to determine the incidence of such presentations using the viewpoint of a large multi-regional cerebral palsy registry.

METHODS: Patient cases with gestational age >35 weeks and an MRI pattern consistent with hypoxic-ischemic injury were extracted and divided according to the presence of neonatal encephalopathy. We extracted data regarding maternal-fetal risk factors, labor and delivery, neonatal course and clinical outcome. Group comparisons were performed using Chi square tests and multivariable logistic regression.

RESULTS: Data from 228 children were extracted from the registry. Neonatal encephalopathy was absent in 77. Variables related to maternal-fetal risk factors did not differ between groups. The group without encephalopathy had less resuscitation, had higher 5-minute Apgar scores, were less likely to have seizures, and were less likely to receive therapeutic hypothermia. Patterns of brain injury and long-term outcomes, including the distribution of cerebral palsy types and the rates of preserved ambulatory function, were similar between groups.

CONCLUSIONS: One third of term-born children with an eventual diagnosis of cerebral palsy and MRI-confirmed

perinatal hypoxic-ischemic injury do not have a history of neonatal encephalopathy. Such children most likely experienced their injury remote from delivery. This remote timing of injury is not associated with specific risk factors and long-term outcomes appear comparable to their peers.

KEYWORDS: Cerebral Palsy, Neonatal Neurology

11. Functional goal setting for botulinum toxin injections in people with cerebral palsy

Gilbert L (St. Louis, MO), Aravamuthan B

OBJECTIVE: To determine how functional goals of care are currently assessed for botulinum toxin injections in people with cerebral palsy (CP)

METHODS: Targeted chemodenervation with botulinum toxin injections can help treat focal hypertonicity and improve range of motion in people with CP, but individualized goal setting is critical to tailor treatment towards optimizing functional outcomes. To evaluate how these functional goals are currently assessed, we performed this prospective cohort study comparing the functional goals documented by botulinum toxin injectors versus referring clinicians for people with CP seen between 8/22/2022-2/23/2023.

RESULTS: Functional goals were documented by both the injectors and referring clinicians in 45% (n=42/94) of people with an ICD-10 diagnosis of CP (age 2.5-18.3 years old, 80% white, 54.8% GMFCS IV-V). Agreement on functional goals between the clinician and the injector occurred only 37% of the time. The top two family-cited functional goals were "easier walking/improve gait pattern" (12.2% of families) and "improve standing/weight bearing" (10.4%). 39% of total goals cited by families were not focused on ambulation with "easier dressing/diapering" (10%) and "lessen pain/discomfort" (8.5%) as the top two non-ambulation focused goals. For independently ambulatory people, the most commonly cited goal was "easier walking/improve gait pattern" (21%). For non-ambulatory people, the most commonly cited goal was "easier dressing/diapering" (15%).

CONCLUSIONS: Individualized function-focused goals for chemodenervation are infrequently and inconsistently documented across care team members. We must improve how clinicians and injectors elicit desired goals from people with CP and their caregivers, a necessary aim to optimize functional outcomes from botulinum toxin treatments.

KEYWORDS: Cerebral Palsy, Movement Disorders, Early Stage Investigator

12. Early Biomarkers in the Prediction of Later Functional Impairment in Preterm Children with Cerebral Palsy

Lambert G (Montreal, QC, Canada), Husein N, Fehlings D, Andersen J, Oskoui M, Shevell M

OBJECTIVE: To identify early biomarkers that could predict later functional capabilities in preterm children with later cerebral palsy (CP).

METHODS: Data from 1112 preterm children with CP were extracted from the Canadian Cerebral Palsy Registry (CCPR). Univariate and chi-square analyses were conducted to measure the association between early objective biomarkers and the later functional outcomes of mobility (GMFCS IV-V) and tube feeding dependence (fed by gavage or via gastrostomy/jejunostomy).

RESULTS: Univariate analysis suggested no significant association between GMFCS levels of IV-V or impaired feeding status and cord or first hour of life pH ≤ 7 [mobility status (odds ratio [OR] 1.67, 95% confidence interval [CI] 0.89-3.05) and feeding status (OR 2.04, CI 0.93-4.08)], MRI findings of white matter injury [mobility status (OR 1.34, CI 0.60-3.27) and feeding status (OR 0.87, CI 0.31-3.07)], abnormal findings on head ultrasound [mobility status (OR 1.97, CI 0.68-7.19) and feeding status (OR 2.21, CI 0.38-41.87)] as well as chorioamnionitis [mobility status (OR 1.03, CI 0.70-1.51) and feeding status (OR 0.91, CI 0.50-1.57)]. A significant association between impaired feeding status and an APGAR score of ≤ 5 at 5 minutes of life (p value 0.04) was detected.

CONCLUSIONS: Prediction of functional outcomes based on specific early biomarkers appears not to be enabled in children with CP born prematurely in contrast to those born at term. The complications and causal pathways inherent to prematurity itself might contribute to make such prognostication more complex and less determinant.

KEYWORDS: Cerebral Palsy, Neonatal Neurology, Neurodevelopmental Disorders

13. Selective dorsal rhizotomy outcomes in children with spastic cerebral palsy: A retrospective study in Jordan

Al-kharabsheh Y (Columbia, MO), Hmade A, Al-Khawaja I, Altaher M, Alfalojy I, Bani-Ahmad A, Anunoby I, Cirstea C

OBJECTIVE: Spasticity management in children with cerebral palsy (CP) is a major challenge for healthcare providers worldwide. In the US, treatment options include non-surgical and surgical (i.e., selective dorsal rhizotomy, SDR) procedures. SDR was recently introduced in Jordan, with the first procedure done in 2019. We were the first to evaluate the long-term effects of SDR on motor function in Jordan.

METHODS: A retrospective analysis of CP children admitted between January 1, 2019, and December 31, 2022, was conducted. Thirty-eight children (22 males; mean±SD age at surgery, 5.6±2.5 years; 27 with diplegia, 10 quadriplegia, 1 hemiplegia) received SDR (37 bilateral, 1 unilateral). Patient Gross Motor Function Classification System (GMFCS), Functional mobility scale (FMS), and modified Ashworth scale (AS) were compared before and at 12 months after SDR. Sex, age at surgery, and post-SDR spasticity treatment were included in the model. SDR-related clinical changes will be compared to those in children receiving non-SDR treatments (ongoing study).

RESULTS: All clinical scores improved significantly at 12-month follow-up: AS decreased across all lower extremity muscle groups ($p<0.001$), GMFCS decreased ($p<0.01$), and FMS increased ($p<0.01$). Changes in FMS negatively correlated with the age at surgery ($r=-0.56$, $p=0.02$). Compared to baseline, post-SDR treatment was reduced (21% no more physiotherapy; none received Botox).

CONCLUSIONS: Our data demonstrated beneficial long-term effects of SDR on motor function, with younger

children (<8 years old) exhibiting the largest improvement. These findings, if further supported by larger data sets, will generate critical data on the therapeutic window for SDR.
KEYWORDS: Cerebral Palsy, Global Neurology

14. Spectrum of common Pediatric Neurological disorders: An experience from three tertiary care centers across Pakistan

Chand P (Karachi, Pakistan), Wasay M

OBJECTIVE: The aim of this study is to identify the commonly presenting neurological disorders among children aged 18 years in Pakistan.
METHODS: The burden of these neurological disorders has been found to be greater in developing countries like Pakistan and there are limited data on the global burden of neurological disorders and its almost non existing from low middle income countries. We conducted a cross-sectional study at three tertiary care hospitals in Pakistan. We included all children presenting to the pediatric neurology clinics during the study period. All cases presenting to these centers were seen by trained pediatric neurologists, and the diagnosis was confirmed by history, neurological examination, and diagnostic tests.
RESULTS: A total of 17,176 children were included in our study; 61.8% were boys and 38.2% females. The most commonly presenting neurological disorder was epilepsy (36%), followed by behavior disorders (16%) and cerebral palsy (10.5%). Gender-wise distribution showed epilepsy to be the most common neurological disorder among both genders, with a significant difference being reported between gender and epilepsy, headache disorders, neuroinflammatory disorders, neurocutaneous syndromes, behavioral diseases, cerebral palsy and movement disorders.
CONCLUSIONS: This study will help health care workers in resource-poor settings within Pakistan to be mindful of the common neurological disorders while diagnosing a child with neurological symptoms in an outpatient setting. Health care providers need to be trained to identify and treat these common conditions; however, there is still a dire need for more trained neurologists across the country.
KEYWORDS: Cerebral Palsy, Behavioral Neurology, Epilepsy

15. Comorbidities of children with cerebral palsy born at term compared to preterm; A Registry-based study

Pekeles H (Montreal, QC, Canada), Husein N, Kirton A, Oskoui M, Shevell M

OBJECTIVE: For individuals with cerebral palsy (CP) and caregivers, comorbidities may be a greater challenge than neuromotor impairment. We compared comorbidities and imaging of children with CP born term to those born preterm.
METHODS: Using data from the Canadian Cerebral Palsy Registry of 2218 children with CP, we compared the comorbidity spectrum of term children (37 weeks and above GA, n=1264) to preterm children (born <37 weeks GA, n=954). To assess differences in MRI patterns, we classified our groups into categories: 1) normal/other, 2) deep gray matter injury (DGM), white matter (WM) and cortical injury, or near-total brain (NTB) injury (grouped together), 3) WM injury alone, 4) focal insult and 5) malformation.
RESULTS: We found differences in comorbidities in children born preterm vs term for epilepsy (10.7 % vs 21.7%), visual impairment (11.2% vs 18.2%), auditory impairment (13.2% vs 8.0%), communication impairment (58.0% vs 67.5%) and lack of functional hand use [MACS Level IV-V] (22.1% vs 27.9%) (p value for all < 0.05). No significant difference was found for tube feeding dependence, cognitive impairment, or non-ambulation [GMFCS Level IV-V]. MRI findings were more dispersed across categories for term infants, with more focal injury, malformation, and widespread injury (DGM injury, WM and cortical injury, or NTB injury) compared to the preterm group where WM injury was predominant.
CONCLUSIONS: Children born term had more frequent comorbidities compared to children born preterm and more varied MRI findings, supporting that causal mechanisms for their CP are likely more widespread. Surveillance efforts should target different comorbidities in these populations.
KEYWORDS: Cerebral Palsy, Neonatal Neurology, Neurodevelopmental Disorders

16. Quantitative thalamic injury patterns in bilateral cerebral palsy: associations with neuropathic pain symptoms

Chin E (Baltimore, MD), Gorny N, Riordan H, Hoon A, Jantzie L, Robinson S

OBJECTIVE: Assess the relationship between thalamic injury profiles and neuropathic pain in adults with cerebral palsy (CP)
METHODS: We recruited adult volunteers (a group with CP and a healthy, typically-developed group [TD]). Adults with CP had predominant bilateral white matter injury (WMI), were independently communicative, and were able to lie still.
Participants self-reported neuropathic pain (PROMISv2 T-scores) and underwent 3T MRI. Thalamic nucleus group volumes were computed from (1mm)3 MPRAGE and FGATIR images (FreeSurfer v7.3.2). We examined group differences using t-tests/proportion tests and biomarker-pain score correlations in terms of ρ2(% shared variance) tested against H0 of no correlation.
RESULTS: Study groups (n=6 each) were similar in age (CP mean±SD: 35±6; TD: 31±9; p=0.4) and sex distribution (p=0.22). Neuropathic pain scores were increased in adults with CP (CP: 43±37; TD: 37±0; p=0.02).
Volume was significantly reduced (20-44%) in five of six nucleus groups (posterior, medial, ventral, intralaminar, and lateral; Bonferroni-corrected p<0.05). More severe volume loss was associated with greater neuropathic pain scores for all nuclear groups (posterior/ventral/intralaminar [all with ρ2=69%] > medial [ρ2=43%] > anterior [ρ2=29%] > lateral [ρ2=7%]), though associations were not significant.
CONCLUSIONS: Posterior, ventral, intralaminar, and medial thalamic nuclei– those that directly receive spinothalamic afferents– showed the most consistent volume loss in adults with CP+WMI, and injury to these nuclei was

most strongly associated with neuropathic pain. While validation and larger study groups are needed, this pattern of findings suggests that spinothalamic deafferentation is linked to neuropathic pain in adults with CP+WMI as is seen in central neuropathic pain syndromes.
KEYWORDS: Cerebral Palsy, Neuroimaging, Lifespan Manifestations of Childhood Onset Conditions

17. Pathogenic variation in RARB causes cerebral palsy without microphthalmia

Calame D (Houston, TX), Fatih J, Hull M, Parnes M, Schwabe A, DiCarlo S, Farach L, Tremblay A, Lupski J, Michaud J

OBJECTIVE: RARB encodes retinoic acid receptor beta and is responsible for syndromic microphthalmia 12 (MCOPS12). Here we describe a role for pathogenic RARB variation in the etiology of cerebral palsy (CP) without microphthalmia.
METHODS: Patients underwent clinical exome sequencing and were identified in clinical practice or through diagnostic laboratory queries. In vitro transcriptional assays were used to assess variant pathogenicity.
RESULTS: We identify three patients with CP without microphthalmia and likely pathogenic RARB missense variant alleles NM_000965.5:c.844G>A; p.(G282S), c.854T>G; p.(L285R), and c.848T>C; p.(L283P). Dystonia was a prominent feature and refractory to medical treatment in one case. Two patients had normal IQ and scholastic performance; the other patient had microcephaly and cognitive impairment. As RARB regulates dopaminergic receptor expression in the mesolimbic pathway, levodopa-carbidopa was trialed in two patients but was unsuccessful. c.844G>A; p.(G282S) increases RARB transcriptional activity whereas c.854T>G; p.(L285R) has a dominant negative effect. Functional characterization of c.848T>C; p.(L283P) is ongoing.
CONCLUSIONS: RARB was first linked to MCOPS12, a severe developmental disorder characterized by microphthalmia, diaphragmatic hernia, and severe developmental delay. These studies demonstrate pathogenic RARB variants also cause CP with dystonia, normal intellect, and without congenital anomalies. As RARB-related CP results from gain-of-function or dominant negative alleles, allele-specific antisense oligonucleotides may be a viable treatment option. Further case identification is needed to understand the prevalence, phenotypic spectrum, and natural history of RARB-related CP.
KEYWORDS: Cerebral Palsy, Neurogenetics, Movement Disorders

18. Steps towards development of a toolkit for early detection and intervention for young children with cerebral palsy

Majnemer A (Montreal, QC, Canada), Boychuck Z, Ogourtsova T, Fehlings D

OBJECTIVE: i) to develop user-friendly tools to enhance earlier detection of cerebral palsy (CP) by primary care providers, for referral to medical specialists for diagnostic assessment, and ii) to ensure that evidence-based early interventions are utilized.
METHODS: A series of studies were carried out to develop a toolkit to optimize early detection and intervention for children with CP. International guidelines exist for identification of CP in high-risk infants, however close to half of children with CP are low-risk. Consensus on clinical attributes associated with CP was determined using nominal group techniques. International validation of attributes and referral recommendations was conducted using Delphi techniques. Review of evidence (2010-, PEDro Scale quality rating) of interventions for young children with CP was synthesized for clinicians and families.
RESULTS: Consensus groups included 29 clinician-scientists, healthcare professionals and parents, and 6 attributes and 2 warning signs were determined and subsequently validated by 51 international experts. Twenty-two interventions were coded by level of evidence, as related to type/severity of CP. A website was launched to include early detection tools and evidence-based interventions, and dissemination strategies are underway.
CONCLUSIONS: Children at low-risk for CP experience substantial delays in diagnosis and interventions, important for adaptive plasticity and better functional outcomes. A toolkit (https://www.childhooddisability.ca/edit-cp-toolkit/) has been developed to address knowledge gaps by primary care providers and rehabilitation specialists. Toolkit uptake will ensure timelier referral to neurologists for diagnostic assessment, and more optimal family adaptation. Furthermore, use of evidence-based early interventions is critical in enhancing child and family outcomes.
KEYWORDS: Cerebral Palsy, Cerebral Palsy, Education

19. Characterization of Clinical MRI Findings in Moderately-Late Preterm Infants Diagnosed with Cerebral Palsy: A Single Center Retrospective Study

Fisher E (Chicago, IL), Jaju A, Aw-Zoretic J, Mithal D

OBJECTIVE: The central hypothesis in the project is that moderately premature infants, with defined, acquired brain injuries have a more severe clinical presentation than those with non-specific MRI findings. The study categorizes the spectrum of moderately pre-term CP patients MRI findings and comparing clinical parameters.
METHODS: A retrospective cohort study of patients at our center seen between 2007 and 2020 identified all children with a CP ICD code. Patients born between 32 and 34 WGA were selected as a moderately premature. Clinical data, including MRI data was extracted from the electronic medical record. Two independent, board-certified pediatric neuroradiologists reviewed the imaging patterns. MRI were grouped into five categories based on existing literature for moderately premature brain imaging.
RESULTS: 5014 total patients with CP were identified of whom 104 were born between 32 and 34 WGA, and 64 had MRI imaging available for review. 54% had a defined causal injury, 10% had a structural abnormality, 30% had nonspecific findings that were not a definitive cause of CP and 5% were normal. Importantly, patients with nonspecific MRI findings, had statistically similar rates of a gastrostomy, tracheostomy or epilepsy as patients with severe, causal imaging patterns.
CONCLUSIONS: In addition to findings of brain injury, children with CP who are born moderately preterm frequently

have structural abnormalities or nonspecific MRI findings. The imaging findings do not correlate with overall disease severity, indicating that for this population, the brain injury on MRI is a poor predictor of neurologic outcome. The risk factors conferring poor neurologic outcome require further investigation.
KEYWORDS: Cerebral Palsy, Neuroimaging

20. Quantifiable features of leg dystonia severity in people with cerebral palsy

Rust A (St. Louis, MO), Suh N, Blackburn J, Gelineau-Morel R, Kruer M, Mingbunjerdsuk D, O'Malley J, Tochen L, Waugh J, Wu S, Aravamuthan B

OBJECTIVE: Noting that leg dystonia is grossly underdiagnosed in people with cerebral palsy (CP), our objective was to help guide clinical dystonia diagnosis by determining the specific movement features that guide expert assessment of leg dystonia severity in people with CP.
METHODS: In this prospective cohort study, eight movement disorder neurologists from different academic institutions graded lower extremity dystonia severity in 193 videos of seated young people with CP (age 5-18) performing a hand open-close task. Dystonia severity was rated on the 10-point Global Dystonia Severity Rating Scale (0 – no dystonia; 10 – severe dystonia). Informed by expert discussion and our previous work demonstrating that variable leg adduction correlated with leg dystonia severity during gait, we used open-source pose estimation software (DeepLabCut) to help determine quantitative analogs of expert-cited features that correlated with experts' leg dystonia severity scores.
RESULTS: Variables assessing adduction variability (inter-knee distance, inter-ankle distance, and inter-toe distance variances) and leg elevation variability (knee to ground, knee to ankle, and ankle to toe distance variances) were significantly different between people with and without dystonia ($p<0.001$, t-test). These variables were also significantly linearly correlated with experts' dystonia severity scores ($p<0.001$, $R2=0.1$-0.4 across variables, Pearson correlation).
CONCLUSIONS: Leg adduction and elevation variability are quantifiable features that correlate with experts' assessments of leg dystonia severity during a seated task in people with CP. Consideration of these features could help standardize the clinical assessment of leg dystonia in people with CP, including in those who are not independently ambulatory.
KEYWORDS: Cerebral Palsy, Movement Disorders

DIVERSITY, EQUITY, INCLUSION

21. Disparities in Rehabilitation After Pediatric Neurologic Injury

Pal R (Palo Alto, CA), Saynina O, Lee S, Wise P

OBJECTIVE: We seek to identify disparities provision of acute inpatient rehabilitation in critically ill pediatric patients with acquired neurologic injury.
METHODS: This is a retrospective cohort study using publicly available California Department of Health Care Access and Information data from 2014-2020. 4462 patients 1-18 years hospitalized in California were included if the hospitalization record included proxies for critical illness (e.g. arterial line placement) and ICD9/10 codes for ischemic or hemorrhagic stroke, traumatic brain or spine injury, or inflammatory myelopathy or polyradiculopathy. Patients were excluded if their length of stay was fewer than 5 days, greater than 180 days, or if they were discharged as deceased, as patients with minor or catastrophic insults are often regarded as poor candidates for rehabilitation (low likelihood of quantitative improvement in assessments of daily function). Chi-square tests for independence were performed across clinical and demographic variables including age, race/ethnicity, geographic region, neurologic diagnosis, and comorbidities.
RESULTS: We found statistically significant differences ($p < .01$) in in-hospital rehabilitation by age, geographic region, rurality as defined by ZIP code, neurologic diagnosis, existing comorbidities, and insurance. No statistically significant differences were found across gender, race/ethnicity, or income (using ZIP code to estimate percentage of federal poverty level).
CONCLUSIONS: Prior work has established that rehabilitation services can improve functional recovery in children with acquired neurologic injury. Population-level disparities in the provision of these services, as suggested in this study, imply preventable inequities in trajectories after neurologic insult and an opportunity for more specific clinical guidelines for inpatient rehabilitation.
KEYWORDS: Diversity, Equity, Inclusion, Neurocritical Care, Practice Parameters

22. Navigating Caregiver-Patient Discord in the Sexual and Gender Minority Community

Kernan-Schloss F (Portland, OR), Christy A

OBJECTIVE: Pediatric neurologists are familiar with the complex ethics of decisional discord: when caregivers and children disagree on treatment and the plan of care. A novel discord can arise when a child identifies as a sexual and gender minority (SGM) that is different from the one assigned at birth, and does not receive support from their caregiver. Because the child is the vulnerable party when there is discord around the child's gender or sexuality, we asked adolescents how clinicians can best navigate this conflict in a clinical setting.
METHODS: Five adolescent patients who identified as sexual and gender minorities (but did not necessarily experience familial discord themselves) were interviewed about how they would prefer a clinician handle certain clinical scenarios: 1) caregiver "deadnaming" (referring to a person by a name they used prior to transitioning); 2) accidental misgendering with pronouns; 3) insistent or intentional misgendering with pronouns; 4) explicitly stated denial of the patient's identified gender.
RESULTS: Our patients gave us different options for clinicians to consider in each scenario.
CONCLUSIONS: Respectful communication with both caregivers and patients is crucial for maintaining therapeutic

alliances with families. Clinicians must thus consider the various ways we can respond in a challenging moment before it occurs.

KEYWORDS: Diversity, Equity, Inclusion, Ethics, Education

23. Inclusion of Medically Underserved Populations in a Cohort with Developmental and Epileptic Encephalopathies

Peck S (Chapel Hill, NC), Heinzen E, Shiloh-Malawsky Y, Felton T, Wilson S, Foss K, Gonzalez Y, Fan Z, Gucsavas-Calikoglu M, Hunter S

OBJECTIVE: Our study (Genetic Determinants of Neurological and Developmental Disorders) seeks to identify genetic variations in patients with developmental and epileptic encephalopathies (DEE). The frequency of rare variants - and significance of their detection - can be confounding in individuals from diverse ancestral backgrounds due to limited diversity in genetic research. We prioritize ancestral diversity per the National Human Genome Research Institute Strategic Vision. Thus, we conducted a pilot study to determine the feasibility of enrolling ≥ 60% of participants from medically underserved populations (historically underrepresented in research) to obtain genomic sequencing data in a DEE cohort.

METHODS: In our single center prospective study, we recruited individuals diagnosed with DEE and their biological relatives for whole exome and genome sequencing. We employed new and existing recruitment and enrollment techniques to achieve robust participation from medically underserved individuals, including racial/ethnic minorities and those with non-English preferred language.

RESULTS: Among 68 subjects, 82% were from medically underserved populations: 50% racial/ethnic minorities, 10% non-English language, 53% from tier 1 or 2 designated counties, and 68% with public insurance (Medicaid) or uninsured. Of those with completed research genomic sequencing we identified likely pathogenic (GRIA2) and pathogenic (somatic MTOR) variants. The pathogenic variant was identified in a subject with limited clinical testing due to language barriers.

CONCLUSIONS: Epilepsy patients are more likely to represent underserved populations, but less likely to be included in genetic research. Our study demonstrates the feasibility of prioritizing inclusion and diversity in genetic research, aligning with the NHGRI Strategic Vision.

KEYWORDS: Diversity, Equity, Inclusion, Epilepsy, Neurodevelopmental Disorders

24. From Resident To Chair: Evaluating Gender Disparities In Child Neurology Pipeline

Rakolle K (New York City, NY), Etienne M, Darrell M

OBJECTIVE: Achieving gender equity is fundamental to creating a balanced healthcare workforce. This study analyses trends in the proportion of male-to-female residents in child neurology and compares this data to the gender diversity of the current pediatric neurology department leadership.

METHODS: This is a retrospective analysis of data extracted from the Accreditation Council of Graduate Medical Education (ACGME) Data Resource Books between 2011 and 2022. The data collection and trend analysis were conducted on Microsoft Excel. We utilized the Child Neurology Society program guide to identify the chair/director of each pediatric neurology department/division and the residency program director (PD). We utilized the pronouns used in their publicly available biographies to classify their gender.

RESULTS: From 2011 to 2022, female representation in Child Neurology residency increased from 60% to 69%. The representation of female residents is approximately 30% higher than male residents for each academic year ($p<0.01$). Of the seventy-five pediatric neurology programs evaluated, 24% of chairs/department directors and 60% of program directors were female.

CONCLUSIONS: More than two-thirds of pediatric neurology trainees are women; however, women make up less than 30% of department/division leadership demonstrating a gender disparity in career progression. It is important to ensure that female physicians are represented in leadership and compensated equally and fairly to achieve gender equity. Women in these roles can serve as role models and increase the likelihood of women pursuing medicine and academia. Medical practice should promote integrated patient care, diversity, and equitable career opportunities and progression regardless of gender identity.

KEYWORDS: Diversity, Equity, Inclusion

25. Recruiting and Retaining a Diverse Child Neurology Workforce: A Remedy for Disparities in Child Neurology Residency Programs

Rakolle K (New York City, NY), Etienne M

OBJECTIVE: The number of child neurologists in the US is 20% below the national necessity and this shortage is more pronounced in underserved communities. Black and Hispanic patients are 30% and 40%, respectively, less likely to receive continual outpatient neurological care than their White counterparts. Physicians from demographics underrepresented in medicine (URiM) are more likely to work in underserved communities. In this study, we explore trends in URiM pipeline in child neurology residency.

METHODS: This is a quantitative analysis of the Accreditation Council for Graduate Medical Education (ACGME) Data Resource Book from 2011 to 2022. Demographic data, including the race and ethnicity of child neurology residents, were extracted, and analyzed in Microsoft Excel. Chi-Square analysis was utilized, and expected values were calculated using the US census data. The primary outcome was the trend in URiM representation in pediatric residency programs.

RESULTS: There were 4035 child neurology residents between 2011-2022. Chi-square analysis demonstrated significant underrepresentation of Black, Hispanic, and Native Americans ($p<.000001$) in US child neurology training programs. There were 6.9% Hispanic, 3.4% Black, and 0.1% Native American residents. There has been a gradual increase in percentage of Hispanic, however, there has been no significant change in Black and Native American residents.

CONCLUSIONS: Despite ACGME interest in prioritizing expansion and support of a diverse physician workforce, there has been no significant increase in URiM physicians in the Child Neurology pipeline. Medical institutions should be intentional in cultivating diversity by recruiting and retaining URiM residents and creating a culturally informed and inclusive clinical environment.
KEYWORDS: Diversity, Equity, Inclusion

26. Zero gaps in care: designing interventions to reduce racial disparities in ER utilization for break-through seizures in pediatric epilepsy patients

Lin N (Cincinnati, OH), Ritter D, Wesselkamper K, Vawter-Lee M, Bruce J, Clifford L, Whitesell K, Grimm J, Bonjour A, Davis A, Gill M, Kremer K, Holland K

OBJECTIVE: Epilepsy is one of the most common neurological conditions of childhood with significant associated comorbidities. Increasing body of literature reveals racial disparities in SUDEP rates or in people with epilepsy (PWE) being referred for epilepsy surgery evaluation. Through the Cincinnati Children's Hospital Medical Center (CCHMC) Health Equity Network with a multi-disciplinary team of physicians, nurses, case managers, social worker, and patient family advocates, we aim to decrease disparities between black/African-American and non-black/African-American PWE under age 21 years that present to the CCHMC emergency department (ED) and urgent care (UC) for seizures.
METHODS: Using quality improvement (QI) methodology, we use Plan-Do-Study-Act (PDSA) cycles to design interventions based on the key driver diagram and Pareto charts to decrease this significant gap in care.
RESULTS: Our baseline data shows a significant disparity between black/African American versus non-black/African American PWE utilization of the ED/UC for break-through seizures. We have constructed a key driver diagram. We have identified barriers to medication adherence as one of our key drivers. Our next step is designing interventions, likely utilizing toolkits provided by Epilepsy Foundation and in co-production with our other community partners such as Legal Aid.
CONCLUSIONS: There is an urgent need to design interventions that will reduce racial disparities in our care of PWE. By using a multi-disciplinary approach, we aim to use QI to reduce those gaps. Our global aim is to achieve a zero gap in pediatric health outcomes by race and socio-economic status.
KEYWORDS: Diversity, Equity, Inclusion, Epilepsy

27. Evaluating current perception, cultural beliefs, and associated social stigma of autism spectrum disorder in Uganda. Insights from an educational Intervention study.

Hoche F (Boston, MA), Tiiti P, Odama C, Nakalule J

OBJECTIVE: Autism spectrum disorder (ASD) is a neurodevelopmental condition that affects communication, social interaction, and behavior. In Uganda, there is widespread misconception and stigma associated with ASD. Autism is considered a shameful condition that leads to discrimination and ostracizing of affected individuals. This study aimed to address the perceptions and stigma associated with ASD in Uganda through an educational intervention program.
METHODS: A mixed-methods approach employed both quantitative and qualitative data collection using pre- and post-intervention surveys and interviews with parents and teachers of children with ASD. The educational intervention program was delivered through a 2-day conference workshop targeting teachers, parents, and community leaders. The workshop covered topics related to the characteristics of ASD, its diagnosis, and management. The program also aimed to improve the participants' understanding of the needs and challenges faced by individuals with ASD.
RESULTS: N=84 participants attended the educational conference. N=22 participants completed both parts of the pre- and post-intervention survey. Results showed a significant improvement in the participants' knowledge and attitudes towards ASD after the intervention program. The study identified factors contributing to stigma, such as misconceptions, lack of awareness, and cultural beliefs.
CONCLUSIONS: Perception of stigma associated with ASD in Uganda can be addressed through educational intervention. EI can improve the knowledge and attitudes of teachers, parents, and community leaders towards ASD. Learners can assume the role of community teachers and thus expand their impact by educating others. Further research is needed to determine if stigma reduction improves health outcomes for those with autism and their families.
KEYWORDS: Diversity, Equity, Inclusion, Behavioral Neurology

28. Racial disparities in access to exome sequencing for children with neurological disorders: When in the diagnostic trajectory do they appear?

Cole J (St. Louis, MO), Sellitto A, Balls-Berry J, Gurnett C

OBJECTIVE: To evaluate the severity and potential causes of disparities in access to genetics services among patients seen in a tertiary care child neurology clinic.
METHODS: Electronic health record data on all patients seen in a tertiary-care child neurology clinic between July 1, 2018 to January 1, 2020 were obtained. Demographic features of patients completing each step along the diagnostic trajectory toward completion of genetic testing were compared. Due to small numbers of other racial/ethnic identities, only non-Hispanic white and Black race/ethnicity were analyzed.
RESULTS: 10,684 patients identifying as white (83.8%) or Black (16.2%) were seen during study dates. Rates of referral to Genetics Clinic did not differ by race/ethnicity (2.8% of white vs. 2.3%of Black patients; p=0.22). Black patients were nearly 3x less likely to complete Genetics visits after referral (OR 2.7, 95% CI 1.3-5.5). Black patients were also nearly 3x less likely to receive ES (OR 2.8, 95% CI 1.3-6.1). However, among those who did complete Genetics visits, there was no significant difference in ES rates (16.3% of white vs.16.8% of Black patients, p=0.98).
CONCLUSIONS: We have identified a key point in the diagnostic trajectory to ES at which Black patients are particularly vulnerable. It is strongly suspected that the inequity in genetics

referral completion is at least in part due to structural racism. Other contributors may include differences in perceived utility of genetic testing, strength of recommendation by providers, and/or medical mistrust. Which of these factors is most remains unknown and future work will explore this.
KEYWORDS: Diversity, Equity, Inclusion, Neurogenetics

29. Health disparities encountered by two patients with developmental disabilities

Runco A (Houston, TX), Levine J, Guzman-Karlsson M, Fisher K, Risen S

OBJECTIVE: To describe two cases that illustrate healthcare inequities that can be encountered by patients with developmental disabilities.
METHODS: Case-series of 2 patients
RESULTS: A 15-year-old Hispanic male with MEHMO syndrome presented to the emergency department (ED) with acute inability to walk, apparent lower extremity sensitivity, and autonomic instability requiring anti-hypertensives. He remained in the ED and received a negative evaluation for trauma and infection. Over 24 hours later, neurology was consulted and observed a history and exam consistent with Guillain-Barré syndrome. He was treated with IVIG (intravenous immunoglobulin) and plasmapheresis, given severity of presentation, including intubation. His MRI and CSF studies confirmed the diagnosis.
A 19-year-old male with CHARGE syndrome who communicates using American Sign Language presented to the ED with new urinary retention, constipation, lower extremity weakness, and difficulty walking, for which a foley catheter was placed, and he was discharged. Three days later, he represented with progression of weakness and new lower extremity paresthesias and neurology was consulted. He was found to have extensive transverse myelitis and serum myelin oligodendrocyte glycoprotein (MOG) positivity. He was treated with high dose steroids and IVIG.
CONCLUSIONS: These two cases clearly demonstrate healthcare inequities that can be met by patients with developmental disabilities and highlight that they often are faced with barriers in communication and common misconceptions or stigma among healthcare providers. The assumption that new symptoms could be attributed to prior diagnoses led to delays in diagnosis and treatment for both patients.
KEYWORDS: Diversity, Equity, Inclusion, Neuroimmunology, Neurodevelopmental Disorders

EDUCATION

30. Design Principles and Insights into Flipped Classroom Learning in Graduate Medical Education: An Educational Design Research Study

Lazar S (Houston, TX), Kannan V, Risen S, Davila-Williams D, Malbari F

OBJECTIVE: "Flipped classroom" educational strategies have grown in popularity across all levels of medical education. Most literature supporting these strategies are not necessarily transferrable to the Graduate Medical Education (GME) context. The objective of this study is to determine design-principles needed for the successful design and implementation of a Cognitive-Load Theory informed Team-Based Learning (TBL) curriculum within a child neurology residency program.
METHODS: An Educational Design Research (EDR) methodology using iterative cycles of analysis and exploration, design and implementation, and evaluation and reflection was used. Primary outcomes include design principles and a mature educational product. Program evaluation incorporated both qualitative focus groups and quantitative post-session surveys that evaluated learner reactions, knowledge acquisition, and self-reported behavioral changes based on Kirkpatrick's Evaluation Framework.
RESULTS: Four cycles of TBL session design were completed. A needs assessment determined curriculum content that balanced both content expertise of the facilitators and learner knowledge and skill gaps. Core design principles for successful implementation of a flipped learning session in GME include: concordance of preparatory material with didactics, use of brief high-yield preparatory materials to limit cognitive load, provide protected time for preparation, and overtly link material to clinical practice.
CONCLUSIONS: Using the pragmatic and contextual approach of EDR we were able to integrate educational theory into curriculum development to help understand, adapt to, and overcome educational challenges of implementing a flipped classroom design in the GME space. Key design principles were developed to allow transferability to other curriculum designers in GME in other contexts.
KEYWORDS: Education

31. An Overview of ICD Code Development in Pediatric Neurology

Baker M (Salt Lake City, UT), Bonkowsky J

OBJECTIVE: Querying large datasets in the U.S. is challenging due to limitations of International Classification of Diseases 10th edition Clinical Modification (ICD-10-CM) codes. ICD codes were developed for tracking mortality and for billing purposes but are also the most widely used data structure to represent clinically significant and distinct disorders. We report an approach for developing new ICD codes based on our work creating new codes for leukodystrophies.
METHODS: Important steps in ICD-10-CM code development include: working with the ICD-10-CM Coordination and Maintenance (C&M) Committee, a subset of the National Center of Health Statistics (NCHS); working to ensure the code has the best placement and is appropriate for submission; presenting the code and accompanying proposal (rationale) at a C&M committee meeting; and requesting letters of support and addressing concerns raised by various groups.

RESULTS: We describe the historical development of ICD codes as well as their current hierarchical structure. Important features for successful code development included: consulting future ICD-11-CM code structure; determining which codes are of most importance to the community; having a multidisciplinary approach; and obtaining organizational and institutional support.
CONCLUSIONS: Focusing on the clinical importance of leukodystrophy codes was important for their approval. Although challenging, there is a route for new code development, and we were ultimately successful in obtaining approval for 10 new leukodystrophy ICD-10-CM codes. Understanding ICD codes and their structure, consideration of their usage for clinical and research work, and an appreciation of how new codes can be developed, is important for the pediatric neurology community.
KEYWORDS: Education

32. Enhancing Child Neurology Resident Knowledge and Residency In-Training Examination (RITE) Scores with Twice-Weekly, Interactive Small-Group Teaching in Child Neurology

Youssef P (Rochester, MN), Fine A, Hanson M, Halliday A, Wirrell E

OBJECTIVE: To augment the clinical knowledge base of child neurology trainees, we implemented a novel series of faculty-led teaching conferences on core child neurology topics for residents rotating on our inpatient service. We sought to determine if this intervention led to improvement in performance on the pediatric neurology section of the Residency In-Training Examination (RITE) scores.
METHODS: Beginning in mid-2016, twice weekly 30-minute interactive teaching sessions were provided by faculty, typically in their area of subspecialty expertise. A combination of case-based and didactic teaching sessions reviewed high yield topics in child neurology. Resident scores on the pediatric neurology section of the RITE exam were reviewed pre-intervention from 2011-2016 and compared to post-intervention scores from 2017-2022 to determine effectiveness of the series.
RESULTS: Resident's exam scores pre-intervention from 2011-2016 (N=10) were compared to those scores post-intervention from 2017-2022 (N=12) using the independent samples t-test. After implementation of the core teaching series, the mean percentage scores (SD) on the pediatric neurology section of the RITE from PGY3-4 improved from 6.1% (SD 9.3) pre-intervention to 6.8% (SD 8.1) post-intervention ($p=0.42$) and from PGY4-5 improved from 5.9% (SD 6.1) pre-intervention to 10.7% (SD 6.8) post-intervention ($p=0.05$).
CONCLUSIONS: Implementation of twice-weekly, focused child neurology teaching sessions showed a strong trend toward improvement in pediatric neurology RITE exam scores amongst PGY4-5 residents. This trend likely also reflects the majority of core child neurology training occurs in the PGY4-5 years. Future work should evaluate if the series leads to sustained improvement amongst a larger group of trainees.
KEYWORDS: Education

33. Faculty Evaluation by Residents in A Small Training Program: Improving Timely Feedback and Ensuring Confidentiality

Fine A (Rochester, MN), Jones B, Youssef P, Halliday A, Hanson M, Wirrell E

OBJECTIVE: Ensuring feedback from residents to teaching faculty in small programs can be challenging given the need to maintain resident confidentiality. We present a novel mechanism to provide timely, actionable feedback to faculty to enhance their teaching skills and ability to provide constructive feedback to learners.
METHODS: Our program consists of only 2 trainees per year, in each of the 3 core Child Neurology years. Previously resident evaluations were embargoed for a year or longer and only released in groups to ensure anonymity of raters. However this presented challenges in providing timely feedback to faculty to improve their teaching skills. We report on a novel feedback tool which has been employed since January 2019.
RESULTS: All PGY3-5 Child Neurology residents meet in a group with the program coordinator twice yearly and feedback is then provided as a group to individual faculty. For each faculty member, feedback is sought specifically regarding approachability and professionalism, role as a clinician educator, ability to provide appropriate trainee autonomy and efficiency in both inpatient and outpatient settings. In addition, all faculty are provided with comments on what they are doing well and should continue, as well as what should be done more or differently. Since using this tool, we have seen both improvement in resident ratings of faculty teaching and in faculty satisfaction with resident feedback.
CONCLUSIONS: We provide a novel feedback tool which could be used in other small training programs to provide timely and actionable feedback to teaching faculty, while ensuring rater confidentiality.
KEYWORDS: Education

34. Neurological Conferences: A Comparison Study

Spivey T (Cincinnati, OH), Gilbert D, Alperin S

OBJECTIVE: To evaluate how neurology societies inform and educate members through annual conferences.
METHODS: Conference sessions at 5 to 10 in-person meetings for seven societies (American Academy of Neurology – AAN, American Clinical Neurophysiology Society – ACNS, American Epilepsy Society – AES, American Headache Society – AHS, Child Neurology Society – CNS, Movement Disorder Society – MDS, World Muscle Society – WMS) were included. Length, costs (society membership and member-rate registration fees), and total educational content hours were tabulated. We categorized and tallied sessions based on type (Symposium/Plenary, Course/Lecture, Workshop, Other) and content (Clinical Care, Research, Career Development, Global Health, Public Health, Quality Improvement, Billing). To account for differences in conference length, we compared features based on per-day calculations.

RESULTS: Average hours of educational content per conference day ranged from 3.9 (WMS) to 85 (AAN). Average total (membership plus conference registration) annual fees ranged from $515 (WMS) to $1340 (AAN). Most conferences focused on clinical content (> 50% of session-hours), except for AHS (40%) and WMS (12%). Research was the second most common focus (<50%) except for AHS (50%) and WMS (72%). Most meetings presented the majority of sessions as courses, often running concurrently. Plenary sessions were most common in AHS (67%) and CNS (49%). Average annual cost per hour of available education was highest for CNS ($100) and WMS ($129) and lowest for AAN ($16) and AES ($33).
CONCLUSIONS: Neurological society meetings emphasize clinical care-related content but vary in number of concurrent courses versus plenary sessions, and fees per hour of education.
KEYWORDS: Education

35. Improving Epilepsy Education in LMIC Schools: Reducing Misconceptions about Epilepsy to Improve Epilepsy Awareness in Pakistan and India

Dhoot R (Durham, NC), Sabha N, Hume C, Karthikeyan L, Hwang J, Dubey S, Mohammed S, Zafar M

OBJECTIVE: This study evaluates baseline epilepsy knowledge, assesses seizure education material effectiveness, and identifies knowledge gaps in interventions teaching seizure first aid in school settings.
METHODS: In-person educational sessions were conducted by volunteers in five schools in Pakistan (n=540; ages 10–15) and five in India (n=459; ages 10-15). Two flyers, a seizure action plan and an epilepsy factsheet, were distributed in English and local languages. We conducted pre- and post-surveys with open-ended and multiple-choice questions that measured educational outcomes. McNemar's and chi-squared tests validated the results.
RESULTS: Supernatural cause attributions for epilepsy decreased from 51.9% to 10.9% in India and from 47.2% to 17.5% in Pakistan after intervention. Belief that epilepsy was contagious also reduced from 46.1% to 5.6% in India and from 30.2% to 7.5% in Pakistan. Knowledge on proper seizure first-aid increased from 46.2% to 94.7% in India and from 62.1% to 87.2% in Pakistan. Long-term epilepsy management knowledge increased from 36.9% to 84.9% in India and from 23.3% to 75.0% in Pakistan. McNemar's tests comparing pre- and post- results were significant ($p<0.001$) for Indian respondents, while chi-squared tests for Pakistani respondents were also significant ($p<0.05$).
CONCLUSIONS: Misconceptions about epilepsy significantly reduced in schools after intervention. Findings highlight the value of targeted early-intervention school programs to address knowledge gaps and stigmas. Refresher sessions in schools are suggested to promote knowledge retention and reduce long-term negative effects of stigmas, including social isolation, hindered psychosocial growth, and school drop-out rates.
KEYWORDS: Education, Epilepsy, Global Neurology

36. Family-Clinician Partnership to Educate Families Affected by Pediatric Stroke or Brain Injury and Their Providers

Yale M (Framingham, MA), Musolino P, Wishart B, Ballasiotes M K

OBJECTIVE: Clinic visits are short. Physicians must focus on medical issues. The journey for children impacted by pediatric stroke or brain injury may involve delayed diagnosis, years of therapy, accommodations at school, accessible recreation, and eventually transitioning to adult medical, therapeutic, vocational support. By partnering, families and clinicians can develop educational resources then strategically direct families to appropriate help.
METHODS: Build a team of family members and clinicians to develop educational resources. Include a lived experience story in each session. Curate live virtual events via recorded videos and documents. Survey the audience for new topics, potential speakers, and other needs. Share resources with families via the internet, advocates, and in the context of medical encounters. Use resources to raise awareness about pediatric stroke with emergency service providers and pediatricians.
RESULTS: • 40 sessions delivered in past 5 years
• Typical live attendance of 20-80
• 16 videos viewed more than 100 times, top video viewed nearly 1000 times
• International audience of family members and clinicians
• Contributions by speakers from more than a dozen organizations
CONCLUSIONS: The audience continues to grow for educational materials about pediatric stroke and brain injury. Families, advocates, and clinicians attend. Early efforts show that pediatric stroke clinic visits may be enhanced by pointing individual families to resources that relate to their child's current challenges. Through patient-reported outcomes and a quality-of-life survey, we are assessing the impact. We aim to continue to curate materials while simultaneously reaching an increasingly diverse population of families and medical providers.
KEYWORDS: Education, Stroke, Lifespan Manifestations of Childhood Onset Conditions

37. Rescheduling Child Neurology Trainee Continuity Clinics: Gauging Potential Impacts on Accessibility and Patient Attendance

Applbaum E (New York City, NY), Bell L, Murphy A, Nelson A

OBJECTIVE: NYU Langone Health/ Bellevue Hospital child neurology residency continuity clinics have been historically held weekday mornings. To address increasing conflicts between resident education that occurs simultaneously in inpatient (morning hospital rounds) and outpatient (clinics) settings, all child neurology residency clinics were rescheduled to weekday afternoons. The goal of this study was to determine if these changes impacted child neurology clinic patient attendance.
METHODS: In anticipation of a planned shift of all child neurology residency program continuity clinics from

mornings to afternoons, the no-show rate was tracked to establish a clear pre-intervention baseline. Clinics were then moved from mornings (9AM-noon) to afternoons (1PM-4PM), and no-show rates were prospectively tracked. Actual versus expected no-show rates were then compared pre- and post-intervention.

RESULTS: There was no significant difference in no-show rates for any of the child neurology continuity clinics with the move from mornings to afternoons. There was neither a clear improvement nor an increase in no-shows despite the change.

CONCLUSIONS: Moving continuity clinics from the mornings to the afternoons did not negatively impact patient attendance. As this was a considerable schedule change, one might have anticipated that in the short-term, patients' personal schedules or the abrupt nature of the change would have transiently increased patient no-show rates. In the long-term, however, it is possible that afternoon clinics will in fact have a lower no-show rate due to decreased conflict with school or parents' work, which will now be assessed longitudinally.

KEYWORDS: Practice Parameters, Education

EPILESPY

38. Cannabidiol Use in Children with Epilepsy: Time to Treatment Failure

Harowitz J (Philadelphia, PA), Catenaccio E, Mohanty S, Kessler SK

OBJECTIVE: Pragmatic evaluation of pharmaceutical cannabidiol (CBD) effectiveness in pediatric epilepsy.

METHODS: This post-marketing single-center retrospective cohort study of patients <18 years prescribed pharmaceutical CBD between 2018 and 2021 used survival analysis methods. Treatment failure was defined as CBD discontinuation or initiation/uptitration of another therapy. Other factors' effects on time to treatment failure were assessed using Cox proportional hazards models.

RESULTS: The analysis cohort included 149 patients (52% female). Median follow-up time was 27 months. Sixty-four patients had Lennox-Gastaut syndrome (LGS); 13 had Dravet syndrome (DS). For all patients, probability of treatment failure was 68% by 12 months and 87% by 24 months. Median time to failure was 8 months. When comparing patients on concurrent clobazam vs those not, there was no significant difference in time to failure (9 vs 7 months, p=0.16). A similar observation was noted for concurrent valproate (9 vs 8 months, p=0.76). Treatment persistence was longer in LGS patients (12 months) than DS patients (4 months) and all others (7 months) (p=0.01). Persistence was also longer in patients with "drop seizures" (tonic, atonic, tonic-clonic) than those without these seizures (11 vs 7 months, p=0.02). In patients discontinuing CBD (n=56), the reason cited was more often lack of efficacy (55%) than lack of tolerability (11%), or both (24%).

CONCLUSIONS: An estimated 32% of children with epilepsy treated with pharmaceutical CBD will continue to take the medication for a year or more without additional therapy. CBD is more often discontinued for lack of efficacy than lack of tolerability.

KEYWORDS: Epilepsy

39. Changes in the occurrence and causative virus type in benign convulsions with mild gastroenteritis during COVID-19: a single center study

Kim YO (Gwangju, South Korea), Na H

OBJECTIVE: Benign convulsions with mild gastroenteritis (CwG) is prevalent in East Asian countries during the winter. Rotavirus was the most common causative pathogen of CwG before rotaviral vaccine introduction; however, norovirus is now the most common causative pathogen. As coronavirus disease 2019 (COVID-19) affects the incidence of neurologic diseases, we investigated its effects on CwG.

METHODS: The medical records of 41 patients with CwG (3-36 months) admitted to the Chonnam National University Children's Hospital between March 2017 and February 2023 were reviewed retrospectively. The incidence and viral type were compared between period I (March 2017-February 2020) and period II (March 2020-February 2023).

RESULTS: There were 18 and 23 patients in the period I and II groups, respectively. A stool virus panel was tested in 97.6% of cases. Viruses in stools were isolated in 92.5% of cases: 88.2% in period I (N=15) and 95.7% in period II (N=22). Norovirus type 2 was the most commonly isolated pathogen and was present in 60.0% of all cases, 58.8% in period I (N=10) and 60.9% in period II (N=14). Adenovirus was the second most common, present in 20% of all cases, 5.9% in period I (N=1) and 30.4% in period II (N=7). Sapovirus (N=3) and rotavirus (N=2) were also observed. CwG even occurred during the summer and autumn in period II (43.5%), whereas it occurred sparsely in period I (11.1%).

CONCLUSIONS: After COVID-19, the incidence of CwG did not decrease and even occurred in the summer and autumn. In addition, adenoviral CwG increased.

KEYWORDS: Epilepsy, Neuroinfectious Disease, Global Neurology

40. Folic acid recommendation rates for adolescents with epilepsy at two Level IV Pediatric Epilepsy Centers and possible barriers to following AAN/CNS Guidelines

Railean A (Lewisville, NC), Singh S, Ciobanu M, Popli G

OBJECTIVE: Despite the recommendation for all FWE (females with epilepsy) on ASMs (anti- seizure medications) from puberty to menopause to be prescribed folic acid, there remains a paucity to this practice.

The first aim was to determine the rate at which pediatric neurologists recommend folic acid. The second aim was to identify barriers to counseling about folic acid via provider survey.

METHODS: We reviewed the charts of 340 FWE ages 12-18 years diagnosed with epilepsy based on ICD10 code, prescribed at least one ASM, and had at least 2? visits at the

outpatient neurology clinic over 5 years: January 1, 2017-December 31, 2022. Additionally, a survey of 12 questions via RedCap was administered to 21 providers located at both locations.

RESULTS: Initial query was done by using I2B2 analysis tool for patient identification through Epic database for the two centers. Of 776 patients, 37 (4.7 %) had an active folic acid prescription. A subsequent manual retrospective chart review found a discussion about folic acid supplementation in 38 of visits (11.2%).

19 out of 21 respondents completed the survey. Only 3/19 (14.3%) felt very comfortable in discussing birth defects/ teratogenicity related to ASMs; 14/29 (66.7%) reported that they never, seldom or sometimes will recommend folic acid. The main barrier to this practice was limited time in clinic.

CONCLUSIONS: Prescribers' level of comfort and time constraints are the biggest barriers to recommending folic acid for adolescent FWE, resulting in a majority of these patients not being adequately counseled. Our results likely represent a national trend.

KEYWORDS: Epilepsy

41. Preferences and Experiences of Parents/Guardians of Adolescents and Young Adults with Epilepsy and Intellectual Disability on Sexual and Reproductive Health Care Counseling

Vasudevan G (Pittsburgh, PA), Filipink R, Gaesser J, Kazmerski T, Sogawa Y, Kirkpatrick L

OBJECTIVE: To explore the experiences and preferences of parents/guardians of adolescents and young adults (AYA) of childbearing potential with co-occurring epilepsy and intellectual disability (ID) regarding counseling by neurologists on sexual and reproductive health (SRH) topics such as pregnancy, contraception, menstruation, and folic acid supplementation.

METHODS: We conducted semi-structured interviews with parents/guardians of female AYAs (12-28 years old) with co-occurring epilepsy and ID, recruited from a tertiary-care children's hospital. We confirmed the diagnoses of epilepsy and ID with the patient's neurologist and parent/guardian. All degrees of ID (e.g. mild/moderate/severe) were eligible. We audio-recorded and transcribed interviews. Two coders performed qualitative thematic analysis.

RESULTS: Twenty-five parents/guardians completed interviews. Themes included: 1) heterogenous opinions surrounding the desired extent and perceived relevance of SRH counseling; a common opinion was to perceive counseling on menstruation as more relevant than pregnancy 2) Parents/guardians want neurologists to initiate annual comprehensive SRH counseling at puberty but report they often initiate SRH discussions themselves 4) parents/guardians believe their child to be immune from sexual abuse due to supervision, yet desire counseling about abuse recognition/prevention, which they report not occurring 5) parents/guardians reported a lack of counseling on folic acid, teratogenesis, and antiseizure medication/contraceptive interactions.

CONCLUSIONS: Parents/guardians of AYAs with epilepsy and ID want more frequent, neurologist-initiated, comprehensive conversations surrounding SRH particularly emphasizing menstruation and sexual abuse recognition/prevention. Findings may inform professional and patient education, and health systems interventions including development of discussion guides and/or decision aides to improve SRH care for AYAs with epilepsy and ID.

KEYWORDS: Epilepsy

42. Examining Behavioral Health Needs of Parents of Children with Epilepsy

Gemmell M (Atlantic Beach, FL), Sahai A, Shapiro J, Lin N, Thio L L

OBJECTIVE: To investigate the prevalence of behavioral health needs among parents of children with epilepsy (PCE) whose children are admitted to the Epilepsy Monitoring Unit (EMU) at a quaternary care children's hospital.

METHODS: A behavioral health therapist evaluated 247 PCE. Of these, 180 agreed to be screened with standardized behavioral health assessments, including the Patient Health Questionnaire (PHQ-9), General Anxiety Disorder-7 (GAD-7), and Edinburgh Postnatal Depression Scale (EPDS). Follow-up/therapy referrals were made for those with scores over threshold values of 6+ on the GAD-7/ PHQ-9 and scores of 12+ on the EPDS.

RESULTS: A total of 180 parents participated in the study, of whom 98% were female, 71% identified as white, 15% identified as black, 98% were non-Hispanic or Latino, and 56% had completed a 4-year college degree or higher.

Among the PCE screened, 46% scored above the threshold for behavioral health service referrals on at least one of the screening forms. Specifically, 28% scored above the threshold on the EPDS, 59% scored above the threshold on the GAD-7, and 58% scored above the threshold on the PHQ-9. The mean scores were 9.0 (SD=5.6, IQR: 5-13) for the EPDS, 7.8 (SD=6.7, IQR: 2-13) for the PHQ-9, and 5.7 (SD=5.3, IQR: 1-9) for the GAD-7.

CONCLUSIONS: A significant proportion of PCE whose children were admitted to the EMU exceeded the threshold for behavioral health service referrals. The high prevalence of mental health concerns among this population highlights the need for increased support and resources to address the mental health needs of PCE.

KEYWORDS: Epilepsy, Behavioral Neurology, Education

43. AAI-SAP Study in developing countries. (Awareness, Availability, and Implementation of a Seizure Action Plan).

Khalid W (Durham, NC), Hwang J, Dubey S, Alvi J, Sabah N, Zafar M, Sulttan H, Chand P, Morris L, Sultan T, Iqbal M

OBJECTIVE: Awareness, availability, and implementation (AAI) of seizure action plans (SAP) in low-or-middle income countries lack consensus. The study measures changes in AAI before and after the introduction of SAP in Pakistan.

METHODS: We conducted an interventional pilot study in eight schools in Pakistan. SAP was translated, distributed and explained to teachers and school staff members. A dichotomous survey was designed to measure AAI parameters before

and after (8-week follow-up) the introduction of SAP. A descriptive analysis was conducted of the pre-intervention survey findings.

RESULTS: Among 41 participants, 85.4% were teachers (n=35). 65.90% (n=27) of participants were unaware of SAP, and 78% reported SAP unavailability at their schools (n=32). 78% (n= 32) were unaware of SAP components. Lack of awareness (73.2%; n=30), understanding (61%; n=25), availability of electronics at schools (41.5% n=17), funding to print (41.5%; n=17), and lack of health care providers to provide SAP to patients (68.3% n=28) were the major factors for limited SAP access. Only 14.6% of the participants knew how to administer first aid (n=6) and emergency medicine (n=6) for seizure events. 85.5% of participants agreed that SAP should be available at schools (n= 35). Among 8 schools, only 4 teachers from two private schools reported implementing SAP.

CONCLUSIONS: This study highlights the importance of providing school staff with SAPs to ensure child safety during seizure-type events. We hope to use the findings of the current study when creating programs to promote AAI of SAP in Pakistan and other South-Asian countries.

KEYWORDS: Epilepsy

44. Predicting Repeat Inpatient Visits in Persons with Epilepsy using Machine Learning

Baker M (Salt Lake City, UT), Cuma M, Sant D, Hernandez E, Bonkowsky J

OBJECTIVE: Over 3 million people in the United States have epilepsy, and these individuals are frequent visitors to the ER/ICU due to breakthrough seizures. The purpose of this study was to identify factors leading to repeated inpatient epilepsy-related visits on the patient level.

METHODS: We conducted a retrospective study using the publicly available MIMIC IV v2 database. Variables in this dataset include age, gender, type of insurance, race, diagnoses, procedures, and medications. Our outcome was frequency of visits per year which was divided into 3 categories (<1 visit per year, 1-2 visits per year, and >2 visits per year). Except for frequency of visits, only data that was available before a patient's initial epilepsy diagnosis was included for analysis. The top 10 variables were selected based on Shapley analysis, and we used four machine learning algorithms (logistic regression, xgboost, random forest, and support vector machine (SVM) to generate 4 new models for prediction. The models were evaluated based on their F1 score.

RESULTS: After variable encoding, our dataset included 1380 patients with 774 variables. After using this set of variables to perform feature selection we built our models. The F1 score for the models were 0.64 for logistic regression, 0.72 for random forest, 0.76 for xgboost, and 0.80 for SVM, respectively.

CONCLUSIONS: We found that for patients with <1 visits/year, that "Consultation, evaluation, and preventative care", "Essential Hypertension" had a significant role in prediction. For patients with >2 visits/year, the largest impact was from being male.

KEYWORDS: Epilepsy, Lifespan Manifestations of Childhood Onset Conditions, Early Stage Investigator

45. Risk of ADHD in Children with Childhood Absence Epilepsy versus Controls: A Population-Based Study

Jones B (Rochester, MN), Nickels K, Fine A, Wong-Kisiel L, Wirrell E

OBJECTIVE: Children with childhood absence epilepsy (CAE) are deemed higher risk of ADHD, however magnitude of risk has not been assessed in a population-based study. Our goal was to address this utilizing the new-onset epilepsy in children database, from the Rochester Epidemiology project which identified all children with a diagnosis of newly-diagnosed CAE between 1980-2018.

METHODS: For each case, four age- and gender-matched controls without CAE were identified. Records of cases and controls screening positive for ADHD were reviewed for confirmation. Those with ADHD and CAE were further assessed to determine if ADHD diagnosis preceded or followed the epilepsy diagnosis and the impact of ADHD treatment on seizure exacerbation.

RESULTS: Forty-two cases of CAE were identified and matched to 168 controls. Co-morbid ADHD was significantly more common in children with a history of CAE (17/42, 40.5%) than controls (12/168, 7.1%) ($p<0.001$). There was no difference in the proportion of cases or controls who were treated with ADHD therapy (16/17 vs 11/12, respectively, $p = 0.80$). Of those with CAE, the diagnosis of ADHD followed that of epilepsy in 87% of cases. Of the 16 treated CAE cases, no child stopped stimulant therapy due to seizure exacerbation. There was no significant difference in the proportion showing excellent response to first ADHD treatment (8/16 cases versus 3/11 controls, $p=0.24$).

CONCLUSIONS: In our population-based study, we found ADHD to be 5.7 fold more common in CAE than controls. Treatment with stimulants is highly effective in the majority of cases and is not associated with worsening of seizures.

KEYWORDS: Epilepsy

46. Pre-Existing Vagal Nerve Stimulation and Post-Operative Stridor: A Pediatric Case Report

Sheppard C (Edmonton, AB, Canada), Liu N

OBJECTIVE: Vagal nerve stimulation (VNS) is a method of neuromodulation used in drug-refractory epilepsy (DRE), with potential side effects including cough and voice hoarseness due to anterograde activation along the recurrent laryngeal nerve. While one case with pre-existing VNS post-operative stridor with right sided vocal cord paralysis associated with anterior cervical surgery has been described in an adult patient, there are no prior case reports of right sided vocal cord paralysis in pediatric patients with VNS following intubation.

METHODS: We describe a single case of a 17-year-old boy with DRE due to a 1q22 microdeletion, with implantation of VNS in July 2021. Following months of titration of VNS settings, in combination with multiple medications and ketogenic diet, he attained a period of 9 months of seizure

freedom. Prior to February 2023, he had no significant complications with his VNS.
RESULTS: In February 2023, the patient underwent surgery for a Mitrofanoff and appendicostomy. His postoperative course was complicated by stridor and oxygen desaturations with intermittent exacerbations coincidental with intermittent VNS activation. Laryngoscopy revealed new complete right-sided vocal cord paralysis, with a previous laryngoscopy revealing normal vocal cords bilaterally.
CONCLUSIONS: We describe a novel pediatric case with pre-existing VNS and post-intubation respiratory complications. Our case illustrates that intubation in patients with a pre-existing VNS may confer an increased risk of vocal cord paresis. While further research is required, pre-surgical planning for patients with VNS in situ should consider the potential for increased risk of vocal cord injury with intubation.
KEYWORDS: Epilepsy, Neurodevelopmental Disorders, Neurogenetics

47. Real-World Experience of Treating Patients Aged <12 Years with Perampanel

Ngo L (Nutley, NJ) Garcia-Ron A, Chez M, Auvin S, Wu T, D'Souza W, Samad O, Villanueva V

OBJECTIVE: To assess the effectiveness and safety/tolerability of perampanel (PER) when used in pediatric patients in everyday clinical practice.
METHODS: Patient data from patients aged <12 years included in PERMIT, a pooled analysis of 44 PER clinical practice studies, and PROVE, a Phase IV study of PER when used during routine clinical care were pooled (PERMIT Extension). Retention was assessed after 3, 6 and 12 months. Effectiveness was assessed by seizure type (focal, generalized) at the last visit (last observation carried forward). Effectiveness assessments included responder rates (≥50% seizure frequency reduction) and seizure freedom rates (no seizures since at least the prior visit). Adverse events (AEs) were also evaluated.
RESULTS: Overall, 297 patients aged <12 years were included (50.0% male; mean age, 7.7 years; mean epilepsy duration, 5.3 years). Baseline seizure types were focal only (60.6%), generalized only (32.6%) and both focal and generalized (6.8%). At 3, 6 and 12 months, retention rates were 80.4%, 69.1% and 52.4%, respectively. At last visit, responder and seizure freedom rates were, respectively, 52.2% and 32.6% for focal seizures, and 50.0% and 17.9% for generalized seizures. AEs were reported for 34.9% of patients (most commonly: aggression [4.9%], behavioral disorders [3.5%], irritability [3.5%]). Discontinuation rate due to AEs was 15.0%. Psychiatric AEs were reported for 20.1% of patients; 10.6% of those with psychiatric AEs discontinued.
CONCLUSIONS: PER was effective and generally well tolerated when used to treat patients aged <12 years with focal and generalized seizures in everyday clinical practice.
Supported by Eisai
KEYWORDS: Epilepsy

48. Are Other Options Absent?: Vagus Nerve Stimulation in the Treatment of Drug-Resistant Absence Epilepsy

Wessel C (Louisville, KY)

OBJECTIVE: Drug-resistant absence epilepsy (DRAE) occurs in about 20-30% of patients and has been associated with poor clinical and psychosocial outcomes. We investigated the therapeutic efficacy of vagus nerve stimulator (VNS) in treating DRAE.
METHODS: Patients were identified by a retrospective review of the Norton Children's Hospital VNS surgery database between 2010 and 2022. All pediatric patients diagnosed with absence epilepsy based on clinical features and electroencephalography findings with a normal brain MRI were eligibl:e for inclusion. The primary outcome measure was seizure frequency after VNS implant compared to baseline.
RESULTS: Thirty-two patients (M/F:18/14) were identified, with an average age of seizure onset of 6.1 years (SD: +3.8). Patients had an average of 6.3 seizure days (+1.6) per week, and there was no significant difference (p=0.86) in seizure frequency between males and females. Patients failed an average of 5 anti-seizure medications (+2) prior to VNS implant, and the average time from first seizure onset to VNS implant was 5.9 years (+3.5). The average duration from VNS implant to the most recent follow up appointment was 5.6 years (+4.4), with patients reporting an average of 2.6 seizure days (+2.8) per week. On average patients reported a 57+47% (p=0.069x10-7) decrease in weekly absence seizure frequency after VNS, with 72% of patients reporting a greater than or equal to 50% reduction in seizure frequency regardless of implant age (p=0.78) or time from seizure onset to VNS implant (p=0.93).
CONCLUSIONS: VNS may be an effective adjunctive therapy in treating DRAE independent of VNS implant age and seizure onset.
KEYWORDS: Epilepsy

49. Use of Acetazolamide for Electrical Status Epilepticus during Slow-wave Sleep

Khan M (St. Louis, MO), Kaulas H, Fenton G

OBJECTIVE: We report the use of Acetazolamide (AZM) in a cohort of children with the EEG pattern of electrical status epileptics in slow-wave sleep (ESES).
METHODS: We assembled a cohort of patients with an EEG pattern of ESES who were treated with AZM between January 2015 and October 2022 at an academic children's hospital. A retrospective chart review was done to retrieve data pertinent to demographics, dose, duration of treatment, efficacy and side effects of AZM.
RESULTS: We reviewed a total of ten patients with ESES. Eight patients were prescribed AZM as a second-line medication for ESES, first being a benzodiazepine - diazepam or clobazam. Out of whom, six patients tolerated the medication well, while two discontinued due to side effects namely acidosis and encephalopathy. AZM was effective in four of the six patients (66%). All four patients not only showed cognitive and behavioral improvement, significant improvement

on EEG was also noted. Spike-wave index (SWI) improved by > 50% in these patients.
CONCLUSIONS: The literature is limited on AZM use for ESES. We note that AZM has shown efficacy (66%) comparable to BZDs (60% in other studies), both clinically and electrographically. Since, it is better tolerated we support the consideration of an AZM trial as a second-line medication in patients who have failed or did not tolerate BZDs, prior to initiation of steroids.
KEYWORDS: Epilepsy

50. Lasting Electrographic Footprint of Familial Hemiplegic Migraine

Khan M (St. Louis, MO), Morris C, Goretzke S

OBJECTIVE: We describe a case of familial hemiplegic migraine whose EEG showed uni-hemispheric slowing during the episode and weeks following it.
METHODS: N/A
RESULTS: A twelve-year-old, previously healthy, right-handed girl presented to the
emergency department with sudden onset right arm weakness, aphasia and
confusion. Altered mentation, expressive aphasia and right hemiparesis were
noted.She underwent emergent MRI brain for concerns of acute stroke, which ruled out the same. Continuous EEG monitoring showed marked left hemispheric slowing but no focal seizures. For suspicion of complex hemiplegic migraine, she received a combination of ketorolac, diphenhydramine and prochlorperazine. This led to resolution of weakness and aphasia, along with return to baseline mentation. However, left hemispheric slowing persisted on EEG even at the time of discharge. Two weeks later, a repeat routine EEG showed continued slowing in the left occipital region, while patient clinically continued to function at baseline and had not had any further episodes. Four weeks after the original event, EEG returned to symmetric brain activity with no other abnormalities. Subsequently, family shared that patient's mother and maternal aunt experience symptoms consistent with hem legic migraines, but had never been formally diagnosed. With this crucial information, we proceeded with genetic testing which revealed a mutation in the ATP1A2 gene, establishing the diagnosis as Familial Hemiplegic Migraine (FHM).
CONCLUSIONS: With limited literature on EEG abnormalities seen in pediatric migraines, specifically familial hemiplegic migraines, our case is the first report of EEG changes persisting for weeks beyond the resolution of symptoms from an acute episode.
KEYWORDS: Epilepsy, Headache

51. Vigabatrin in a neonate with GABRB3 gain-of-function mutation.

Sun F (Indianapolis, IN), Wing S

OBJECTIVE: Variants in the GABRB3 gene encoding for a GABA-A receptor Beta-3 subunit are known to cause various developmental and epileptic encephalopathies (DEE). There are two types of GABRB3 disease-causing variants: variants that cause the loss-of-function (LOF) of the gene, and variants that cause a gain-of-function (GOF) of the gene. Typically, the GOF variants produce more severe presentations, with profound intellectual disability and intractable epilepsy that begins within the first few months of life. No effective therapeutic regimen has been found. We herein share the clinical course of one neonate who was found to have a gain-of-function GABRB3 mutation and intractable epilepsy.
METHODS: Whole Genome Sequencing revealed a heterozygous, likely pathogenic, de novo, c.841 A>G (Thr281Ala) GABRB3 mutation that causes a GOF of the GABA-A receptor Beta-3 subunit. Using reports of other cases, many antiepileptic drugs were trialed, including Vigabatrin, which in GOF variants, has been found to cause a hypersensitive reaction to alleviate seizures with lower concentrations of GABA, though has also caused severe adverse side effects.
RESULTS: Of the many antiepileptic drugs tried, many were ineffective at best; Vigabatrin began to show most improvement at 30mg/kg/day. However, this patient passed before further titration could be completed.
CONCLUSIONS: We share this case and its clinical course in hopes that others who have similar GOF-GABRB3-related DEE may try Vigabatrin sooner as it was showing the most improvement of all of the anti-seizure medications trialed for this neonate.
KEYWORDS: Epilepsy, Neurogenetics

52. Medical and environmental factors associated with perceived quality of life in adolescents with epilepsy

Yiu A (Orange, CA), Arellano J, Cohen A, Arshad A, Phillips D, Sayrs L, Shrey D

OBJECTIVE: In adolescents with epilepsy, factors such as number of medications and adequate seizure control affect their perceived quality of life. What is unknown is whether societal and environmental conditions are contributing factors. The purpose of this study was to understand the possible interplay between environmental conditions and epilepsy characteristics with perceived quality of life in adolescents with epilepsy.
METHODS: This retrospective study analyzed data using bivariate analysis using Spearman's rho for 526 adolescent epileptic patients from the ages of 11 to 18 years. Multiple measurements of epilepsy severity were extracted from the medical record. Health-related quality of life was determined through the self-reported Pediatric Quality of Life Inventory - Epilepsy (PedsQL-E) Module 3.0 under 5 separate dimensions. The Child Opportunity Index (COI) was utilized to assess the possible impact of environmental and neighborhood conditions.
RESULTS: Older children were associated with higher perceived quality of life on the PedsQL-E cognitive function dimension. Children with a greater number of seizure medications and higher number of neurological diagnoses was modestly associated with lower perceived quality of life in PedsQL-E scoring on the impact, cognitive function, and executive function dimensions. Higher COI was weakly associated with higher perceived quality of life on the PedsQL-E impact and cognitive function dimensions.

CONCLUSIONS: The perceived quality of life in adolescents with epilepsy is impacted by both medical, environmental, and socioeconomic factors. Understanding the role of environmental, neighborhood, and socioeconomic factors affecting one's community may lead to strategies to improve their perceived quality of life.
KEYWORDS: Epilepsy, Diversity, Equity, Inclusion

53. Long-term Safety and Efficacy of Add-on Cannabidiol (CBD) for Seizures Associated With Tuberous Sclerosis Complex (TSC): 3-Year Results From GWPCARE6 Open-Label Extension (OLE)

Thiele E (Boston, MA), Bebin E, Filloux F, Jansen F, Kwan P, Loftus R, Sahebkar F, Sparagana S, Lawson J, Wheless J

OBJECTIVE: To report safety (for the full follow-up) and efficacy (through 156 weeks) of CBD in patients with TSC treated in an OLE (NCT02544750).
METHODS: Patients completing GWPCARE6 RCT enrolled to receive CBD (Epidiolex®; 100 mg/mL) starting at 25 mg/kg/d with titration up to maximum 50 mg/kg/d. Primary endpoint: safety. Secondary endpoints: percentage change in TSC-associated (countable focal and generalized) seizures, responder rates, and Subject/Caregiver Global Impression of Change (S/CGIC).
RESULTS: Of 201 RCT completers, 199 (99%) entered OLE. At baseline, median age was 10.7 years and number of ASMs was 3. Most common concomitant ASMs: valproate (43%), vigabatrin (37%), and clobazam (35%). Baseline median (Q1, Q3) monthly TSC-associated seizure frequency: 57 (28, 109). Thirty-four patients (17%) completed treatment; most common reason for withdrawal was transition to commercial product (93 [56%]). Median (range) treatment time: 631 days (18–1462). AE incidence: 96% of patients, serious AE incidence: 28%; discontinuation because of an AE: 9%. Most common AEs: diarrhea (47%) and seizures (30%). Overall, 7% of patients had elevation in ALT levels and 5% in AST levels. There was 1 death due to cardiopulmonary failure, deemed not treatment related. Median percentage reduction in TSC-associated seizures was 53%–90% and seizure responder rates (≥50%, ≥75%, and 100%) was 52%–78%, 29%–69%, and 6%–31% across 12-week windows. Improvements on S/CGIC were reported by 89% and 93% of subjects/caregivers at 52 and 104 weeks.
CONCLUSIONS: Add-on CBD was well tolerated and continued to reduce TSC-associated seizures for up to 156 weeks in patients treated in OLE.
Study funded by Jazz Pharmaceuticals.
KEYWORDS: Epilepsy

54. Focal occipital epilepsy due to SCN1B pathogenic variant. A case report expanding the GEFS+ spectrum associated with SCN1B mutations.

Litten R (Memphis, TN), Ghosh A, Chourasia N

OBJECTIVE: SCN1B associated genetic disorder includes phenotypic spectrum of generalized epilepsy with febrile seizures plus (GEFS+) and developmental and epileptic encephalopathies. Focal seizures described independently and in patients with GEFS+ phenotype include temporal lobe (TLE) or frontal lobe epilepsy. Focal occipital epilepsy (Panayiotopoulos syndrome or self-limited epilepsy with autonomic features), however, has not been described previously. We expand the spectrum of seizure types associated with SCN1B genetic change in a six-year-old boy with febrile convulsive seizures and focal occipital epilepsy.
METHODS: We retrospectively evaluated the clinical, video electroencephalogram (EEG), brain magnetic resonance imaging (MRI) in a 6-year-old boy with febrile and afebrile seizures in the setting of pathogenic SCN1B genetic change.
RESULTS: Our index case is a six-year-old boy with normal development and attention deficit hyperactivity disorder with onset of febrile convulsive seizures at 2 years. He subsequently developed afebrile seizures at 4 years of age with prolonged focal autonomic symptoms including emesis, malaise and pallor with lack of awareness. EEG showed independent left and right bi-phasic/triphasic occipital spikes with fixation off sensitivity. Brain MRI was normal. He responded well to oxcarbazepine monotherapy with occasional focal seizures, although he continues to have yearly febrile convulsions in the setting of illness. A proband only epilepsy gene panel revealed heterozygous pathogenic SCN1B [c.363C>G (p.Cys121Trp)] genetic change which has been previously described in association with febrile seizures(FS) alone, FS+, GEFS+ and TLE.
CONCLUSIONS: Our report illustrates that SCN1B pathogenic genetic variant can present with focal occipital epilepsy in combination with febrile seizures.
KEYWORDS: Epilepsy, Neurogenetics

55. Reducing underdosing of rectal diazepam as home seizure rescue medication after hospitalization

Silver M (Philadelphia, PA), Means M, Abend N, Caffeé L, Fried L, Gonzalez A, Kaufman M, Ramos M, Zook J, Press C, Molisani S

OBJECTIVE: Seizure rescue medications are commonly prescribed to children with epilepsy and are dosed in a weight-dependent manner. Ensuring that medications are not underdosed is important to terminate seizures. We aim to reduce the rate of underdosed rectal diazepam prescriptions for children discharged from the inpatient neurology service at our institution from 6% to 3% by July 2023.
METHODS: This quality improvement project was completed using our institution's Improvement Framework. Prescription data from the electronic health records (EHR) were used to generate a dashboard and a statistical process control (SPC) p-chart for our primary outcome measure, monthly percentage of underdosed rectal diazepam prescriptions for patients discharged from the inpatient neurology service. Interventions aimed at the identified root causes were implemented via iterative plan-do-study-act cycles.
RESULTS: Between July 2020 and January 2023, rectal diazepam was prescribed 343 times to patients admitted to neurology, with a monthly average of 11 prescriptions. During this period, rectal diazepam was underdosed for 6% of patients. Root cause analysis revealed contributing factors to underdosing included lack of provider familiarity with age

and weight-based dosing and lack of an easily accessible orderset in the EHR. As our primary intervention, we have created an EHR orderset to facilitate accurate prescribing.
CONCLUSIONS: The baseline rate of rectal diazepam underdosing at our institution is 6%. We have developed an EHR orderset to facilitate accurate prescribing, and we are now beginning assessment. If this approach is effective, then it may be feasible for spread to outpatient and ED settings.
KEYWORDS: Epilepsy

56. The clinical utility of finding unexpected subclinical spikes detected by high-density EEG during neurodiagnostic investigations

March M (Chandler, AZ), Bar O, Chadehumbe M, Catterall K, Mintz M

OBJECTIVE: This study aimed to analyze the frequency of unexpected subclinical spikes (USCS) in pediatric patients who underwent high-density electroencephalogram (HD-EEG).
METHODS: Patients were included in the study if they were less than 21 years old and had at least one successful resting HD-EEG at our institution between January 2010 and December 2020. We classified HD-EEG reports as normal, abnormal, SCS or USCS according to a schema based on factors such as the impression in the report, prior epilepsy diagnosis or history of seizure-like events, and the presence or absence of spike and slow waves or electroclinical correlates.
RESULTS: Of the 4481 successful HD-EEG studies, 18.5% (829) were abnormal, and 49.7% of these abnormal studies showed SCS, of which 64.1% were USCS. USCS were found to be correlated with attention/concentration deficits and executive dysfunction, often accompanied by the dual psychiatric diagnosis of ADHD. MRI revealed abnormal findings in 32.6% of the subjects with USCS, such as abnormal signal or signal hyperintensity in brain parenchyma, temporal or arachnoid cysts, and vascular malformations. Moreover, the USCS group who received neuropsychiatric testing scored lower than the population mean on several metrics, including Full Scale Intelligence Quotient. There were also three notable examples where the finding of USCS prompted further neurodiagnostic testing and/or therapeutic interventions that caused a major change in clinical management and improved clinical outcomes.
CONCLUSIONS: This study highlights the potential of USCS as biomarkers that can lead to changes in clinical management and outcomes, provide valuable information about pathophysiological mechanisms, and suggest potential treatment pathways.
KEYWORDS: Epilepsy, Behavioral Neurology, Neuroimaging

57. Seizure Outcomes With Cannabidiol (CBD) in Pediatric Versus Adult Patients With Lennox-Gastaut Syndrome (LGS) and Dravet Syndrome (DS): Subgroup Analysis of BECOME, a Caregiver Survey

Saurer T (Carlsbad, CA), Berg A, Dixon-Salazar T, Meskis M, Danese S, Le N, Perry M

OBJECTIVE: To evaluate seizure-related outcomes in pediatric (<18 years) versus adult (≥18 years) patients from the cross-sectional caregiver survey BECOME (BEhavior, COgnition, and More with Epidiolex®).
METHODS: The US-based caregivers (N=498) of patients with LGS (80%) or DS (20%) who received ≥3 months of CBD treatment (Epidiolex®, 100 mg/mL oral solution) compared the past month with the period before CBD initiation.
RESULTS: Mean (standard deviation) patient age: 16 (11) years; median (IQR) CBD dose: 14 mg/kg/d (8–19 mg/kg/d); median concomitant ASMs: 4. Most caregivers of pediatric (n=315) and adult (n=183) patients reported any improvement in seizure frequency (84% each) and severity (77% and 75%). Worsening in seizure frequency was reported by 7% and 5% of caregivers of pediatric and adult patients, respectively; 10% and 6% reported any worsening in seizure severity. Caregivers of pediatric and adult patients reported any decrease in the frequency of specific seizure type as follows: convulsive (72% each), drop (71% each), nonconvulsive/nondrop (66% and 69%), and night-time seizures (61% and 63%). Similar proportions of caregivers of pediatric and adult patients reported improvements in seizure-free days/week for ≥1 seizure type (65% and 70%) and seizure freedom in the past month (18% and 15%). Many respondents in both groups reported reductions in rescue medication use (57% each), emergency room visits (56% and 51%), hospitalizations (55% and 50%), and occurrence of seizure-related injuries (48% and 49%).
CONCLUSIONS: A substantial proportion of caregivers of patients with LGS or DS, regardless of age, reported improvements in seizure-related outcomes with CBD treatment.
Funding by Jazz Pharmaceuticals.
KEYWORDS: Epilepsy

58. Nonseizure Outcomes With Cannabidiol (CBD) in Pediatric Versus Adult Patients With Lennox-Gastaut Syndrome (LGS) and Dravet Syndrome (DS): Subgroup Analysis of BECOME, a Caregiver Survey

Dixon-Salazar T (San Diego, CA), Berg A, Meskis M, Danese S, Saurer T, Le N, Perry M

OBJECTIVE: To evaluate nonseizure behavioral and cognitive outcomes in pediatric (<18 years) vs adult (≥18 years) patients from the cross-sectional caregiver survey BECOME (BEhavior, COgnition, and More with Epidiolex®).
METHODS: US-based caregivers (N=498) of patients with LGS (80%) or DS (20%) who received ≥3 months of CBD treatment (Epidiolex®, 100 mg/mL oral solution) compared the past month with the period before CBD initiation.
RESULTS: Mean (standard deviation) age of patients: 16 (11) years; median (IQR) CBD dose: 14 mg/kg/d (8–19 mg/kg/d); median concomitant ASMs: 4. A similar proportion of caregivers of pediatric (n=315) and adult (n=183) patients reported any improvement in ≥1 question of the following domains: alertness, cognition, and executive function (87% and 81%) and emotional and social function (82% and 80%). A numerically greater proportion of caregivers of pediatric versus adult patients reported any improvement in ≥1 question of the language and communication (verbal patients: 81% vs 63%; nonverbal patients: 85% vs 68%),

physical functioning (53% vs 33%), sleep (53% vs 48%), and daily activities (56% vs 44%) domains. Rates of worsening varied by behavior and ranged from 0% to 20% of respondents. In pediatric patients, the most common improvements were in the ability to learn new things (76%) and in nonverbal patients, looking up or smiling at mention of their name (76%). For adult patients, the most common improvement was in alertness (70%).

CONCLUSIONS: A substantial proportion of caregivers of patients with LGS or DS, regardless of age, reported improvements in outcomes beyond seizure control since initiating CBD treatment.

KEYWORDS: Epilepsy

59. Effectiveness of Diazepam Nasal Spray Does Not Vary Across Times of Day in Pediatric Patients With Seizure Clusters

Cook D (San Diego, CA), Wheless J, Segal E, Misra S, Carrazana E, Rabinowicz A

OBJECTIVE: Diazepam nasal spray is approved for treatment of seizure clusters in patients with epilepsy age ≥6 years. Nasal administration is designed to bypass the stomach, avoiding variable drug absorption due to the fed/fasted state. The independence of fed/fasted state and diazepam effectiveness was assessed among pediatric patients.

METHODS: Data from the phase 3 safety study of diazepam nasal spray on the use of second doses within 24 hours, a proxy for effectiveness, was assessed over 12-hour and 4-hour periods. This post hoc analysis tested the hypothesis that if bioavailability were delayed due to gastric absorption, use of second doses would be elevated during the fed versus the fasted state.

RESULTS: Overall, 78 pediatric patients (aged 6–17 years) received ≥1 dose of diazepam nasal spray. Of 1634 treated seizure clusters, 186 (11.4%) were treated with a second dose, of which 70 (37.6%) were treated within 4 hours of first dosing. Of all second doses, 49.5% were given in the daytime (8AM–8PM, likely fed) and 50.5% were given at night (8PM–8AM, likely fasting). The proportion of second doses given within 4 hours of the first was lower in the daytime (44.3% vs 55.7%). Analysis by 4-hour period showed no trends with fed/fasted states.

CONCLUSIONS: No clear association was found between time of day and administration of second doses among pediatric patients. These findings reinforce that diazepam nasal spray is absorbed intranasally and bypasses the stomach, and, thus, effectiveness is not associated with the fed/fasted state.

KEYWORDS: Epilepsy

60. Efficacy and Safety of Add-on Cannabidiol (CBD) for Seizures Associated With Tuberous Sclerosis Complex (TSC) in Pediatric Patients Enrolled in a Phase 3 Trial With an Open-Label Extension (OLE)

Thiele E (Boston, MA), Lawson J, Kotulska K, Sahebkar F, Greco T, Saurer T

OBJECTIVE: CBD reduced TSC-associated seizures in the randomized controlled trial (RCT) GWPCARE6 and its OLE. This post hoc analysis evaluated efficacy and safety in pediatric (<18 years) patients of GWPCARE6.

METHODS: Patients received placebo or CBD (Epidiolex®; 100 mg/mL) 25 mg/kg/d (CBD25) or 50 mg/kg/d (CBD50) in RCT (4-week titration+12-week maintenance). In OLE, dose started at 25 mg/kg/d with maximum up to 50 mg/kg/d. TSC-associated seizure responder rates with ≥50% and ≥75% reductions from baseline were evaluated for RCT maintenance and OLE.

RESULTS: Of 224 patients in RCT, 166 (74%) were pediatric with median age, 8 years. At RCT baseline, patients were taking median 3 antiseizure medications and had median (interquartile range) 62 (29–125) TSC-associated seizures/28 days. Of 166 patients, 153 (92%) continued to OLE (median treatment duration, 680 days). During RCT, ≥50% (CBD25, 47%; CBD50, 52%; placebo, 21%) and ≥75% (CBD25, 24%; CBD50, 28%; placebo, 5%) responder rates were greater for CBD than placebo. This is consistent with (≥50% rate: CBD25, 39%; CBD50, 50%; placebo, 22% and ≥75%: CBD25, 20%; CBD50, 27%; placebo, 5%) the overall population. In OLE, ≥50% and ≥75% responder rates were 53% and 33%, respectively. AE incidence: placebo, 68% of patients; CBD25, 69%; CBD50, 71% during RCT and 97% in OLE. Diarrhea was the most common AE in RCT (placebo, 23%; CBD25, 22%; CBD50, 36%) and OLE (35%).

CONCLUSIONS: Efficacy of CBD in pediatric patients was consistent with the overall population during RCT. Response was durable and maintained throughout OLE. Safety profile was consistent with the overall population.

KEYWORDS: Epilepsy

61. Prediction Model for Electrographic Status Epilepticus in Critically Ill Children

Fung F (Philadelphia, PA), Parikh D, Jacobwitz M, Topjian A, Abend N

OBJECTIVE: High seizure burden (electrographic status epilepticus, ESE) is associated with unfavorable outcomes whereas isolated electrographic seizures (ES) are not. We aimed to develop a model to predict ESE.

METHODS: A prospective observational study of critically ill children with encephalopathy who underwent continuous EEG (CEEG). We performed univariate analyses to identify variables predictive of ESE. Variables with p-value <0.2 from the univariate analyses were entered into a multiple logistic regression model, and stepwise selection approach identified the most parsimonious model. We calculated model specificity, sensitivity, PPV, and NPV.

RESULTS: ESE occurred in 5.6% (79/1399) of subjects. The optimal model for ESE prediction yielded an AUROC of 0.81 and included four variables: (1) metal status at CEEG initiation, (2) seizures prior to CEEG, (3) EEG background category and (4) epileptiform discharges, both in the initial 30 minutes of CEEG. A 0.03 cutoff yielded sensitivity of 91% and specificity of 56%. Based on the ESE incidence of 5.6%, the PPV was11.0% and NPV was 99.1%. If the model were applied to our cohort, then 53% (744/1399) of patients would not undergo CEEG and 8% (7/79) of patients experiencing ESE would be missed.

CONCLUSIONS: Models focused on ESE identification, rather than detection of isolated ES may reduce CEEG utilization although some patients with ESE would be missed. A limitation is that most patients with seizures were treated with antiseizure medications. Additional patients may have experienced ESE if seizures were not aggressively identified and managed, potentially yielding a larger cohort with different predictors and model performance.
KEYWORDS: Epilepsy

62. Comparative effectiveness of levetiracetam and oxcarbazepine as first drug monotherapy in children with focal epilepsy

Chang G (Philadelphia, PA), Wilson J, Massey S, Piccoli C, Worden L, Kessler S

OBJECTIVE: To compare effectiveness of levetiracetam (LEV) and oxcarbazepine (OXC) as first line antiseizure medication (ASM) for children with focal epilepsy
METHODS: In this single-center, multi-site retrospective cohort study of patients 1-17 years old with newly diagnosed focal epilepsy between January 1, 2008 and June 30, 2014, we compared freedom-from-failure rates of LEV and OXC monotherapy using survival analysis. Treatment failure was defined as discontinuation of first ASM (excluding discontinuation for seizure remission) or addition of a second ASM. Factors influencing freedom-from-failure were evaluated with Cox proportional hazards models.
RESULTS: Of the 483 patients in the cohort (41% female, median age 7 years, IQR 4-11 years), first line therapy was LEV in 208 and OXC in 275. For all patients, the probability of remaining on the first ASM without additional therapy was 74% at 12 months (95% CI 70-79%), and 66% at 24 months (95% CI 61-70%). Freedom-from-failure for LEV was 68% at 12 months (95% CI 61-74%) and 58% at 24 months (95% CI 51-65%), and for OXC was 79% at 12 months (95% CI 74-83%) and 71% at 24 months (95% CI 65-76%). OXC had substantially higher freedom-from-failure than LEV (unadjusted hazard ratio 0.59, $p<0.001$), which persisted with adjustment for potential confounders including age, sex, initial presentation to emergency department, lesional etiology, and abnormal EEG (adjusted HR 0.58, $p<0.001$). Adverse effects were more often noted with LEV than with OXC (53.4% versus 41.1%, $p=0.008$).
CONCLUSIONS: OXC is more effective than LEV as initial monotherapy for new onset focal epilepsy in children.
KEYWORDS: Epilepsy

63. Early-onset Epileptic Encephalopathy and Rett Syndrome

Radhakrishna S (Bronx, NY), Polavarapu A, Duberstein S

OBJECTIVE: To describe a case of epileptic encephalopathy and hypsarrhythmia in a 16-month-old girl with R168X MECP2 mutation
METHODS: Case report
RESULTS: A 4-month-old female patient presented to an outside hospital with episodes of hand flexion, generalized shaking, and unresponsiveness concerning for seizures. Her routine EEG showed spike and slow wave discharges and she was treated with valproate. She then presented to our institution for EEG monitoring at 16 months of age. At this time, her exam and developmental history were notable for generalized hypotonia and inability to roll, babble, or make purposeful movements. She had no history of developmental regression or stereotypies. The interictal EEG demonstrated hypsarrhythmia with multifocal spikes and background slowing. Vigabatrin was started once seizures recurred. Genetic work-up showed a heterozygous R168X MECP2 mutation.
CONCLUSIONS: Rett Syndrome is a neurodevelopmental disorder caused by mutations in the gene encoding methyl-CpG binding protein-2 (MECP2). R168X is one of the most common mutations and is associated with a more severe phenotype. The typical syndrome is characterized by rapid regression of milestones, a plateau period, and possible late motor deterioration. Epilepsy is comorbid in about 60% of patients with MECP2 mutations and typically presents after 3 years of age with focal or generalized tonic-clonic seizures. While hypsarrhythmia has been described in patients with CDKL5 mutations with a Rett syndrome-like phenotype, no cases to date exist in the literature for patients with an R168X MECP2 mutation. This case provides evidence that the spectrum of pathogenic R168X MECP2 mutation can include early-onset epileptic encephalopathy and hypsarrhythmia.
KEYWORDS: Epilepsy, Neurodevelopmental Disorders, Neurogenetics

64. Utilization of Long-Term Video EEG Monitoring in Pediatric Patients: Experience of a Large Pediatric Tertiary Care Center

Sanghi A (Atlanta, GA), Lin J, Phlibrook B, Bhalla S, Al-Ramadhani R

OBJECTIVE: Long-term video EEG monitoring(LTVM) aids in identifying subclinical seizures. An ongoing struggle exists of how to balance limited resources with the demand of patients. The aim of this study is to retrospectively describe our experience of LTVM inpatient clinical utilization.
METHODS: A retrospective review was conducted over a 2 month period from August 1–September 30, 2021. Inclusion criteria included LTVM of pediatric patients ages 0–21 years. Exclusion criteria were EEG's done outpatient or in the Epilepsy Monitoring Unit. Demographic, clinical, and seizure data were reviewed.
RESULTS: There were 276 LTVM studies and 9,192 hours 44 minutes of EEG data. The mean daily total LTVM EEG data was 150 hours 42 minutes. Median duration of a study was 33 hours 18 minutes(1 hour 55 minutes to 205 hours 34 minutes). The median age of patients was 5.2 years(0 days to 20.7 years) with 33%(n=92) children 1-10 years, 30% (n=82) infants, 24%(n=66) over 10 years, and 13%(n=36) neonates. Most common indications included seizure-like activity(53%, n=145), AMS(9%, n=26), status epilepticus(8%, n=23), and breakthrough seizures(8%, n=21). Seizures were recorded on EEG in 26%(n=72). 47% (n=33) were electrographic, 40%(n=28) clinical, 10%(n=7)

both, 3%(n=2) on the ictal-interictal continuum. In a subanalysis of subclinical seizures, 10/19(52%) patients had seizures within 1 hour of LTVM initiation, 18/19(94%) within 24 hours, and 19/19(100%) within 72 hours.
CONCLUSIONS: Children 1-10 years and infants were the most common age groups. Most common indication for LTVM was seizure-like activity. Seizures were recorded 26%, which 40% were electroclinical. 94% of subclinical seizures were detected within 24 hours.
KEYWORDS: Epilepsy

65. TBC1D24 Syndromes in 10 Pediatric Cases

Mondragon E (Dallas, TX), Armstrong D, Sirsi D

OBJECTIVE: TBC1D24 regulates both oxidative stress tolerance and neurosynaptic vesicle trafficking. Pathogenic variants in this gene are associated with a clinical spectrum ranging from isolated deafness to early-onset infantile encephalopathies. Unfortunately, no consensus has been reached regarding genotype-phenotype correlations or optimal therapies. We describe TBC1D24-related cases seen in our institution's pediatric neurology department.
METHODS: Health records were reviewed across the available clinical course of 10 patients with confirmed TBC1D24 mutations, ranging from early infancy to 21 years old.
RESULTS: Delays in motor development (fine and gross) and speech are ubiquitous, and several patients are on the autism spectrum. Movement disorders occur in the majority (N=8) and improve with rest, clonazepam, trihexyphenidyl, and botulinum toxin. An overwhelming majority have epilepsy that initially presented with focal myoclonic seizures (9/10) with recurrent status epilepticus. Carbamazepine and oxcarbazepine were ineffective (4/5), but seizure burden consistently responded to benzodiazepines, cannabidiol, and to menstrual suppression in the two adolescent females in the cohort. Novel use of everolimus improved seizures and autistic features (2/2).
CONCLUSIONS: We summarize the salient clinical characteristics of 10 patients with TBC1D24-related syndromes, five of whom share the relatively undescribed c.845C>G variant. There is a high incidence of both seizures and movement disorders, with semiology corroborating prior literature. Everolimus improved seizure burden and autistic features. Such results correlate with the known pathophysiology of TBC1D24 dysfunction. Further investigation is needed into potential disease-modifying therapies, such as everolimus (given indirect associations between TBC1D24 and mTOR), and effective seizure and movement disorder therapies.
KEYWORDS: Epilepsy, Movement Disorders, Neurogenetics

66. Efficacy and Safety of Add-on Cannabidiol (CBD) for Seizures Associated With Tuberous Sclerosis Complex (TSC) in Pediatric Patients Enrolled in a Phase 3 Trial With an Open-Label Extension (OLE)

Thiele E (Boston, MA), Lawson J, Kotulska K, Sahebkar F, Greco T, Saurer T

OBJECTIVE: CBD reduced TSC-associated seizures in the randomized controlled trial (RCT) GWPCARE6 and its OLE. This post hoc analysis evaluated efficacy and safety in pediatric (<18 years) patients of GWPCARE6.
METHODS: Patients received placebo or CBD (Epidiolex®; 100 mg/mL) 25 mg/kg/d (CBD25) or 50 mg/kg/d (CBD50) in RCT (4-week titration+12-week maintenance). In OLE, dose started at 25 mg/kg/d with maximum up to 50 mg/kg/d. TSC-associated seizure responder rates with ≥50% and ≥75% reductions from baseline were evaluated for RCT maintenance and OLE.
RESULTS: Of 224 patients in RCT, 166 (74%) were pediatric with median age, 8 years. At RCT baseline, patients were taking median 3 antiseizure medications and had median (interquartile range) 62 (29–125) TSC-associated seizures/28 days. Of 166 patients, 153 (92%) continued to OLE (median treatment duration, 680 days). During RCT, ≥50% (CBD25, 47%; CBD50, 52%; placebo, 21%) and ≥75% (CBD25, 24%; CBD50, 28%; placebo, 5%) responder rates were greater for CBD than placebo. This is consistent with (≥50% rate: CBD25, 39%; CBD50, 50%; placebo, 22% and ≥75%: CBD25, 20%; CBD50, 27%; placebo, 5%) the overall population. In OLE, ≥50% and ≥75% responder rates were 53% and 33%, respectively. AE incidence: placebo, 68% of patients; CBD25, 69%; CBD50, 71% during RCT and 97% in OLE. Diarrhea was the most common AE in RCT (placebo, 23%; CBD25, 22%; CBD50, 36%) and OLE (35%).
CONCLUSIONS: Efficacy of CBD in pediatric patients was consistent with the overall population during RCT. Response was durable and maintained throughout OLE. Safety profile was consistent with the overall population.
KEYWORDS: Epilepsy

67. Proposed Diagnostic Criteria for Bilateral Rasmussen's Encephalitis

Trapp N (Madison, WI), Knox A

OBJECTIVE: Bilateral Rasmussen's encephalitis (RE) is a rare variant of a unihemispheric autoimmune encephalitis. A European Consensus Statement (Bien 2005) established diagnostic criteria for unilateral RE, but does not provide criteria for the bilateral variant. Published reports of bilateral RE vary substantially in quality of evidence supporting bihemispheric disease. We evaluate reports of bilateral RE using the Bien criteria, and propose diagnostic criteria for bilateral RE.
METHODS: Literature review identified 24 cases of bilateral RE. Cases were labeled as "Meets Criteria" if they fulfilled the following:
1. Satisfy Bien criteria for RE
2. Have epilepsy
3. Meet at least one of the following:
a. Bilateral histopathology consistent with RE
b. Disease recurrence in contralateral hemisphere following hemispherotomy
c. Bilateral T2/FLAIR hyperintensities with bilateral focal seizures
Cases in which bilateral histopathology and MRI were not obtained that otherwise met Bien criteria and were suggestive

of bilateral disease were classified as "Probable"; cases were otherwise classified as "In Doubt."
RESULTS: 23 of 24 identified cases met Bien criteria for RE. Four (17%) had bilateral histopathology, eight (35%) had bilateral T2/FLAIR hyperintensities on MRI, and seventeen (74%) had bilateral seizures. Overall, 11 of 23 cases met these criteria for bilateral RE.
CONCLUSIONS: For patients with epilepsy who satisfy the Bien diagnostic criteria for RE and have suspected bihemispheric involvement, we propose that at least one of the following is sufficient to confirm bilateral RE: (1) bilateral histopathology consistent with RE; (2) disease recurrence in contralateral hemisphere following hemispherotomy; and/or (3) bilateral T2/FLAIR hyperintensities with bilateral focal seizures.
KEYWORDS: Epilepsy, Neuroimmunology, Neuroimaging

68. Electroencephalography predictors of cerebral injury and in-hospital mortality after pediatric cardiac arrest

Smith J (Washington, DC), Keenan J, Staso K, Conley C, Harrar D, Sansevere A

OBJECTIVE: To assess associations between electroencephalography (EEG), diagnostic imaging and mortality after pediatric cardiac arrest (CA).
METHODS: This review of prospectively collected data analyzed patients in the PICU at Children's National Hospital from July 2021 to January 2023. Patients with continuous EEG after cardiac arrest greater than 5 minutes were included. EEG background features included background severity (mild abnormality/slow disorganized, moderate abnormality/discontinuous, severe abnormality/burst suppression and attenuated), epileptiform discharges (ED), periodic patterns, and electrographic seizures (ES). Descriptive statistics and odds ratios (OR) were used to describe associations of EEG background features with neuroimaging and mortality.
RESULTS: We included 48 patients with a mean age of 4.16 years (SD=6). The most common EEG background was slow/disorganized (40%), followed by attenuated/featureless (31%), burst suppression (23%), and normal (6%). The most common periodic pattern was lateralized periodic discharges (15%). Thirteen percent of patients had focal ES, 6% met criteria for myoclonic status epilepticus associated with generalized periodic discharges. Sixty percent had abnormal imaging and 97% of these had global anoxic injury. Epileptiform discharges were associated with cerebral injury OR=13 (95% CI 1.53-110.73, p=0.01). The presence of ED did not correlate with mortality OR=1.43 (95% CI 0.41-4.99, p=0.23), nor was there significance between mortality and ES OR=0.96 (95% CI 0.19-4.84, p=0.48). There was strong association between severely abnormal EEG background and mortality OR = 88 (95% CI 9.45 - 819.07, p=0.00).
CONCLUSIONS: EEG features impart significant prognostic value after pediatric CA. In the future, we hope to elucidate electrographic signatures, corroborated with imaging, that confer diagnostic prediction.
KEYWORDS: Epilepsy, Neurocritical Care, Neuroimaging

69. Yield and utility of genetic panel testing among patients with epilepsy aged 0-8

Grew E (Newark, NJ), Reddy M, Hashim A

OBJECTIVE: Epilepsy is a neurological disorder with challenging etiological diagnosis. We aim to examine the yield of genetic testing and correlate outcomes with patients' history.
METHODS: We reviewed third-party saliva genetic sequencing results analyzing 302 epilepsy-associated genes and medical records from neurology patients aged 0-8 from 7/2021-3/2023. Analysis variables were positive results (pathogenic genes or variants of uncertain significance (VUS)); total genes identified; age; sex; seizure type; development, tone/movement, dysmorphism, and seizure history scores; epilepsy family history; and abnormal EEG or MRI. Data was analyzed using SPSS v.25.
RESULTS: 47 patients with mean age 4.6 were included. 57.4% were male. 38.3% were Black/African-American, 17% Hispanic, 4.3% Asian, 14.9% identified as other, and 25.5% did not respond. 12 patients had pathogenic genes (25.5%), 26 had VUS (55.3%), and 9 tested negative (19.1%). Among positives, 2.4 genes on average were identified. 18 pathogenic genes were identified, including: ATAD1, CLN8, FOXG1, SCN1A, and TSC1/2. Positive results were unassociated with age, sex, seizure type, clinical survey scores, abnormal MRI or EEG, or family history. Number of genes inversely correlated with abnormal EEG (p=.019, [-3.408,-.327]), and was unassociated with abnormal MRI or family history.
CONCLUSIONS: We found a positive yield of 80.9%. Positivity was not associated with family history or clinical features. Mutations identified have implications for treatment (SCN1 has specific drugs approved for use); comorbidity screening (TSC1/2); reproduction (ATAD1, PSAT1, and CLN8 are recessive); and prognostication (FOXG1 is associated with autosomal dominant Rett Syndrome). In sum, epilepsy genetic testing is valuable and relevant to patient education and counseling.
KEYWORDS: Epilepsy, Neurogenetics, Neonatal Neurology

70. Variable clinical and epilepsy phenotypes within a family harboring a novel deletion in NPRL3

DeKorver N (St. Louis, MO), Thio L

OBJECTIVE: We describe the variable clinical phenotypes within a family harboring a novel deletion in NPRL3 ranging from pharmacoresponsive epilepsy to drug resistant multifocal epilepsy with epileptic spasms.
METHODS: Case Report
RESULTS: Genetic variants in sub complexes of GTPase activating protein complex that inhibits RAG-dependent activation of TORC1 (GATOR1) including DEPDC5, NPRL2 and NPRL3 are associated with epilepsy and brain malformations with variable clinical phenotypes. Here, we describe the varying phenotypes within three family members carrying a novel deletion [arr[GRCh37] 16.p13.3 (148142_148300)] involving exon 9 in the NPRL3 gene. Our index patient is a young male with seizures starting shortly after birth that evolved to drug-resistant multifocal epilepsy and epileptic spasms. His MRI demonstrated

multifocal pachygyria of right temporal, occipital, and inferior parietal lobes. FDG-PET while on ketogenic diet revealed marked hypermetabolic activity in similar areas with concomitant EEG showing on-going seizures. Patient's seizures were refractory to medications, ketogenic diet, and temporal-occipital posterior motor disconnection, but improved following hemispherectomy. Pathology of resected temporal operculum demonstrated cortical dysplasia. Our patient's mother had focal cortical dysplasia and medically refractory epilepsy treated with surgical resection. Patient's maternal grandfather has pharmacoresponsive epilepsy.
CONCLUSIONS: This case provides clinical data on the phenotypic variability of NPRL3 related epilepsy within families. A "two-hit" hypothesis has been proposed as a possible explanation for this variability. Further genetic testing of our patient's family may be able to provide further support for this hypothesis. Understanding factors modifying clinical phenotypes can improve patient care and identify new therapeutic targets.
KEYWORDS: Epilepsy, Neurogenetics

71. Seizure Resolution and Anti-Seizure Medication Discontinuation in Neonates with Hypoxic Ischemic Encephalopathy Undergoing Therapeutic Hypothermia: An Observational Study

Squire M (Chapel Hill, NC), Hunter S, Broman-Fulks J, Malawsky D, Shiloh-Malawsky Y

OBJECTIVE: We aimed to analyze the course of seizures in neonates undergoing therapeutic hyperthermia for hypoxic ischemic encephalopathy (HIE) during initial admission and assess the safety of early discontinuation of anti-seizure medications (ASMs) prior to hospital discharge. Observational studies suggest discontinuation of ASM prior to discharge is safe (1) but there is no consensus regarding medication (2, 3) and electroencephalogram (EEG) management. (4)
METHODS: We conducted a retrospective study of infants with HIE who underwent therapeutic hypothermia from 2017 to 2021. We included only subjects with EEG data. We recorded demographic data, clinical course, clinical and electrographic seizures, ASM use, and ASM continuation on discharge.
RESULTS: Among the 99 infants included, 41 had clinical seizures, and 34 had seizures recorded on EEG. The mean day of life of the last seizure was 2.65 days (SD 1.35). Out of 21 infants who had a second EEG after initial monitoring during 3 days of hypothermia, only three had seizures. One had seizures on day of life 5, and two had continued seizures and were diagnosed with medication-resistant genetic epilepsies. A total of 53 infants received ASMs during admission, with 42 discontinuing the medication. Only 11% continued ASM on discharge.
CONCLUSIONS: Clinical and electrographic seizures in this retrospective study of acute HIE resolved by day of life 5, except for two patients with neonatal-onset genetic epilepsy. Discontinuing ASMs prior to discharge may be safe, as there is a low risk of seizure recurrence during initial admission for neonates with HIE undergoing hypothermia.
KEYWORDS: Epilepsy, Neonatal Neurology, Neurocritical Care

72. Improving Medication Non-Adherence Screenings in Children with Epilepsy – One Center Experience as part of the Epilepsy Learning Healthcare System

Lin N (Cincinnati, OH), Clifford L, Buchhalter J, Grimm J, Cronin S, Whitesell K, Bruce B, Hagans C, Clements M, Holland K

OBJECTIVE: Medication non-adherence is associated with increased risks of seizures, healthcare costs and morbidity/mortality in children with epilepsy. The identification of medication nonadherence is crucial for appropriate provider treatment recommendations. In partnership with Epilepsy Learning Healthcare Network (ELHS), pediatric psychology and the pediatric epilepsy division at Cincinnati Children's Hospital Medical center, we aim to improve our medication nonadherence screening rates
METHODS: This is a quality improvement project where we implemented the 18-item Barrier to Medication Adherence Screening Tool adopted by ELHS to increase our screening for our follow up patients with epilepsy. All epilepsy providers were included. Our Plan-Do-Study-Act (PDSA) cycles were previously focused on interventions using the paper form for barriers. As of March 2023, we have integrated a digital questionnaire with automated data pull using EPIC electronic medical system.
RESULTS: Using the paper form, we increased our screening rates from baseline 21% to 36%. Our goal is to screen 90% of our patients with epilepsy. As of March 2023, there has been a 36% completion (baseline) of the electronic system. We are now actively collecting data to see how much our screening rates have improved using the electronic system.
CONCLUSIONS: Implementation of the formal ELHS Adherence Screening Tool allowed us to screen for barriers to nonadherence at a rate higher than our previous screening methods. With now implementation of an automated electronic health record survey, there can be an automated collection of longitudinal data including demographics and diversity data.
KEYWORDS: Epilepsy

73. Enteral Ketamine for Status Epilepticus in Children with Epilepsy

DiDomenico L (Cincinnati, OH), Broomall E, Poisson K, Garrity L

OBJECTIVE: Status epilepticus (SE) is a neurologic emergency. Approximately 10-20% of children with epilepsy experience SE, and children with seizure clustering are at higher risk. Emergent intubation for refractory seizure clusters or non-convulsive status epilepticus (NCSE) is often undesirable with recognized risks. Ketamine is growing in use for SE. The goal of this case series is to examine the efficacy and safety of enteral ketamine in the treatment of NCSE and convulsive status epilepticus (CSE) characterized by recurrent seizure clusters in children with epilepsy.
METHODS: This case series is a retrospective chart review. Patients with epilepsy aged 1 to 21 years presenting in SE and receiving enteral ketamine were identified. Resolution or reduction in seizure frequency was assessed. Clinical presentation, endotracheal intubation, duration of hospitalization, and side effects were noted. Readmission for SE was also examined.

RESULTS: Nine patients aged 2 to 20 years were identified. Six patients presented in CSE characterized by recurrent seizures, and three patients presented in NCSE. Four patients had underlying genetic mutations, including PCDH19 and MECP2. Seven patients saw resolution or reduction in seizures within 48 hours of ketamine initiation. Two patients were intubated. Three patients reported side effects, predominantly emergence, psychotomimetic, or mood-related. Hospitalization duration ranged from 1 to 34 days. Three patient readmissions with early ketamine retreatment resulted in shorter hospital time.
CONCLUSIONS: Enteral ketamine is an effective and well tolerated treatment for nonconvulsive and convulsive status epilepticus in children with epilepsy and may prevent endotracheal intubation and reduce hospitalization duration.
KEYWORDS: Epilepsy, Neurocritical Care

74. A Case of Refractory Seizures in a Neonate with Resolution of Seizures Following Surgical Intervention

Garavatti E (Portland, OR), Yamamoto E, Collins K, Selden N, Roberts C, Bushlin I

OBJECTIVE: Onset of epilepsy in neonates with tuberous sclerosis complex (TSC) is rare and is associated with multiple brain lesions. Isolated FCD have been reported with TSC1 mutations, but has not been documented in a neonate. Presentation on day 1 of life with a single lesion and surgical resection before day 30 has not been previously described.
METHODS: Describe clinical course for novel presentation.
RESULTS: An infant was born at 38w1d by urgent c-section for placental abruption and met physiologic criteria for therapeutic hypothermia. Refractory seizures started in 1st hour of life, on EEG arising from left central region. MRI on day 4 demonstrated a left frontal lobe lesion. Seizures were refractory to 5 antiseizure medications; the patient began having hemodynamic compromise secondary to medications and required vasoactive support. On day 15, the patient was transferred to a tertiary care center. Exam on arrival was notable for profound encephalopathy. EEG showed near-continuous discharges at C3. The lesion was surgically resected on day 18, following which there was significant improvement in encephalopathy with spontaneous eye opening and movement. Rapid whole exome sequencing (WES) demonstrated a novel missense mutation in TSC1. No other clinical characteristics of TSC were identified. There were no further concerns for seizures. The infant was discharged on day 33 on monotherapy.
CONCLUSIONS: This case demonstrates that surgical intervention can be effective for neonates with pharmaco-resistant seizures associated with focal lesions and that rapid WES in the neonatal period has a high yield for identifying potential cause for seizures.
KEYWORDS: Epilepsy, Neonatal Neurology, Neurogenetics

75. Survey of Pediatric ICU EEG Monitoring – Reassessment After a Decade

Fung F (Philadelphia, PA), Carpenter J, Chapman K, Gallentine W, Giza C, Goldstein J, Hahn C Loddenkemper T, Matsumoto J, Press C, Riviello J, Abend N

OBJECTIVE: In 2011 we conducted a survey regarding continuous EEG (CEEG) utilization in critically ill children. In the interim decade, the literature has expanded, and guidelines and consensus statements have addressed CEEG utilization. Thus, we aimed to characterize current practice related to CEEG utilization in critically ill children.
METHODS: We conducted an online survey of pediatric neurologists from 50 United States (US) and 12 Canadian institutions in 2022.
RESULTS: We assessed responses from 48 of 62 (77%) surveyed institutions. Reported CEEG indications were consistent with consensus statement recommendations and included altered mental status after a seizure or status epilepticus, altered mental status of unknown etiology, or altered mental status with an acute primary neurological condition. Since the prior survey, there was a 3-4-fold increase in the number of patients undergoing CEEG per month and greater use of written pathways for ICU CEEG. However, variability in resources and workflow remained, particularly regarding technologist availability, frequency of CEEG screening, communication approaches, and electrographic seizure management approaches.
CONCLUSIONS: Among the surveyed institutions, which included primarily large academic centers, CEEG use in pediatric intensive care units has increased with some practice standardization, but variability in resources and workflow remained.
KEYWORDS: Epilepsy, Neurocritical Care

76. Safety and Effectiveness of Diazepam Nasal Spray With Concomitant Cannabidiol: Post Hoc Analysis of Pediatric Patients From a Phase 3 Safety Study

Peters J (Boston, MA), Puri V, Segal E, Misra S, Rabinowicz A, Carrazana E

OBJECTIVE: People with epilepsy may receive cannabidiol (CBD) as part of their daily treatment regimen. Drug interactions have been described between CBD and other antiseizure drugs. This post hoc analysis from a long-term, open-label safety study (NCT02721069) examined safety and effectiveness of diazepam nasal spray in pediatric patients also receiving CBD. Diazepam nasal spray (Valtoco®) is approved for acute treatment of seizure clusters in patients with epilepsy aged ≥6 years.
METHODS: Patients (6–65 years) were administered diazepam nasal spray to treat seizure clusters. Concomitant CBD use, treatment-emergent adverse events (TEAEs), and number of episodes treated with second doses within 24 hours of the first (proxy for effectiveness) were collected. Descriptive statistics for pediatric patients (aged 6–17 years) were calculated.
RESULTS: Among 78 pediatric patients, 44 (56.4%) did not receive CBD, 22 (28.2%) received the FDA-approved, highly purified oral-solution CBD, and 12 (15.4%) received another form of CBD. Most patients in each group (>70%) had epileptic encephalopathies. TEAE rates were greatest in the other CBD group (100%) vs no CBD (81.8%) and oral-solution CBD (90.9%). Treatment-related TEAEs were lowest in the oral-solution CBD group (9.1%) vs no CBD (11.4%) and other CBD (25.0%). Second dose use (effectiveness) was similar between no CBD (12.0%) and oral-

solution CBD groups (8.4%), and slightly higher for the other CBD group (16.4%).
CONCLUSIONS: CBD did not appear to influence the safety or effectiveness of diazepam nasal spray in this pediatric cohort. These results support concomitant use of CBD in pediatric patients.
KEYWORDS: Epilepsy

77. Ketogenic Diet as a Safe and Effective Treatment for Infantile Spasms Secondary to Holoprosencephaly

Moyen S (Memphis, TN), Patterson A, Walsh L, Rivas-Coppola M

OBJECTIVE: Objective: To report the safety and efficacy of the Ketogenic diet (KD) as an adjunctive therapy in patients with infantile spasms (IS) secondary to holoprosencephaly (HPE).
METHODS: Methods: Through retrospective chart review, we analyzed the clinical course and outcomes of two patients with IS due to HPE, whose seizures were controlled after KD initiation.
RESULTS: Results: Patient A was born full term with cleft lip and palate. At 2 months old, she was diagnosed with Diabetes Insipidus and MRI brain revealed a semi-lobar/lobar HPE. At 9 months, patient was diagnosed with IS and started on Sabril. She had recurrent IS at 4 weeks for which adjunctive KD treatment was initiated with complete resolution of the IS in 3 weeks. Patient B was born at 32 weeks gestation via cesarean section due to preterm labor. Neonatal period was complicated by focal seizures that were refractory to phenobarbital, Keppra, and clonazepam. At 10 months, patient was referred to our center for epilepsy evaluation and was diagnosed with IS and HPE. Sabril and ACTH was initiated, however IS continued, thus KD was added to Sabril, with complete resolution of the IS in 4 weeks.
CONCLUSIONS: Conclusion: To our knowledge, this is the first case report of patients with refractory IS secondary to HPE treated with KD. Both patients had complete resolution of IS after KD was initiated and tolerated treatment, despite the endocrinopathies associated with HPE. We illustrate that KD seems to be an effective and safe option for patients with IS secondary to HPE.
KEYWORDS: Epilepsy, Experimental Therapeutics

78. Utilizing Adult Clinician Transition Surveys to Improve Transition Process

Griffaton S (Philadelphia, PA), Thomas B, Stoney S, Hartmann N, Bullock A, Jangam K, Caffee L, DiGiovine M, Fried L, Greenberg A

OBJECTIVE: As patients transition from pediatric to adult care, adult providers can encounter challenges throughout the process. The survey addressed adult providers' satisfaction with the current transition process (initiated by the pediatric epilepsy program) and identified areas for improvement.
METHODS: A 10-question survey was distributed via Redcap to adult providers at an epilepsy program within a large, urban adult medical system. After the initial distribution, the survey was edited to focus provider responses to patients who transferred through the existing transition process, compared to those who had not.
RESULTS: The survey was distributed to 21 providers in three cycles, for a total of 19 responses. 79% (n=15) responded that the transition program was beneficial for patients and 90% (n=9) were more comfortable assuming their care, opposed to patients transferred outside the program. 47% (n=9) of providers reported having sufficient information for the first visit but 36% (n=7) specifically cited not having access to images. 52% (n=10) of respondents wished patients were aware that providers may not have access to all patient data and that care coordination may not be as robust within the adult medical system.
CONCLUSIONS: These brief surveys validated the value of the transition program for adult epilepsy providers and provided clear paths for actionable process improvement: ensuring images are transferred and expectation setting prior to transfer. The secondary benefit to this process improvement effort was reinvigorated transition collaboration between the pediatric and adult medical systems.
KEYWORDS: Epilepsy, Education, Lifespan Manifestations of Childhood Onset Conditions

79. Predictive analysis of response in children with treatment naïve West syndrome, to hormonal therapy using neurophysiological, radiological and biochemical markers: An observational study

Gulati S (New Delhi, India), Sharma R, Kamila G, Saini G, Kumaran S, Bhat P, Sharma R, Ahmadulla S, Chakrabarty B, Jauhari P, Pandey RM, Gandhi T

OBJECTIVE: The gold standard of treatment for West Syndrome(WS) has long been hormonal therapy, but only 50-70% of children respond to it, and 30-40% relapse. Our objective was to predict response to hormonal therapy(ACTH/oral steroids) in children with treatment naïve WS using clinic-electrographic features, Functional connectivity-fMRI, serum IL-1b and IL-1RA levels.
METHODS: Children upto 2-years with electro-clinical diagnosis of WS with clinical spasms in the last 48 hours were included. Burden of AmplitudeS and Epileptiform Discharges(BASED) score was done on most severely abnormal 5-minutes sleep epoch which would provide the highest score. All of them underwent Q-EEG, fMRI and serum samples for IL-1b and IL-1RA levels were collected.
RESULTS: Fifty-five children who were scheduled for hormonal therapy during the study period were included. No clinical characteristics at baseline had statistically significant association with non-response/relapse to hormonal treatment. Complete electroclinical resolution was predicted by the baseline BASED score of 3(p value: 0.018). Area under the BASED score(cut-off >3) ROC curve-0.67(95%CI: 0.53-0.8); sensitivity-81.5%(95%CI: 61.9-93.7); specificity-55.6%(46.5-80.3). On functional neuroimaging there was significantly increased functional connectivity among the group that was resistant to treatment. There was no significant difference in power spectral density for the five-frequency band and the baseline mean values of IL1b and IL-1RA among responders and non-responders.

CONCLUSIONS: Baseline EEG based score has both diagnostic and prognostic value in management of West syndrome. Compared to grouped multifocal spikes with paroxysmal voltage attenuation, multifocal epilepsy hypsarrhythmia pattern exhibited significantly higher relapse rates. Increased delta power could be a potential prognostic marker of non-responsiveness to hormonal therapy.
KEYWORDS: Epilepsy

80. Rapid Initiation of Rescue Treatment with Diazepam Nasal Spray Leads to Faster Seizure Termination in Pediatric Patients with Seizure Clusters

Misra S (San Diego, CA), Jarrar R, Stern J, Rabinowicz A, Carrazana E

OBJECTIVE: Diazepam nasal spray (Valtoco®) is approved for treatment of seizure clusters in patients with epilepsy age ≥6 years. Seizure clusters can lead to seizure emergencies such as status epilepticus. Delay in treatment for status epilepticus is associated with negative outcomes; however, the impact of timing of benzodiazepine treatment for seizure clusters remains unknown. This post hoc analysis investigated temporal patterns of seizure clusters among pediatric patients treated with intranasal diazepam.
METHODS: Seizure cluster timing data were collected during a phase 3, long-term, open-label, repeat-dose safety study of diazepam nasal spray in patients aged 6–65 years with epilepsy and frequent seizure clusters. Analysis was based on timing of diazepam administration after seizure recognition: <5, 5–15, and >15 minutes. Data preparation included exclusion of observations with seizure duration >24 hours, negative duration, and invalid dose date/time values. Medians were calculated.
RESULTS: 78 pediatric patients (aged 6–17 years) received ≥1 dose of intranasal diazepam. Of 1658 analyzed observations, 1175 seizure clusters were treated <5 minutes with median times of 1 minute to treatment and 3 minutes from treatment to seizure termination of. In comparison, a delay in treatment >15 minutes was associated with a >2-fold increase in time to seizure termination (median 8 minutes).
CONCLUSIONS: Among pediatric patients, faster time to administration of diazepam nasal spray was associated with shorter time to seizure termination, suggesting that prompt treatment may provide benefit. Further research is needed to clarify the relationship between treatment timing and seizure termination time.
KEYWORDS: Epilepsy

81. The United States Pharmaceutical Supply Chain of Anti-Seizure Medications

Meylor J (Milwaukee, WI), Shahrukh S, Javarayee P

OBJECTIVE: To delineate the anti-seizure medications (ASM) pharmaceutical supply chain of the United States of America (US).
METHODS: Using the FDA's National Drug Code (NDC) database and the U.S. National Library of Medicine's DailyMed website (Sept 2022 data), ASM details, including the type of FDA-drug application, country of manufacturing, and NDC associated with relabeling/repacking ASM were compiled.
RESULTS: 3190 unique NDCs (94.2% related to oral formulation) and 449 FDA application numbers (87.1% were abbreviated new drug applications) were associated with 26 ASMs. Gabapentin (16.3%), pregabalin (14%), lamotrigine (9.7%), and levetiracetam (9.3%) accounted for the majority of ASM NDCs in the FDA database. Twenty-four countries were associated with ASM manufacturing, with India (50.1%) and the US (25%) accounting for a majority of manufacturing locations of ASM pharmaceutical companies (information about manufacturing location was not available in 9.9% of NDC). In addition, 49.6% of ASM NDCs were associated with repacking/relabeled meds. 177 (5%) NDCs were related to intravenous (IV) and intramuscular formulation ASM; only three companies were identified with IV valproic acid manufacturing.
CONCLUSIONS: This study delineating the US ASM supply chain underscores the reliance on global ASM manufacturing and limited manufacturing facilities of critical ASMs like IV valproic acid. Future studies should focus on both ASM supply chain information and market share data to help understand the pricing and availability of ASM in the US.
KEYWORDS: Epilepsy

82. Real-World Retrospective Outcomes With Inter-Seizure Cluster Interval and the Number of Seizures per Cluster Following Rescue Medication Administration

Chiang S (San Francisco, CA), Moss R, Misra S, Carrazana E, Rabinowicz A

OBJECTIVE: Rescue medication (RM) is a cornerstone for acute termination of seizure clusters. Recently published phase 3 data on diazepam nasal spray demonstrated possible longer-term impact of RM on time in days between seizure clusters (SEIzure interVAL [SEIVAL]). Here, we tested the hypothesis that RM administration is associated with prolonged time to the next seizure cluster in a retrospective analysis of real-world outcomes from the Seizure Tracker® database.
METHODS: We analyzed Seizure Tracker® data on benzodiazepine RM administrations and seizure timing from patients with self-reported seizures between December 1, 2007, and August 8, 2022. Time to the start of the next seizure cluster or RM administration was compared via a log-rank test between RM administrations and clusters for which RM was not administered within 4 hours of cluster onset. The number of seizures per cluster was compared between clusters with and without RM administration using mixed-effects analysis.
RESULTS: A total of 10,889 RM administrations among 220 people with self-reported seizures (64.5% pediatric, 35.5% adult) were included. Number of days to the next seizure cluster or RM administration was longer after RM administration compared with clusters for which RM was not administered. RM administration was associated with fewer seizures per cluster when given earlier in the cluster.

CONCLUSIONS: These findings support the hypothesis that the time in days between seizure clusters tends to be longer when RM is given and that administration of RM earlier in the cluster is associated with earlier termination of seizure clusters.
KEYWORDS: Epilepsy

83. YouTube Analytics demonstrates high volume of organic traffic to Spanish language epilepsy content

Le Pichon J (Kansas City, MO), Varela V, Horton S, Abdelmoity A, Hoffman M

OBJECTIVE: Managing epilepsy in children and youth requires parental engagement and parental engagement is contingent on knowledge of epilepsy. Children living in rural and underserved areas are at a significant disadvantage in terms of managing epilepsy effectively. As part of a project dedicated to developing medical homes for children with epilepsy in rural Kansas, we developed a series of 17 videos in English and Spanish and made them available on YouTube.
METHODS: Video content related to the management of epilepsy was developed by physician experts. The videos are uploaded to YouTube and associated with a dedicated channel. Patients were directed to the REACT site within our hospital web page and also reached the content organically. We accessed YouTube analytics to evaluate patterns of online traffic to the video content.
RESULTS: The REACT Channel had 8,581 total views, 217,676 impressions, 232.72 hours of total watch time, and 145 total shares. Spanish language videos had 6,364 views compared to 2,217 English language videos. The total watch time for the Spanish language videos is 187.06 hours compared to 45.67 hours for English language videos. This is despite the English-language videos having more impressions (123,869 vs. 93,506).
CONCLUSIONS: Our work demonstrates that paired development of English and Spanish language clinical content can meet a strong need among the Spanish-speaking community. Deploying video content through YouTube offers a number of benefits, including global access and the ability for the video developers to analyze significant data.
KEYWORDS: Epilepsy, Telemedicine, Diversity, Equity, Inclusion

84. Long-term treatment with ganaxolone for seizures associated with CDKL5 Deficiency Disorder: 2-year open-label extension follow-up

Miller I (Radnor, PA), Demarest S, Bahi-Buisson N, Pestana-Knight E, Devinsky O, Amin S, Marsh E, Aimetti A, Hulihan J, Olson H

OBJECTIVE: Cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) is a developmental and epileptic encephalopathy characterized by global developmental impairment and early-onset, refractory seizures. In a double-blind placebo-controlled study, ganaxolone significantly reduced major motor seizure frequency (MMSF) in patients with CDD. Here we report safety and clinical outcomes data through 2 years open-label extension (OLE) treatment.
METHODS: Patients with CDD (aged 2-19 years) who completed the double-blind phase were eligible to receive ganaxolone in the OLE. Assessments included percent changes in MMSF from pre-randomization baseline to 3-month intervals in the OLE, as well as safety, and tolerability. All patients in this analysis had entered the OLE at least 2 years prior to data cut off.
RESULTS: Eighty-eight (of the 101 randomized) patients (87.1%; median age of 5; 79.5% were female) continued into the OLE. The median baseline 28-day MMSF was 50.6. Thirty-seven patients discontinued for various reasons: lack of efficacy (n=13), withdrawal by caregiver (n=11), adverse event (n=10), physician decision (n=2), and death (n=1). Using all available data at 2 years in the OLE (Months 22-24), patients (n=50) experienced a median 48.2% reduction in MMSF. The most commonly reported treatment-emergent adverse events within 2 years in the OLE were somnolence (17%), seizure (11.4%), and decreased appetite (5.7%). There was one death reported, which was deemed unrelated to study treatment.
CONCLUSIONS: Sustained reductions in MMSF at 2 years provide supportive evidence for the maintenance of effect of ganaxolone in seizures associated with CDD. Ganaxolone was generally well-tolerated with safety findings consistent with the double-blind phase.
KEYWORDS: Epilepsy, Neurodevelopmental Disorders

85. The use of YouTube videos in engaging children with epilepsy and their families

Horton S (Kansas City, MO), Le Pichon J, Abdelmoity O, Waller M, Abdelmoity A

OBJECTIVE: This study is a part of an effort to develop medical homes for children with epilepsy. One of the principal targets in developing this project was to improve patient and parental engagement. To achieve this goal, we developed short videos and assessed level of interest and improvement in knowledge.
METHODS: A total of 17 videos were created in English and Spanish by epileptologists. Each video was designed to be less than 5 minutes in length. The patients were directed to view one or two videos as part of their discharge instructions from the clinic. Every subject was asked to complete a short survey before and after viewing each video to assess knowledge improvement. Improvement was ranked on a three-point Likert scale.
RESULTS: The majority of families identified as non-Hispanic ethnicity (83%), and came from a suburban region (55%). More than 90% had at least high school degree. The vast majority of responders were female (85%). Of the 60% of subjects who completed at least one video, the average number of videos viewed was 2.6 and the average improvement in the knowledge survey was 0.28.
CONCLUSIONS: In this study we attempted to use short teaching videos to improve family engagement. We show that the use of these videos can be an effective tool to reach families and improve engagement. In a second phase of the study we assessed the broader impact of these videos.
KEYWORDS: Epilepsy, Telemedicine, Education

86. Use of surveys from patients who have transferred care to improve the process.

Griffaton S (Philadelphia, PA), Thomas B, Stoney S, Hartmann N, Bullock A, Jangam K, Caffee L, DiGiovine M, Fried L, Greenberg A

OBJECTIVE: The transition from pediatric to adult care for patients is difficult. The objective is to assess the transition process and to identify process areas that need improvement. For this project, we gathered feedback from recently transitioned patients on their experiences with the transition process with the goal to use data collected to both improve the transition process and better prepare future patients for the transition.

METHODS: The transferred patient survey was distributed in three successive rounds via RedCap to 272 unique patients ages 19-44 who transferred their epilepsy care between large, urban, free-standing pediatric and adult medical centers. Surveys were sent to patients via a link embedded in a text message.

RESULTS: The survey was sent to 272 unique patients in three successive rounds. The survey had a total of 53 unique patient responses. 90% (n=47) reported that their pediatric provider discussed transition. 79% (n=41) felt prepared for transition to adult care. 10% (n=5) reported that the adult epilepsy provider did not understand their epilepsy history at the initial visit; 29% (n=15) reported that they understood it very well. 69%(n=36) also reported that there was no additional information that they would have liked prior to transfer. 50% (n=26) reported having a copy of the most recent seizure action plan. Individual comments were collected as well.

CONCLUSIONS: Transition of care is a complicated process that warrants investment of resources to improve transition readiness and to ensure that adult providers understand their patients' medical history.

KEYWORDS: Epilepsy, Education, Lifespan Manifestations of Childhood Onset Conditions

87. Cyclical trends in Emergency Room visits for Seizures in Pediatric and Adult Patients

Velez D (New Hyde Park, NY), Nath M, Suri C, Kothare S

OBJECTIVE: Endogenous factors influencing seizure presentation are well studied, but we can learn more about exogenous factors. In epilepsy, seizures can occur in predictable cycles organized in annual, multidien (multi-day), circadian (24 hours), and ultradian (shorter than a day/longer than an hour), raising questions about exogenous factors affecting seizure cyclicity. We aim to determine cyclical trends in Emergency Room Visits for Seizures (ERVS) in adult and pediatric patients.

METHODS: A retrospective chart review of 56,974 (10,902 pediatric patients) ERVS was performed in adult and pediatric patients from May 2013-November 2020 within a large healthcare in a metro area. Using chi-squared analysis, we compared an annual, monthly, and hourly number of ERVS.

RESULTS: Our data show a statistically significant trend of ERVS in pediatric patients on an annual, monthly, and hourly basis. Higher average monthly ERVS occurred between July and December ($p<0.05$). We observed significantly higher hourly ER visits between 9 AM and 9 PM compared to 9 PM and 9 AM ($p<0.005$).

CONCLUSIONS: ERVS varies on an annual, monthly, and hourly due to intrinsic neuro-hormonal factors or extrinsic factors like seasonal variations in the duration of daylight, religious practices, and access to medical care. Further retrospective chart review will reveal correlations between meteorological variables (temperature, precipitation, barometric pressure) and the influence of epilepsy type on these ERVS. These findings may contribute to a better understanding of the mechanisms of nonrandom distribution of seizures and may provide information for individualized treatment options.

KEYWORDS: Epilepsy

88. Experience with the Ketogenic Diet in GNAO1-related Epilepsy

Becton J (Charlottesville, VA), Axeen E, Gulotta D, Boguszowsky K, Viehoever A

OBJECTIVE: Epilepsy in GNAO1-NDD is most commonly an early onset pharmacoresistant developmental and epileptic encephalopathy (DEE). Caregivers report on average 3 or more medications with continued seizures[1]. Ketogenic diet (KD) was reported to make one seizure free[2]). We sought to identify efficacy and experience on KD in the ultra-rare GNAO1-related DEE.

METHODS: Caregivers of participants with GNAO1 were consented and enrolled with IRB Approval by two US academic medical institutions. Data were obtained via survey, medical record review, and/or interview with dietician.

RESULTS: Five participants reported experience with dietary therapy. All have pharmaco-resistant DEE with an onset of seizure onset by two months. No participants became seizure-free on KD. One participant reported definite improvement in seizure frequency with KD representing the most effective treatment. Three expressed either no change or uncertainty as to the effect on KD on seizures and one noted worsening of seizures on two separate trials of dietary therapy. All five rated a different treatment as most effective.

CONCLUSIONS: No participants in our cohort of GNAO1-related DEE became seizure free on dietary therapy. One of five reported improved seizures with no significant improvement in three. One had exacerbation of seizures. While dietary therapy can be considered, it is unlikely to result in uniformly positive improvement in seizure frequency.

KEYWORDS: Epilepsy, Neurodevelopmental Disorders, Neurogenetics

89. The Use of Fenfluramine in Genetic DEEs and Refractory Epilepsy: A Two Center Experience

Varughese R (New Hyde Park, NY), Nath M, Marti C, Poduri A, Kothare S

OBJECTIVE: To study the efficacy of fenfluramine in genetic epileptic encephalopathies by studying the responder

rate, median seizure reduction, median dose for seizure reduction, and safety profile of this medication in the pediatric population.

METHODS: Seizure reduction, median reduction in seizure frequency, and responder rate were primary outcomes investigated and tabulated as four distinct quartile categories in post-fenfluramine assessment. Related-Samples-Friedman's two-way ANOVA-by-rank-summary-test was used for the statistical analysis of between-group differences of continuous variables to evaluate mean reduction in seizure frequency pre-and-post-fenfluramine treatment. Mann-Whitney-U test and Independent-Samples Kruskal-Wallis test was used to compare between-group differences of continuous variables.

RESULTS: There were 14 patients on fenfluramine. The pre-and-post mean seizure frequency was 22.85 and 18.7 and median seizure frequency per month was 28. Mean and median percent seizure reduction was 18.17% and 0%, respectively (p=0.046). Overall, 28.5% (n=4) patients showed more than 40% response to fenfluramine treatment of which 3 patients showed >85% reduction in mean seizure frequency. 13 (92.8%) patients had $^{3}2$ seizure types. Patients who had generalized tonic, clonic or tonic-clonic seizures in addition to other seizure types had a 18.4% decrease in mean seizure frequency (p=0.046). Patients who had myoclonic seizures (n=5) and atonic seizures (n=7) in addition to other seizure types showed 34.13% and 34.08% reduction in mean seizure frequency however this was not significant.

CONCLUSIONS: Within this genetic DEE cohort, there was minimal overall mean and median seizure reduction. Limitation includes small sample size. Patients that achieve early improvement while on fenfluramine continued to experience seizure reduction on subsequent follow-up.

KEYWORDS: Epilepsy

90. Memantine as precision therapy for de novo novel GRIN1-related epilepsy in a neonate

Reecher H (Milwaukee, WI), Eiler I, Adams S, Cabacungan E, Carlton K, Cohen S, Jozwik J, Singh A

OBJECTIVE: We report a case of novel GRIN1-related early-infantile developmental and epileptic encephalopathy (DEE) highlighting the patient's phenotype, targeted therapy, and its implications for future treatment strategies in GRIN1-related disorders.

METHODS: A retrospective study was conducted for a male neonate with GRIN1-DEE after informed consent. Data review included clinical presentation, EEG, brain MRI, genetic testing and therapeutic interventions.

RESULTS: A 37-week male neonate manifested clinical and electrographic seizures from day one of age, accompanied by apnea. Initial EEG exhibited burst suppression and focal seizures, progressing to tonic seizures, epileptic spasms, and choreiform movements. Brain MRI displayed extensive polymicrogyria without evidence of ischemic injury. The patient remained refractory to multiple antiseizure medications (phenobarbital, levetiracetam, clobazam, clonazepam, vigabatrin) with frequent tonic seizures with apnea requiring frequent resuscitations. Whole-exome sequencing revealed a de-novo, likely pathogenic GRIN1 variant (1916t>G,p.Phe639Cys). As gain-of-function variant was suspected based on phenotype, memantine and magnesium were introduced at 3.5 months, yielding a significant improvement in seizures. This allowed for discharge with hospice care, fulfilling the family's goals of care. The patient remained home for 19 days before seizure frequency worsened, and he ultimately died from respiratory failure at 4.5 months.

CONCLUSIONS: This study summarizes the phenotype of a novel GRIN1-DEE case, emphasizing the potential of memantine as a precision therapy. The observed clinical improvement exemplifies the importance of investigating targeted therapies for GRIN1-DEE for potential improvement in patient outcomes and quality of life. Further research is warranted to better understand the underlying pathophysiology for optimization of treatment strategies for GRIN1-associated conditions.

KEYWORDS: Epilepsy, Neurogenetics, Neonatal Neurology

91. Panayiotopoulos When Autonomics and Neurology Collide: Lessons from a Patient with Panayiotopoulos Syndrome

Massrey C (Houston, TX), Wells D, Risen S

OBJECTIVE: We describe a patient with Panayiotopoulos syndrome and why autonomic symptoms should not be dismissed.

METHODS: Not applicable.

RESULTS: A 7-year-old child presented to neurology with concern for "abnormal spells" for over 1 year. Patient had episodes that began with neck pain and shortness of breath progressing to drooling, nausea, vomiting and diarrhea. Episodes lasted up to 1 hour and the patient would develop a loss of tone without a loss of consciousness. After the events, the patient would be tired and would sleep for several hours. She had several ER visits for which she was discharged home without intervention. She was eventually seen by a cardiologist and started on propranolol for concern for presyncope which did not alter the frequency of the events. After a year of having these episodes, she was started on Keppra for concern for seizures after which she went without an episode for 4 months. Ultimately, she was admitted to the EMU and monitored on cEEG for 5 days during which Keppra was discontinued. Her EEG showed mixed generalized and focal epileptiform process from the left central area along with right central and bilateral occipital lobes while awake and in sleep.

CONCLUSIONS: Panayiotopoulos syndrome is a benign childhood epilepsy that presents with seizures characterized by variable autonomic symptoms. Seizures are typically prolonged (lasting up to 2 hours) and can have retained awareness. EEG shows spikes in the occipital lobe. Being able to identify children with Panayiotopoulos syndrome can help prevent status epilepticus and unnecessary treatment for other conditions.

KEYWORDS: Epilepsy, Autonomic Disorders

92. Evaluating the phenotype and genotype of a brother and sister with the same CDKL5 mutation

Tambunan D (Atlanta, GA), Davids L, Keller S, Zhang G

OBJECTIVE: To evaluate the phenotype and genotype of a brother-sister duo with CDKL deficiency disorder.

METHODS: Retrospective chart review, including clinical information and ancillary testing was collected.
RESULTS: Two siblings (brother and sister) were found to have the same pathogenic variant in CDKL5 that was not found in biological mother. Despite their opposite genders, the siblings had similar seizure presentation and semiology. MRI was normal. They have both shown significant regression and developmental delays since seizures started.
CONCLUSIONS: CDKL5 deficiency disorder is associated with severe early onset epileptic encephalopathy. The CDKL5 gene is located in the X chromosome and the protein has a role in axon outgrowth, dendritic morphogenesis, and synapse formation in early postnatal life and in maintaining synaptic function in the adult brain. The vast majority of affected individuals are females and surviving males on average have a more severe clinical course. The pathogenic variant found in these two patients has been previously identified in multiple unrelated individuals with CDKL5 deficiency disorder however not in siblings of opposite genders. Their pattern of inheritance is suggestive of a maternal gonadal mosaicism which has an important relevance in genetic counseling.
KEYWORDS: Epilepsy, Neurogenetics, Neurodevelopmental Disorders

93. A novel technique for illustrating the hypothesized epileptogenic zone in patients undergoing stereoencephalography: a pilot feasibility study

Chiu M (Boston, MA), Park E-H, Rotenberg K, Stone S, Madsen J

OBJECTIVE: Epilepsy surgery is the treatment of choice for patients with drug-resistant epilepsy. Surgical candidacy is predicated on identification of a putative epileptogenic zone (EZ). Some patients require intracranial stereoencephalography (SEEG) to approximate their EZ and/or determine its overlap with eloquent cortex. SEEG involves placing intra-parenchymal depth electrodes based on a tailored implantation plan that investigates a patient's epileptogenic network. We aim to determine the feasibility of a novel technique for illustrating a patient's hypothesized EZ, with the goal of facilitating SEEG implantation planning and optimizing surgical decision-making.
METHODS: All patients who underwent SEEG implantation at a large tertiary pediatric hospital were identified. A pediatric epileptologist retrospectively reviewed the pre-surgical work-up for 5 patients, then outlined 3 circles on their pre-operative MRIs to depict the area(s) hypothesized to be in their EZ at 3 probability levels (red=90%, orange=50%, yellow=10%). SEEG data was reviewed, and the circle-drawing exercise was repeated to illustrate post-SEEG EZ hypothesis.
RESULTS: Five patients were included (2-19 years, 2 boys). Four had lesional epilepsy with diverse etiological substrates: cortical malformation, tuberous sclerosis, post-infectious, post-tumor resection. SEEG captured habitual seizures in all patients. The pediatric epileptologist synthesized a hypothesis of each patient's EZ at two time points (pre-SEEG/post-SEEG), then created probabilistic drawings of their putative EZ accordingly.
CONCLUSIONS: We demonstrate that this novel technique is feasible and distils a patient's surgical workup into a concise pictorial summary of their hypothesized EZ. Further application on a larger data set by a greater number of surgical epilepsy experts is needed for clinical validation.
KEYWORDS: Epilepsy

94. Utilizing Clinical Intracranial Epilepsy Monitoring Infrastructure for Basic Science Research of Speech and Language Development

Hamilton L (Austin, TX), Asghar S, Desai M, Kurteff GL, Field A, Nussbaum N, Clarke D, Tyler-Kabara E, Anderson A, Weiner H

OBJECTIVE: Pediatric epilepsy patients undergoing intracranial monitoring provide a unique opportunity to study the neural development of speech and language. Setting up a separate research electrophysiology system can be a challenge in terms of cost and expertise. Here, we show how to study expressive and receptive language using a Natus Quantum clinical system and minimal hardware, and compare this to a dedicated research system (Tucker Davis Technologies, TDT).
METHODS: We developed tasks for pediatric epilepsy patients that are administered via iPad, including sentence listening, movie watching, and reading aloud. We routed iPad audio to the DC inputs of the Natus Quantum. Neural data were acquired from depth or grid electrodes at 4092 Hz. For expressive language tasks, we recorded high resolution audio (44.1kHz) to an external laptop. Data were preprocessed using custom Python scripts.
RESULTS: We acquired data from 43 patients aged 4 to 20. N=21 surgical epilepsy patients were recorded at Texas Children's Hospital in Houston, TX using the Natus Quantum system and N=22 patients at Dell Children's Medical Center in Austin, TX with a TDT research system. We show localized acoustic and phonetic selectivity during listening, and modulation of auditory cortex during speaking versus listening. A benefit of using the simplified clinical system is its ease and speed of setup.
CONCLUSIONS: We show it is possible to perform research in the EMU on brain signals underpinning speech and language with a relatively simple setup. We encourage other Epilepsy Centers to engage in similar research tasks.
KEYWORDS: Epilepsy, Neuroimaging

ETHICS

95. Withdrawal of Care in Patients with Neurological Conditions the NICU: A Case Report Reviewing Islamic Bioethics

Shoaib A (Cincinnati, OH), Vawter-Lee M, Venkatesan C, Soliman A

OBJECTIVE: As clinicians, it is important to be familiar with religious and cultural perspectives on medical treatment, life-prolonging measures and comfort and palliative care.

There is lack of literature within Child Neurology regarding Islamic perspectives surrounding palliative care.
METHODS: A representative case from the Neonatal Intensive Care Unit (NICU) at Cincinnati Children's Hospital Medical Center is presented that highlight challenges and discussions, including insight provided by Islamic scholars.
RESULTS: Male Muslim infant delivered at 37 weeks by caesarean section for severe polyhydramnios and breech positioning required admission to the NICU for respiratory failure. Neurologic examination showed bilateral clenched hands with arthrogryposis, diffuse hypotonia of face, core and extremities, and lack of cough or gag reflexes. Whole genome testing revealed two genetic diagnoses: congenital myasthenia gravis and Becker muscular dystrophy. The infant continued to decompensate despite escalations in treatment. There were many thoughtful conversations among family, clinicians and religious leaders to discuss goals of care within the context of their Muslim faith and the infant's diagnosis of treatment-resistant congenital myasthenia gravis.
CONCLUSIONS: This case highlights explorations of medical care and end-of-life decisions within the context of Islamic bioethics. The majority of Islamic scholars allow for withdrawal or withholding of medical care in patients with poor prognosis or when treatment is futile. The expertise of clinicians is given significant weight in making these judgments, and as such, families appreciate frank assessment of the situation by the medical team. Physicians should seek counsel and guidance from local Islamic leaders, and support families in their decision-making process.
KEYWORDS: Ethics, Neonatal Neurology, Diversity, Equity, Inclusion

96. Assessing the Emotional Well Being of Caregivers of Children with Medical Complexity and Serious Neurologic Impairment

VanZant J (Pittsburgh, PA), Yu J

OBJECTIVE: This study aims to describe emotional well-being (EWB) of family caregivers of children with chronic health conditions across a spectrum of child neurological impairment.
METHODS: Caregivers of children receiving care within a tertiary-care children's hospital completed a battery of Patient-Reported Outcomes Measurement (PROMIS) instruments assessing caregiver emotional distress, psychological strengths, and sleep-related health. Participants were categorized by their child's health complexity and neurologic impairment status. One-way ANOVA examined associations between caregiver EWB with child health complexity and neurologic impairment status.
RESULTS: Sample population consisted of 263 caregivers; 236 (89.73% were female, 232 (88.21%) were a biologic parent, and 122 (46.39%) reported their child was 1-5 years old. Overall, as the child's health complexity and neurologic impairment increased, caregivers tended to report lower global mental health, increased emotional distress, and poorer sleep-related health. We detected significant differences between caregiver groups in scores for anxiety, depression, emotional regulation, and sleep-related problems ($p<0.05$). Caregivers of children with medical complexity (CMC) and serious neurologic impairment (SNI) reported the most distress, experiencing the highest symptoms of anxiety, fatigue, and emotional dysregulation.
CONCLUSIONS: Family caregiver EWB differs by child's health complexity and neurologic impairment status, with caregivers of CMC experiencing serious neurologic impairment reporting the poorest global mental health, most emotional distress, and worst sleep-related health. Interventions aiming to improve health and well-being among caregivers of CMC with SNI are needed.
KEYWORDS: Ethics, Lifespan Manifestations of Childhood Onset Conditions, Neurodevelopmental Disorders

97. A rare case of bilateral facial palsy in an adolescent: a diagnostic challenge

Anderson T (Cleveland, OH)

OBJECTIVE: To report an adolescent case of bilateral facial palsy misdiagnosed as malingering.
METHODS: Case report.
RESULTS: A 15-year-old African American female with multiple comorbid psychiatric conditions and mild intellectual disability presented to a pediatric emergency room with bilateral facial palsy. MRI and lab results were unremarkable. The patient's story and physical exam were seen as unconvincing by the consulting neurologist and the palsy was judged to be feigned. The patient followed up at the outpatient pediatric neurology clinic. Careful re-examination demonstrated that genuine bilateral palsy was present and not feigned.
CONCLUSIONS: Bilateral facial palsy is exceedingly rare, occurring in 1 in 5,000,000. In the adolescent population, establishing the veracity of reported neurological symptoms is challenging. Reporting of symptoms may include elaboration or exaggeration for emphasis, resulting in a medically non-convincing story. This case highlights the importance of careful differentiation between suboptimal effort, deception, and genuine neurologic findings on physical exams. Additionally, it serves as a reminder of the potential for bias at the intersection of diverse age, gender, race, psychiatric comorbidity, and intellectual disability.
KEYWORDS: Ethics, Diversity, Equity, Inclusion

EXPERIMENTAL THERAPEUTICS

98. RGX-121: An Investigational Gene Therapy for the Treatment of Neuronopathic Mucopolysaccharidosis Type II (MPSII): Interim Analysis from the First-in-Human Study

Pisani L (Rockville, MD), Ficicioglu C, Giugliani R, Harmatz P, Rajan D, Hagood J, Fiscella M, Yang L, Wang H, Gilmor M, Cho Y, Mulatya C, Phillips D, Falabella P

OBJECTIVE: MPS II is an x-linked lysosomal storage disease caused by deficiency of iduronate-2-sulfatase (I2S)

leading to accumulation of glycosaminoglycans (GAGs). Neuronopathic MPS II (nMPS II) results in irreversible neurodevelopmental decline not addressed by intravenously administered enzyme replacement therapy. RGX-121, a recombinant adeno-associated virus serotype 9 capsid containing a human iduronate-2-sulfatase expression cassette (AAV9.CB7.hIDS), administered to the central nervous system (CNS) may provide a permanent source of secreted I2S, potentially correcting neurologic and systemic disease manifestations.

METHODS: CAMPSIITE™ is a phase I/II/III, open-label, 104-week trial enrolling boys 4 months up to 5 years of age with nMPS II (NCT03566043) who receive one image-guided RGX-121 injection to the CNS. Assessments include safety and tolerability; CSF, plasma, and urine biomarkers; neurodevelopmental scales; and imaging. Participants are encouraged to enroll in a long-term follow-up study.

RESULTS: As of January 3, 2023, 15 participants were enrolled in the phase I/II portion of CAMPSIITE in 3 dose cohorts (1.3x1010, 6.5x1010, and 2.9x1011 genome copies/gram brain mass). RGX-121 was reported to be well-tolerated with no drug-related serious adverse events. Longest post-administration follow-up was > 3 years. CSF GAGs showed dose-dependent reductions with D2S6 approaching normal levels in cohort 3 at 48 weeks. Interim neurodevelopmental assessments demonstrated CNS activity up to 3 years after RGX-121 administration. Evidence of systemic enzyme expression and biomarker activity was present after CNS RGX-121 administration. Updated interim results will be presented.

CONCLUSIONS: RGX-121 has the potential to provide sustained CNS clinical outcomes and additional systemic effects in MPS II patients.

KEYWORDS: Experimental Therapeutics, Neurodevelopmental Disorders, Neurodevelopmental Disorders

99. RGX-111: An Investigational Gene Therapy for the Treatment of Severe Mucopolysaccharidosis Type I (MPS I): Interim Analysis from the First-in-Human Study

Pisani L (Rockville, MD), Wang R, Ficicioglu C, Giugliani R, Burke J, Yang L, Wang H, Gilmor M, Cho Y, Mulatya C, Phillips D, Falabella P

OBJECTIVE: MPS I is a rare, autosomal recessive disease caused by deficiency of alpha-L-iduronidase (IDUA), an enzyme required for the breakdown of lysosomal glycosaminoglycans (GAGs). RGX-111, a recombinant adeno-associated virus serotype 9 capsid containing a human IDUA expression cassette (AAV9.CB7.hIDUA) administered to the CNS, may provide a permanent source of secreted IDUA that corrects neurologic and systemic disease manifestations.

METHODS: This phase I/II, first-in-human, 104-week, open-label trial enrolled participants > 4 months of age with severe MPS I or documented CNS involvement (NCT03580083) who received one image-guided RGX-111 injection to the CNS. Assessments include safety and tolerability; CSF, plasma, and urine biomarkers; cognition, language, and motor neurodevelopmental scales; and imaging. Participants are encouraged to enroll in a long-term follow-up study.

RESULTS: As of January 17, 2023, 8 participants were enrolled in 2 dose cohorts (1.0x1010 and 5.0x1010 genome copies/gram brain mass). RGX-111 was reported to be well-tolerated with no drug-related serious adverse events. Post-administration follow-up ranged up to 103 weeks. CSF GAGs were decreased through last time point available. Interim neurodevelopmental assessments demonstrated continued neurodevelopmental skill acquisition on age and developmentally appropriate scales. Emerging evidence of systemic enzyme expression and biomarker activity was present after CNS RGX-111 administration. Updated interim results will be presented. Additionally, follow-up will be reported for a severe MPS I child treated at age 21 months utilizing a single-patient, investigator-initiated Investigational New Drug application.

CONCLUSIONS: RGX-111 has the potential to provide sustained CNS clinical outcomes and additional systemic effects in MPS I patients.

KEYWORDS: Experimental Therapeutics, Neurometabolic, Neurodevelopmental Disorders

100. Real World Data Collection in Niemann-Pick Disease Type C – Data from Expanded Access Program with Arimoclomol

Berry-Kravis E (Chicago, IL), Gallo D, Greene T, Pagano K, O' Reilly R, Donnelly C

OBJECTIVE: Niemann-Pick disease Type C (NPC) is a rare, progressive, neurodegenerative disease with no FDA-approved treatments and persisting unmet medical need.

Rare disease data are sparse and data collection opportunities limited. While randomised controlled trials remain the gold standard, Real-World Data (RWD) provides additional insights as increasingly recognized by regulatory authorities.

RWD collected in an ongoing protocol-driven Expanded Access Program (EAP) aim to expand the understanding of NPC, including in populations not previously studied in controlled clinical trials.

METHODS: The 15-site US arimoclomol EAP was designed to maximize data capture in a rare disease population, while decreasing burden of participation on patients, caregivers, and staff through inclusion of broad geographic site representation, telemedicine consultations, direct-to-patient shipment, and local laboratories for blood tests. Routine clinical care was maintained, with clinical assessments at baseline, 4, 7 and 12 months. Effectiveness and safety data are collected through a secure online portal including 5-domain NPC Clinical Severity Scale scores and adverse events. Data collected will be transferred (with consent) to the International Niemann-Pick Disease Registry (INPDR) to contribute to a single world-wide source of NPC RWD.

RESULTS: The program has provided arimoclomol expanded access to adult and pediatric patients, with maximum patient follow-up spanning greater than 2 years. EAP and RWD collection design will be presented.

CONCLUSIONS: This collection of RWD from NPC patients will expand the understanding of this rare disease and the effectiveness and safety of arimoclomol. Addition of

these RWD to the INPDR may help guide future clinical management and development of treatment options.
KEYWORDS: Experimental Therapeutics, Neurodevelopmental Disorders, Telemedicine

101. Retrospective Matched Analysis of Disease Progression in Intrathecal Adrabetadex-Treated Children with Early-Onset Niemann Pick Disease Type C

Berry-Kravis E (Chicago, IL), Jaeger R, Aufox S, Stampfer M

OBJECTIVE: Adrabetadex (VTS-270, 2-hydroxypropyl-ß-cyclodextrin) is in development for treatment of Niemann-Pick disease type C (NPC), a rare lysosomal storage disorder associated with progressive neurodegeneration, with no current FDA-approved therapies. This study evaluated the effect of 2-weekly intrathecal adrabetadex treatment in young children with early or late infantile onset NPC relative to matched controls.
METHODS: Children with neurological onset and treatment initiation at age <6 years were compared to matched historical controls from a German/Swiss natural history cohort, with matching based on age, motor and/or language delay/regression, neurological symptoms and NPC Severity Scale (NPC-SS) score at treatment baseline. Subsequent disease progression was compared 1-to-1 between treated and control subjects. Kaplan-Meier analysis was based on time to unreversed progression on NPC-SS scores.
RESULTS: 12 treated subjects were matched to one or more of 11 controls. The average difference in NPC-SS at baseline for matched dyads was -0.63 $\pm$ 1.77 points (NS, controls with overall slightly lower NPC-SS scores). Disease progression was compared for 3.5 $\pm$ 1.4 years (0.5-5.8 years) post-treatment initiation for each match. In all cases the treated child showed less progression than the matched control(s). Average annualized change in NPC-SS was 4.3 $\pm$ 1.7 (2.0-7.8) for controls and 0.8 $\pm$ 1.5 (-2.5-3.0) for treated patients ($p<0.001$). Median time to progression in the Kaplan-Meier analysis was not reached for treated children and was 1 year for controls ($p=0.0003$).
CONCLUSIONS: Treatment with adrabetadex in early and late infantile onset NPC is predicted to be effective for management of this aggressive, rapidly-progressive form of the disease.
KEYWORDS: Experimental Therapeutics, Neurogenetics, Neurometabolic

FETAL NEUROLOGY & NEONATAL NEUROLOGY

102. Prenatal imaging findings and MR spectroscopy in pyruvate dehydrogenase complex deficiency

Christoffel K (Washington, DC), Fortin O, Schroeder J, Cilli K, Fraser J

OBJECTIVE: Pyruvate dehydrogenase complex deficiency (PDCD) is an inborn error of metabolism that often presents with neonatal encephalopathy, seizures, hypotonia, with or without persistent lactic acidosis and energy failure. Brain MRI and MR spectroscopy (MRS) findings, although well described postnatally, are not well-established in the fetal brain. This is the largest case series of prenatal brain imaging findings in PDCD, with exploration of MRS in PDCD.
METHODS: Six pregnant women referred to the Prenatal Pediatrics Institute at Children's National Hospital were included due to confirmed diagnosis of PDCD and prenatal imaging. All six women underwent fetal MRI, and brain MRI of the newborn infant occurred in three cases. MRS was obtained in one fetus and two newborns.
RESULTS: Characteristic prenatal imaging features included corpus callosum abnormalities, ventricular abnormalities, cortical abnormalities, cystic lesions in the ganglionic eminences, and small brain volumes. Abnormal lactate peaks were seen on MRS in one fetus with acute energy failure evident immediately at delivery and in a different infant with persistent lactic acidosis at the time of scan. MRS was normal in an infant who had stabilized on ketogenic diet.
CONCLUSIONS: Identifying imaging features of PDCD prenatally may expedite diagnostic testing, inform prenatal counseling for parents, and lead to better care for newborns with this condition. Destructive lesions in the ganglionic eminences may be a prenatal hallmark of neuronopathic PDCD. Further, MRS may identify acute energy failure in PDCD and be a useful diagnostic biomarker of PDCD prenatally.
KEYWORDS: Fetal Neurology, Neurogenetics, Neuroimaging

103. Agenesis of the corpus callosum: clinical characteristics and outcomes among children with complete or partial agenesis in a twenty-year retrospective cohort

Bach A (Philadelphia, PA) Rashid R, Patel V, Saha K, Gebb J, Soni S, Miller K, Cristancho A, Agarwal S

OBJECTIVE: To compare clinical characteristics and outcomes among children with complete or partial agenesis of the corpus callosum (ACC).
METHODS: In this retrospective cohort study, patients were identified with diagnosis codes for ACC (2003-2022). Complete or partial ACC diagnoses were confirmed by fetal or postnatal MRI (<2 years) and classified as isolated or complex (associated with other brain abnormalities). Clinical characteristics and outcomes were collected by chart review. Descriptive statistics were used to summarize data. Kruskal-Wallis or T-test and Chi-square or Fisher's exact test were respectively used to compare continuous and categorical variables.
RESULTS: Of 161 children with ACC, 89 (55%) had complete and 72 (45%) had partial ACC. Complete ACC had a higher rate of prenatal diagnosis than partial ACC (76%-vs-53%, $P=0.002$). There was no significant difference in the proportion of complex ACC, sex, gestational age at delivery, cesarean delivery, birthweight or 5-minute APGAR score by ACC type. There was no difference in age at last neurological evaluation by ACC type (complete: 2.8 years [IQR:1.6, 5.3], partial: 2.3 years [IQR:1.1, 6.6], $P=0.97$). There was a lower rate of cerebral palsy among children with complete than

with partial ACC (9%-vs-21%, P=0.03). By contrast, the rates of ventriculoperitoneal shunt placement, epilepsy, vision or hearing impairment, and motor, social-emotional, language or cognitive delays did not differ between children with complete versus partial ACC.
CONCLUSIONS: In this single-center cohort, children with complete and partial ACC had similar birth characteristics. Children with complete ACC were more frequently diagnosed prenatally and had lower rates of cerebral palsy.
KEYWORDS: Fetal Neurology, Neonatal Neurology, Neuroimaging

104. Outcomes of Children Prenatally Diagnosed with Midline Brain Defects

Coletti M (Salt Lake City, UT), Keene J, Smego A, Young M, Ostrander B

OBJECTIVE: Fetuses with midline brain defects including absent cavum septum pellucidum, abnormalities of the corpus callosum and holoprosencephaly are at risk for adverse endocrine, ophthalmologic, and developmental outcomes. This study's goal was to assess the efficacy of a standardized assessment pathway for postnatal evaluation to improve counseling, timing of diagnostic testing and follow-up.
METHODS: A retrospective review was conducted of all neonates with suspected midline brain anomalies identified prenatally at the only multidisciplinary referral center in a multistate region. We assessed subsequent diagnoses and outcomes after use of a standardized assessment pathway to facilitate the diagnosis of subsequent epilepsy, endocrine, ophthalmologic, and developmental abnormalities.
RESULTS: Of the 102 patients that were evaluated, 8 were lost to follow up after initial consultation and prenatal imaging. 14 of the patients died prior to delivery or within the first 24 hours of delivery either from pregnancy termination, palliative birth or natural causes and did not have diagnostic follow up. Of the remaining 84 patients we found that 41% were diagnosed with at least one endocrine abnormality, 32% with at least one ophthalmologic abnormality,25% had epilepsy and 23% were diagnosed with developmental delay, which varied by type of midline abnormality.
CONCLUSIONS: Our study shows the importance of endocrine and ophthalmic testing and neurological and developmental follow-up for infants identified as having a midline brain defect on prenatal imaging. A detailed analysis of diagnosis timing and testing utility will be essential to further refine our prognostic counseling and post-natal diagnostic approach to this cohort.
KEYWORDS: Fetal Neurology, Neuroimaging, Neonatal Neurology

105. Maternal IL-6 during Pregnancy is Associated with Patterns of Newborn Brain Connectivity

Butler R (St. Louis, MO), Triplett R, Nielsen A, Smyser T, Warner B, Luby J, Barch D, Rogers C, Chen E, Miller G, Smyser C

OBJECTIVE: Maternal poverty has been linked to alterations in child brain development and later neuropsychiatric outcomes. Maternal inflammation in pregnancy is posited as a potential pathway in alterations of fetal brain development related to poverty. This study investigates associations between maternal inflammation, indexed by IL-6, and infant functional connectivity (FC) in a cohort oversampled for social disadvantage, a composite measure of socioeconomic status.
METHODS: Maternal sociodemographic data and serum IL-6 levels were collected longitudinally during pregnancy. Infant MRI scans were performed between 38-45 weeks postmenstrual age (PMA). Infants were excluded for low gestational age (GA) or weight at birth (<34 weeks GA and/or <2 kg). A multivariate support vector regression (SVR) supervised machine learning model was constructed using average maternal IL-6 across trimesters and infant FC data, with GA and PMA as covariates.
RESULTS: 279 mother-dyads were included. Maternal IL-6 was correlated with social disadvantage. Brain-wide patterns of infant FC varied according to maternal IL-6 concentrations during pregnancy (R=.13, p=.02) Networks strongly associated with IL-6 exposure included frontoparietal, cingulo-opercular, salience, ventral attention, and default mode networks, along with the left globus pallidus, right amygdala, right thalamus, and right cerebellum (all p <.02).
CONCLUSIONS: These findings highlight the association between maternal inflammation during pregnancy with infant functional connectivity. Many networks most related to IL-6 overlap with those associated with social disadvantage in our sample and have been shown to correlate with later executive function and socioemotional processing in other samples. Our results support a link between social disadvantage, maternal inflammation, and child neurodevelopment.
KEYWORDS: Neonatal Neurology, Neuroimaging, Neuroimmunology

106. Autonomic seizures as a novel presenting seizure type in a neonate with ANKRD11 genetic disorder. Assessing clinical characteristics and treatment response in five neonates with autonomic seizures.

Litten R (Memphis, TN), Gatewood C, Thomas B, Patterson A, Mudigoudar B, Chourasia N

OBJECTIVE: Neonatal apnea with tonic stiffening can be the presenting seizure type in genetic epilepsies (ex. KCNQ2, SCN2A). ANKRD11 has been previously associated with generalized and focal epilepsies (infancy to teenage years). We describe autonomic seizures as a novel presenting seizure type in ANKRD11 genetic disorder and review clinical characteristics, treatment response in five neonates with autonomic seizures of varying etiologies.
METHODS: A retrospective chart review of five neonates diagnosed with ictal apneic seizures serially identified from clinical practice (January 2020-22) was conducted.
RESULTS: All five neonates presented at term with multiple repetitive paroxysmal autonomic events consisting of apnea and oxygen desaturation without motor movements. Clinical apnea and desaturations corelated with ictal onset and evolution in the temporal region(n=4) and temporal spikes at onset followed by generalized background attenuation(n=1).

Brain MRI was normal in four neonates and Dandy-Walker malformation(DWM) was noted in one. Etiologies included: genetic (n=2)- trisomy 18 and a pathogenic ANKRD11 genetic change[c.4087C>T (p.Arg1363Ter)] in a neonate with dysmorphic facial features, clinodactyly, large fontanelle, infection- S. pneumoniae meningitis(n=1), structural - DWM(n=1) and unknown(n=1). All five neonates received levetiracetam as first ASM with resolution in three, whereas two responded to combination of levetiracetam and a second ASM (phenobarbital or lacosamide).

CONCLUSIONS: Abrupt onset and clustering autonomic symptoms of apnea with desaturation/cyanosis in term neonates should raise suspicion for epileptic seizures. Neonatal apnea with or without motor manifestation can be a presenting seizure type in various genetic epilepsies and is newly described in a neonate with ANKRD11 in this case series.

KEYWORDS: Neonatal Neurology, Autonomic Disorders, Epilepsy

107. Sex Differences in Brain Development and Neurodevelopmental Outcomes at 4.5 years in Children Born Preterm

Christensen R (Toronto, ON, Canada), Chau V, Guo T, Synnes A, Grunau R, Miller S

OBJECTIVE: In preterm infants, sex is associated with differences in outcomes, with males at increased risk for mortality and morbidity relative to females. The objective of this study was to examine sex differences in risk factors, brain development and neurodevelopmental outcomes between preterm males and females.

METHODS: A prospective cohort of very preterm infants, born 24-32 weeks gestation, underwent MRI scans soon after birth, at term-equivalent age, and were followed at 4.5-years with standardized developmental assessments. Risk factors, brain fractional anisotropy (marker of white matter maturation) and neurodevelopmental outcomes were compared between males and females.

RESULTS: In 234 preterm infants, males (N=121) and females (N=113) had no differences in risk factors. There was a significant sex and brain injury interaction for cognitive (P<0.001) and motor scores (P=0.002) with females with brain injury having higher cognitive and motor scores than males. There was a significant sex and brain injury interaction for white matter injury volume (P<0.001) with females with severe brain injury having higher volume of injury than males. There was a significant sex effect on fractional anisotropy with females having higher anterior, central and posterior white matter fractional anisotropy (P=0.01) than males.

CONCLUSIONS: Neurodevelopmental outcomes differ in preterm males and females in the presence of severe brain injury. Preterm females had better cognitive and motor outcomes which may relate to greater brain white matter maturation. Preterm females had better outcomes despite having greater brain injury, suggesting a differential response to brain injury in preterm males and females.

KEYWORDS: Neonatal Neurology, Neuroimaging, Neurodevelopmental Disorders

108. Voxel-wise disconnectome mapping in preterm brain injury and neurodevelopmental outcomes

Selvanathan T (Toronto, ON, Canada), Ufkes S, Guo T, Chau V, Branson H, Ly L, Synnes A, Kelly E, Grunau R, Miller S

OBJECTIVE: The impact of white matter injury (WMI) and periventricular hemorrhagic infarction (PVHI) on brain structural connectivity in preterm infants is unknown. We assessed: (1) the probability of structural disconnections in the brains of preterm infants with brain injury and (2) their associations with neurodevelopmental outcomes.

METHODS: Prospectively recruited 294 very preterm infants underwent early-life brain MRI. 18-month neurodevelopmental outcomes were assessed with Bayley-3; adverse outcomes were defined as composite scores <85. We segmented brain injury (n=61) to develop ma-ps demonstrating voxel-wise probabilities of disconnection. Voxel-wise disconnectome-symptom maps demonstrating associations of disconnections with neurodevelopment were calculated.

RESULTS: Most lesions involved the periventricular white matter with highest probabilities of disconnections in tracts passing through this region. Similar extents of disconnection were observed in WMI and PVHI despite WMI lesions being smaller. Anterior but not posterior WMI was associated with disconnections in tracts passing through the basal ganglia and pons. Voxel-wise disconnectome-symptom maps showed that disconnections involving tracts passing through the basal ganglia and pons were associated with neurodevelopmental outcomes; associations with motor outcomes remained significant after correcting for multiple comparisons.

CONCLUSIONS: In preterm infants with ischemic brain injury, the periventricular white matter was most vulnerable to aberrations in structural connectivity. Disconnections in the tracts passing through the basal ganglia and pons were associated with adverse motor development. We observed similar extents of disconnection in infants with WMI and PVHI despite smaller WMI lesions, highlighting the importance of lesion location relative to white matter tracts in predicting neurodevelopmental outcomes.

Funding: CIHR

KEYWORDS: Neonatal Neurology, Neuroimaging, Neurodevelopmental Disorders

109. Prechtl's General Movements Assessment at writhing age guides MRI use in a clinical implementation network

Chirigos A (Salt Lake City, UT), Ostrander B, Burton V, Mirecki M, Maitre N

OBJECTIVE: We aimed to determine if Prechtl's general movement assessment (GMA) could help target the use of magnetic resonance imaging (MRI) in the neonatal intensive care unit (NICU) to detect infants with neuroimaging abnormalities not detected by cranial ultrasound (CUS) alone.

METHODS: We retrospectively reviewed neuroimaging reports of all infants who had cramped synchronized (CS) GMA between 36 and 44 weeks post-menstrual age at two level III and three level IV NICUs. All three sites used

standard protocols for preterm neuroimaging with at least one CUS in the first week after birth and another near 30 weeks corrected gestational age. If an MRI was obtained (due to clinical suspicion for intracranial abnormality, abnormal CUS findings, or CS GMA) the reason for performing the MRI was recorded.

RESULTS: 144 infants had CS GMA, and of these, only 19 did not receive neuroimaging. Initial neuroimaging demonstrated abnormal (mild and severe) findings in 64.5% and clinically significant findings in 45.6%. When MRI was performed secondarily, agreement between the two types of imaging occurred most of the time. A higher level of insult was present in 20.7% of those receiving a secondary MRI. The frequency of clinically significant abnormal findings on final determination was 48.8%. In 14 cases, secondary MRI was performed in response to GMA CS pattern only; in this case, MRI was abnormal in 11 (76.8%) cases.

CONCLUSIONS: These results suggest that infants with CS GMA at writhing age may represent a population with a high-likelihood of clinically significant abnormal neuroimaging findings.

KEYWORDS: Neonatal Neurology, Neuroimaging, Cerebral Palsy

110. Glucose levels during neonatal encephalopathy and neuropsychological outcomes at early school-age

Lagacé M (Toronto, ON, Canada), Williams T, Kamino D, Chau V, Widjaja E, Ly L, Tam E

OBJECTIVE: To evaluate the relationship between dysglycemia during neonatal encephalopathy (NE) and cerebral visual function and neuropsychological outcomes at early school-age.

METHODS: Standardized evaluation was performed using the Wechsler Preschool and Primary Scale of Intelligence fourth edition (WPPSI-IV), at early school-age in a prospective cohort of NE survivors (≥36 weeks GA) following therapeutic hypothermia and continuous glucose monitoring during the first 72h of life. Hypoglycemia was defined as ≤47mg/dL and hyperglycemia ≥182mg/dL. Using minimum and maximum glucose levels before 48h of life, we built a linear regression model evaluating the association between dysglycemia and neuropsychological outcomes adjusting for sex, maternal education (proxy for socioeconomic status), measures of hypoxic-ischemic encephalopathy severity (umbilical cord pH and Sarnat score), and visual acuity at 36 months.

RESULTS: Twenty-six children (54% male) were assessed at 5.5±0.4 years. Encephalopathy was mild in 2, moderate in 22, and severe in 2 participants. Mean cord pH was 7.02±0.17, and brain injury was seen on neonatal MRI in 7 (27%) participants. 10 (38%) children had hypoglycemia, while 5 (19%) had hyperglycemia. Maximum glucose before 48h was negatively associated with Full-Scale IQ (-0.96 points/mM, 95% CI -1.75 to -0.18, p=0.02) and Verbal Comprehensive Index scores (-0.16 points/mM, 95% CI -2.88 to -0.30, p=0.02). No other WPPSI-IV composite scores including tasks evaluating visual-spatial skills shared this association. Hypoglycemia was not associated with measured outcomes.

CONCLUSIONS: Maximum glucose concentration during NE undergoing therapeutic hypothermia was associated with lower overall intellectual outcomes at early school-age, driven by lower language abilities but not visual-spatial or early memory outcomes.

KEYWORDS: Neonatal Neurology, Neurodevelopmental Disorders

111. Intronic homozygous RNASEH2B variant in a newborn with Aicardi-Goutières syndrome presenting as recurrent hemorrhagic stroke and severe microcephaly

Lee B (Busan, South Korea) Oh S, Choi E, Park J, Lee J, Lee K, Roh D

OBJECTIVE: Aicardi-Goutières syndrome (AGS) is a progressive multisystemic disorder that has an early-onset encephalopathy, and intellectual, or physical disability. Here, we describe genetic mechanisms of a newborn case of AGS with severe neurological symptoms.

METHODS: Clinical information was extracted from the medical record. Results of laboratory tests, brain imaging, and electroencephalography were reviewed. A next-generation sequencing (NGS) based gene panel from GC Genomic diagnostic laboratory was performed from genomic DNA from leukocytes. Segregation analysis and RNA study was done to prove the pathogenic mechanism of patient's variants.

RESULTS: A female child was born at 37 weeks of gestation by elective cesarean section due to breech presentation. Her birth weight was 1,710 g (-3.3 SD), length was 40 cm (-4.2 SD), and head circumference was 28.5 cm (-4.3 SD). The parents are first-degree cousins form Sri Lanka. They are both healthy with no family history of any neurological disease. The patient presented with severe microcephaly, recurrent hemorrhagic stroke, multiple intracerebral hemorrhages, multifocal brain calcification, focal seizures, anemia, thrombocytopenia, and left ventricular hypertrophy. NGS revealed a homozygous variant c.65-13G>A in RNASEH2B. This variant was inherited from her parents with same heterozygous variant. It appears that the RNASEH2B protein is truncated as the creation of a new splice site causes a frameshift (p.Glu22Valfs*7), which was proven by RNA study.

CONCLUSIONS: We report the newborn case presenting with early severe neurological symptoms of AGS due to a biallelic missense variant in the RNASEH2B gene. The pathogenic mechanism of this variant has been elucidated.

KEYWORDS: Neonatal Neurology, Neurogenetics, Stroke

112. Contributing factors to elevated creatine kinase in newborns

Falk E (Boston, MA), Chrzanowski S, Coyne F, Sheldon Y, Cherkerzian S, Parad R

OBJECTIVE: Creatine Kinase (CK) screening at birth can help identify infants with certain conditions that affect the muscles, such as muscular dystrophy, which is of increasing importance with improving therapeutic interventions that are becoming increasingly available early in life. However, CK elevation can also occur with other conditions such as infections, trauma, or certain medications. How these perinatal

factors affect CK levels is currently unknown. Here, we determine the role that conditions in birth and transition play in elevating serum CK levels.
METHODS: >8,000 newborns and their mothers were enrolled in our study, during which CK-MM levels were measured on already-existing dried bloodspot (DBS) samples in conjunction with routine NBS. Review of electronic medical records was subsequently performed in order to analyze perinatal variables and factors.
RESULTS: Factors affecting CK levels included male gender, gestational age more than birth weight, oxytocin induction or augmentation, assistive maneuvers during vaginal delivery, shoulder dystocia, maternal fever, urgency of c-section, failure to progress, and presence of a trial of labor. Lower APGARS and intensive resuscitation were also associated with worse CK.
CONCLUSIONS: Using high powered analyses, we were able to observe that the primary factors contributing to elevated CK during birth were labor prolonging factors, oxytocin, gestational age, gender, and events for which assistive maneuvers and resuscitation were required. Presence of these factors in work up of a patient for muscular dystrophy can help to aid interpretation of elevated CK.
KEYWORDS: Neonatal Neurology, Neuromuscular

113. Child opportunity and social vulnerability indices are associated with language and cognitive outcomes at 4 years in term neonatal encephalopathy

Bach A (Philadelphia, PA), Song E, Barkovich A J, Lambing H, Rogers E, Glass H, Ferriero D, Gano D

OBJECTIVE: To evaluate associations of Child Opportunity Index (COI) and Social Vulnerability Index (SVI) with 4-year language and cognitive outcomes in a cohort of term neonatal encephalopathy (NE).
METHODS: Cross-sectional analysis of 4-year outcomes (IQR:48-52 months) in a prospective cohort of term NE (1993-2017). Therapeutic hypothermia (TH) was implemented in 2007. Severity of watershed and basal ganglia/thalamus injury was scored on day 4 MRI(IQR:3-6) by a blinded pediatric neuroradiologist using published criteria. Zip code at birth determined COI, a metric (0-100) of neighborhood resources and conditions that support child development, and SVI, a metric (0-1) of relative social vulnerability in every census tract. Primary outcome was verbal IQ (VIQ) and full-scale IQ (FSIQ) on Weschler Preschool and Primary Scale of Intelligence-III. Univariate and multivariate linear regression evaluated associations of COI and SVI with VIQ and FSIQ. Covariates were injury pattern, TH, and baseline characteristics comprising TH eligibility.
RESULTS: Of 141 children with NE and 4-year follow-up, 42(30%) had TH. Median COI and SVI did not differ by TH-treatment (treated: COI 79[IQR:54,92], SVI 0.43 [IQR:0.37,0.62]; untreated: COI 73[IQR:41,91]), SVI 0.43 [IQR:0.43,0.6]). Children with above-median versus at-or-below-median COI and SVI had similar frequencies of MRI injury (COI: $\chi2=4.8$,P=0.31; SVI: $\chi2=2.4$, P=0.67). COI and SVI were associated with 4-year VIQ and FSIQ in univariate and multivariate models, adjusting for injury, TH, and predictors of TH (COI: VIQ:Coefficient=0.26[95%-CI:0.13—0.39], P<0.001, FSIQ:Coefficient=0.20[95%-CI:0.07—0.32],P=0.002; SVI: VIQ:Coefficient=-31.2 [95%-CI:-49—-13],P=0.001, FSIQ:Coefficient=-28.2 [-45— -11],P=0.002).
CONCLUSIONS: In term NE, COI and SVI are associated with 4-year verbal and full-scale IQ regardless of MRI injury pattern, TH treatment, and birth characteristics.
KEYWORDS: Neonatal Neurology, Diversity, Equity, Inclusion, Neuroimaging

114. Acoustic biomarkers of cries from newborns admitted to the NICU with hypoxic ischemic encephalopathy

Latremouille S (Montreal, QC, Canada), Onu CC, Wang J, Gorin A, Basfar W, Al Ali A, Sant'Anna GM

OBJECTIVE: To compare acoustic biomarkers of cries from healthy newborns to those with hypoxic ischemic encephalopathy (HIE).
METHODS: Infants ≥36wks gestational age and birth weight ≥1800g with history of perinatal hypoxic insult were eligible and divided in 4 groups: no HIE, Mild, Moderate or Severe HIE by modified Sarnat at admission. Controls were recruited from newborn nursery. Infants' cries were collected (30sec-3min) and Sarnat performed on day of discharge. Cries were segmented into Cry Units (CUs; one voiced expiration) and Pauses (between CUs). From each CU, the mean, standard deviation, min, and max of the pitch (F0) were compared between controls and any HIE level. Controls were also compared with different HIE levels at admission and discharge.
RESULTS: Cries were analyzed from 171 controls (4830 CUs) and 39 with HIE (1760 CUs). Patient demographics and all acoustic biomarkers were significantly different between the groups. HIE group had lower F0, higher variability in F0, and shorter CUs with longer pauses. Differences in biomarkers at discharge of Mild HIE were found when compared to control and Moderate groups; HIE patients discharged with Normal Sarnat have significantly lower biomarker values than controls.
CONCLUSIONS: Acoustic biomarkers are significantly different in newborns with HIE. Cry analysis of Mild HIE (admission or discharge) was different than controls and HIE with Normal discharge Sarnat, raising concerns about brain injury in this group. Differences between healthy controls and HIE patients discharged with Normal Sarnat indicate that acoustic biomarkers may be more sensitive to detect neurological injury.
KEYWORDS: Neonatal Neurology

115. Assessing the relationship between dysglycemia and brain function in neonatal encephalopathy

Varghese J (Toronto, ON, Canada), Pinchefsky E, Moghadam S, Kamino D, Hahn C, Vanhatalo S, Tam E

OBJECTIVE: Hypoglycemia and hyperglycemia are common in term neonatal encephalopathy (NE). Our aim was to investigate changes in brain function during dysglycemic events using continuous electroencephalography (cEEG).

METHODS: 98 neonates with NE ≥36 weeks gestational age underwent cEEG and continuous glucose monitoring for >48 hours. EEG background activity was visually scored as continuous or tracé alternant, tracé alternant with excessive discontinuity, tracé discontinu, depressed/undifferentiated or burst-suppresion, and low voltage. 19 computational EEG parameters were extracted including amplitude, power, and non-linear measures. Five-minute epochs with hypoglycemia (≤47mg/dL) and hyperglycemia (>182mg/dL) were compared to epochs with normoglycemia. Generalized estimating equations for repeated measures were used to assess these relationships after adjusting for markers of NE severity (5-minute Apgar score, umbilical artery pH, and base deficit).
RESULTS: A total of 19 hypoglycemic events were detected in 13 neonates and 19 hyperglycemic events in 16 neonates. Adjusting for NE severity, epochs of hyperglycemia demonstrated worse cEEG background scores (1.32, 95%CI 1.27-1.37, p<0.001), while hypoglycemia demonstrated better scores (-0.31, 95%CI -0.44 - -0.17, p<0.001). Hyperglycemia and hypoglycemia demonstrated opposing associations for the 19 computational EEG parameters: hyperglycemic epochs showed lower mean amplitude (-5.28mcV, 95%CI -5.60 - -4.96, p<0.001) and lower total power (-107.57mcV2/Hz, 95%CI -117.40 - -97.73, p<0.001), whereas hypoglycemic epochs showed higher mean amplitude (4.43mcV, 95%CI 3.60-5.27, p<0.001) and higher total power (145.34mcV2/Hz, 95%CI 119.04-171.64, p<0.001).
CONCLUSIONS: This study demonstrates that hyperglycemia during NE is temporally associated with worse brain function, whereas hypoglycemia is not.
KEYWORDS: Neonatal Neurology

116. Genetic and Congenital Anomalies in Newborns with Hypoxic-Ischemic Encephalopathy

Morell A (San Francisco, CA), Cornet M-C, Monsell S, Comstock B, Glass H, Gonzalez F, Mayock D, Heagerty P, Juul S, Wu Y

OBJECTIVE: Among infants with hypoxic-ischemic encephalopathy (HIE), we determined whether presence of a co-existing genetic and/or congenital anomaly correlates with severity of encephalopathy or with neurodevelopmental outcome.
METHODS: Infants with moderate/severe HIE enrolled in the HEAL Trial underwent genetic testing when clinically indicated (e.g., dysmorphic features, family history, organ anomaly). Congenital anomalies diagnosed prior to hospital discharge were prospectively recorded. Outcomes at 22-36 months of age included death, cerebral palsy (CP), and low (≤ 85) cognitive, language and motor scores on the Bayley Scales of Infant Development-III (BSID-III).
RESULTS: Of 500 infants, 24 ([HG1] 5%, 95% CI 3%-7%) were diagnosed with a genetic abnormality (n=15) and/or structural anomaly of the brain (n=5) or another organ (n=5). Each genetic and congenital anomaly was unique. Infants with genetic and/or congenital anomalies had a similar rate of severe encephalopathy (17% vs. 23%, p=0.62), death (12% vs.14%, p=0.99), and median cord pH (6.90 vs. 6.94, p=0.47) as infants with no co-existing condition. However, infants with genetic and/or congenital anomalies had a higher rate of CP (32% vs. 13%, p =0.02); moderate/severe neurodevelopmental impairment (50% vs. 24%, p =0.005); and low BSID-III cognitive (65% vs. 13%, p=0.02), language (65% vs. 13%, p=0.02), and motor (70% vs. 13%, p=<.001) scores, than did infants without a co-existing condition.
CONCLUSIONS: About 5% of infants with moderate/severe HIE may have a co-existing genetic and/or congenital anomaly. Despite a similar degree of encephalopathy and acidosis, infants with both HIE and an underlying genetic and/or congenital anomaly have significantly worse neurodevelopmental outcomes.
KEYWORDS: Neonatal Neurology

117. A Novel Model of Assessing Parental and Infant Physiologic Stress Response during a Family-Centered Intervention in the NICU.

Garavatti E (Portland, OR), Alsup S, Cimino C, Philips J, Dipietro J, Ondusko D, Mackiewicz Seghete K

OBJECTIVE: Our objective was to develop a methodology for studying physiologic stress response in parents and infants in NICU environment during a family-centered intervention.
METHODS: Participants include parent-infant dyads currently admitted to the NICU. Heart rate data was used as metric of physiologic stress response. To capture parents' heart rate (HR), parents wore a wearable wristband before, during and after intervention. For infants, physiologic data was collected off bedside monitors.
RESULTS: 24 parent-infant dyads were enrolled and 21 completed the study. Infant vital signs were collected for 76% of sessions. Parent wore wristband and data was collected for 100% of sessions, of those, 66% had complete data sets. Of the date available, 8 sessions had usable pre-calculated heart rate variability (HRV). A trend was seen with increase in HRV from baseline (M=36.8) to intervention (M=49.4), and from baseline to post-intervention (M=41.7). All but one participant had increase HRV with intervention as compared to baseline.
CONCLUSIONS: Collection of live-time physiologic stress responding in acute setting is not only feasible, but can be achieved through inexpensive, reusable wearable devices and standard hospital monitors. Trends in data suggest this methodology is promising for capturing acute stress response in live time, and provides means to non-invasively monitor response to acute interventions. Limitations with methodology that had been previously documented for this technology were identified, and solutions have been identified for future studies.
KEYWORDS: Neonatal Neurology, Early Stage Investigator, Behavioral Neurology

118. Developing a Guideline for Parental Holding of Neonates while on Therapeutic Hypothermia

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

OBJECTIVE: Identify stakeholders and barriers to parental holding of neonate during therapeutic hypothermia (TH) for development of a guideline for parental holding during TH.
METHODS: This is a quality improvement project in a Level IV NICU at single institution. Important stakeholders identified included neurophysiologists (EEG readers), NICU

nurses, and neonatologists. First, the prior process was sent by email to EEG readers and requested feedback. An email survey was sent to NICU nurses exploring comfort with both transferring infant and parental holding of infants with different medical interventions commonly used in TH and during TH. This information was combined to create proposal that was presented to neonatologists for approval.
RESULTS: Four of five neurophysiologists responded, concerns included compromising study and dislodging leads, and suggestions included ensuring camera stays on infant, no patting or bouncing of the infant while held. 167 NICU nurses were emailed survey, and 42 responses (25%) were received. Higher discomfort was reported with transferring and parental holding of an infant on TH, followed by parental holding and transferring while on EEG. Concerns included maintaining TH, safety in regards to umbilical catheters and endotracheal tubes, and EEG dislodgement. A proposed guideline was created, with attention to feedback from stakeholders and presented to clinical consensus committee and approved as a clinical consensus guidelines.
CONCLUSIONS: Both concern and support for proposed intervention were raised by all stakeholders. Concerns were addressed in guideline, and was approved by clinical consensus committee. Future direction include quality improvement measurements of the implemented guidelines in the NICU.
KEYWORDS: Neonatal Neurology, Practice Parameters, Early Stage Investigator

119. Evaluating the clinical utility of perioperative EEG monitoring in infants undergoing cardiac surgery with cardiopulmonary bypass

Trapp N (Madison, WI), Wallace A

OBJECTIVE: Neonatal cardiac anomalies often require surgical correction with cardiopulmonary bypass (CPB), increasing risk of neurological injury and seizures. Perioperative EEG monitoring is common since seizures may present subclinically in sedated neonates. Initial studies suggested seizures following surgery with CPB occur in up to 21% of patients, though more recent data suggest this risk is lower. Records of neonates who underwent CPB with EEG monitoring at a single center were reviewed to evaluate risk of neurological injury and assess neuromonitoring protocol utility.
METHODS: Chart review was conducted on patients who underwent neuromonitoring at American Family Children's Hospital (Madison, WI) between 1/2018 and 10/2021. Inclusion criteria: 1). age 0-12 months at admission; 2). congenital cardiac defect; 3). surgical repair requiring CPB; and 4). perioperative EEG monitoring.
RESULTS: 87/94 patients met inclusion criteria. 82/87 patients underwent preoperative EEG, of which 10 were abnormal, and 0 had seizures. 84/87 underwent postoperative EEG, of which 38 were abnormal, 10 had focal epileptiform abnormalities, and 2 had electrographic seizures. Most abnormal EEGs were due to diffuse encephalopathy, and the 2 with seizures occurred in patients on ECMO.
CONCLUSIONS: Identifiable neurologic injury and seizures following CPB were uncommon. Preoperative EEG did not detect actionable findings and provided low clinical utility. Seizures only occurred in the context of ECMO, suggesting these patients may require increased EEG surveillance. Also, the total duration of EEG monitoring can be safely reduced in patients with normal early EEG findings.
KEYWORDS: Neonatal Neurology

120. Quality improvement (QI) approach to reduce time to EEG in neonates with hypoxic-ischemic encephalopathy (HIE) produces sustained effect

Natarajan N (Seattle, WA), Allar N, Lingen L, Forsyth A, Kelly K, Mietzsch U

OBJECTIVE: To reduce time to initiation of EEG monitoring in neonates with HIE undergoing therapeutic hypothermia (TH) by 25% over 12 months and sustain the results 2-years after project completion using a multidisciplinary QI approach.
METHODS: Neonates admitted with HIE undergoing TH during three time-periods "Baseline" (01/2018-06/2019), "Project" (1/2018-11/2020) and "Post-project" (01-12/2022) were included. A multidisciplinary QI approach was used, process maps across disciplines were created. Time from admission to EEG initiation was recorded as outcome measure. Balancing measures were time to first chest radiograph (CXR) and blood gas (BG) to remain within 10% of baseline. Interventions included preadmission huddle and checklist for procedure triaging. Checklist completion was tracked as a process measure. Data review and Plan-Do-Study-Act (PDSA) cycles were conducted monthly during the "project". Time to first seizure was recorded to monitor the impact of outcome measure.
RESULTS: Preadmission huddle and checklists were optimized through PDSA cycles. During the "Project", time to EEG decreased from 320 to 147 min (-54% change) without delay to first CXR or BG. "Post-project", the effect was sustained and further decreased to 129 min (-12% change). In the "Project" and "Post-project" period, 25% of neonates had seizure onset in the time gained from intervention.
CONCLUSIONS: Use of multidisciplinary QI approach significantly reduced time to EEG monitoring and allowed earlier seizure recognition and treatment without delaying critical procedures. Communication across disciplines is crucial for complex interdisciplinary procedures to sustain long-term effect.
KEYWORDS: Neonatal Neurology

121. Improving time to treatment in neonatal seizures

Papas S (Chapel Hill, NC), Olm-Shipman C, Jenkins A, Brown A, Trembath A, Boerwinkle V, Martin J, Thomas M, Broman-folks J

OBJECTIVE: Neonates are the most common age group to develop seizures, often with status epilepticus. Even with standardized pathways for treatment of neonatal seizures, treatment delays can occur. Untreated status epilepticus may contribute to neurologic injury and is associated with worse neurodevelopmental outcomes. Faster treatment of neonatal seizures is associated with improved response to antiseizure medication. This quality improvement project is intended to minimize treatment delays for neonatal seizures, specifically between the time the antiseizure medication is ordered and administered.

METHODS: Primary and secondary drivers of treatment delays were identified. These included errors in ordering medication (for example medications ordered as "routine" vs "STAT") and absence of a shared mental model of urgency for treatment. Specific interventions were developed based on these drivers, which included providing staff education, developing an order set in the electronic medical record, and standardizing communication between those involved in this process.
RESULTS: Baseline data from January 2021 – November 2022 showed a mean of 41.7 minutes from decision to treat to medication administration, with a standard deviation of 31 minutes. Preliminary data as the project was ongoing in February 2023 showed improvement to a mean of 22 minutes and standard deviation of 6.5 minutes.
CONCLUSIONS: In this quality improvement project, implementing simple interventions has, so far, led to improvement in time to treatment of neonatal seizures. This has the potential to have significant impact on the immediate and long-term health of the treated neonates.
KEYWORDS: Neonatal Neurology, Epilepsy

122. A case of newborn refractory seizures in kernicterus secondary to G6PD deficiency

Pehlivan EP (St. Louis, MO), Tabatabai GT, Zerafati GMZJ, Galindo RG

OBJECTIVE: Severe neonatal hyperbilirubinemia can result from kernicterus and can lead to lifelong neurodevelopmental problems including seizures, motor dysfunction, hearing loss, and oculomotor impairment. Limited data is available in the existing literature reporting the clinical course and treatment of seizures associated with acute newborn bilirubin encephalopathy. In this case report, we detail the neurological course and treatment of seizures in a newborn male with G6PD-associated bilirubin encephalopathy.
METHODS: Case report
RESULTS: A 4-day-old term male with an uncomplicated pregnancy and delivery presented with somnolence and decreased oral intake in the setting of severe unconjugated hyperbilirubinemia requiring exchange transfusion. At presentation, his total and direct bilirubin levels were 37.6 mg/ld., and 1.1 mg/dL, respectively. Shortly after admission, he developed apneic episodes requiring intubation. The patient was monitored with continuous EEG which showed multiple multifocal temporal electrographic seizures, some of which were associated with apnea. He was treated with loading doses of phenobarbital and levetiracetam followed by maintenance phenobarbital 6 mg/kg/day and levetiracetam 100 mg/kg/day. MRI brain revealed bilateral globus pallidus hyperintensity consistent with kernicterus. The patient developed recurrent clinical and electrographic seizures refractory to phenobarbital and levetiracetam for which lacosamide was added during the second week of admission. The patient was noted to have total cessation of clinical seizures and subclinical seizures (as noted on repeat EEG) within one day of starting lacosamide.
CONCLUSIONS: These observations suggest that Lacosamide may be a therapeutic option for neonates with medication refractory seizures secondary to bilirubin encephalopathy.
KEYWORDS: Neonatal Neurology, Epilepsy, Neurodevelopmental Disorders

123. Gut Microbiota in Neonatal Hypoxic Ischemic Encephalopathy: a Novel Long-Term Therapeutic Target

Caretti V (Houston, TX), Korf J, Blasco-Conesa M, Ganesh B, McCullough L

OBJECTIVE: Neonatal Hypoxic Ischemic Encephalopathy (nHIE) remains a leading cause of mortality and long-term disability worldwide, despite the implementation of therapeutic hypothermia (TH). Tertiary mechanisms of brain injury may continue for years after HIE. The gut microbiota and its metabolites are crucial for normal brain development. However, gut dysbiosis (perturbation of bacterial homeostasis) was reported in neonates with HIE after TH. It remains unknown whether HIE (with or without TH) results in persistent gut dysbiosis throughout development.
METHODS: C57BL/6 pups (n=6 for female and male/group) at post-natal day 9 (corresponding to term neonates) underwent the modified Rice-Vannucci Model (RVM) or sham surgery (controls) followed by hypoxia. Fecal samples, plasma, and brains were collected 1 day and 3 months (corresponding to young adulthood) after surgery. 16s RNA sequencing and mass-spectroscopy analysis were performed on stool and plasma/brain, respectively.
RESULTS: The gut microbiota of HIE pups 1 day after injury had a lower α-diversity (Simpson analysis) in comparison to controls, corresponding to a lower mean relative abundance of Lactobacillus genus. This depletion persisted 3 months after HIE with the additional loss of the Bifidobacterium genus. Lactobacillus and Bifidobacterium are known for their importance in brain development. Additionally, metabolites exclusively produced by gut microbes and with key roles in neurodevelopment were altered in plasma and brains of RVM pups but not controls. Results were statistically significant at $p<0.05$.
CONCLUSIONS: Hypoxic ischemic brain injury causes gut dysbiosis in pups at acute and chronic time points, underscoring the potential of gut modulation as a long-term treatment for nHIE.
KEYWORDS: Neonatal Neurology, Experimental Therapeutics

124. Neonatal neurological assessment of Molybdenum Cofactor Deficiency Type A mouse model to inform development of a gene-targeted therapy

Shamber C (Boston, MA), Misko A, Alyea E, Musolino P, Schwarz G

OBJECTIVE: To characterize the neurological deficit present in the MoCD Type A mouse model and develop a strategy for assessment of gene therapy efficacy.
METHODS: Survival, weight, health assessments and neurological assessments were applied to the MOCS1 knockout mouse model. Health assessments involved observations during the neonatal period to determine levels of distress in knockout mice. Possible indicators of distress were reaction to tactile stimuli, skin color, spontaneous movement, skin turgor and milk spot visibility. Neurological assessments adapted for

neonatal mice were used to determine developmental delays and neurological deficits. These tests included motor exams that tested neonatal mouse instinctual behaviors such as ambulation, righting reflex, cliff aversion and hindlimb suspension.
RESULTS: MOCS1 deficient mice showed 100% mortality at 15 days of life. These mice also showed a failure to thrive, presenting with less than 50% of the body weight of their littermates by day 8 of life. During motor assessments, knockout mice showed less ambulation than control counterparts. The knockout mice failed neurological tests that assessed instinctual reflexes such as the righting reflex, negative geotaxis and hindlimb suspension. By day 6 of life, 100% of knockout mice failed the cliff aversion test. Knockout mice also showed inability to perform grasping reflex from day 5 of life.
CONCLUSIONS: The MoCD Type A mouse model presents a severe neurological phenotype that leads to 100% mortality at 15 days of life. The knockout mice show stark inability to perform instinctual reflexes due to their severe neurological deficit, increased muscle tone and inability to ambulate.
KEYWORDS: Neonatal Neurology, Neurodevelopmental Disorders, Neurometabolic

125. Infantile Spasms in an Infant with a history of Neonatal COVID Infection

Hernandez C (Rochester, NY), Rosati J , Shehanaz E, Bearden D

OBJECTIVE: The emergence of the novel human coronavirus SARS-CoV-2 (COVID-19) was initially perceived to predominantly affect adults and was thought that vertical transmission was unlikely. Recent studies however estimate the risk of vertical transmission from a COVID infected mother to be 3.2%. Neurologic complications/manifestations of COVID-19 have mainly been described in adults and older children, but less is known in the neonatal population. We present a case of infantile spasms in an infant with a history of neonatal COVID-19 infection acquired by vertical transmission.
METHODS: The patient we describe is a late preterm infant who presented with seizures and encephalopathy in the setting of maternal COVID-19 infection at delivery. The patient tested positive for COVID-19 on DOL 1. Magnetic Resonance Imaging (MRI) demonstrated a diffuse pattern of white matter diffusion restriction which resolved over the patient's hospitalization on repeat imaging. He was followed in our pediatric neurology clinic and at 7 months of age the patient developed electro-graphically confirmed infantile spasms that readily responded to high dose prednisolone. Spasms resolved after one day of high dose prednisolone, repeat EEG at three weeks showed resolution of hypsarrhythmia. The patient has microcephaly, global developmental delay and spasticity.
RESULTS: Rapid whole genome sequencing and metabolic work up for infantile spasms did not reveal a possible etiology, we suspect development of infantile spasms could be related to his history of neonatal COVID.
CONCLUSIONS: The presentation we describe here has not been described in prior reports and could represent a potential risk associated with neonatal COVID infection.
KEYWORDS: Neonatal Neurology, Epilepsy, Neuroinfectious Disease

126. Early disruption of epigenetic and transcriptomic organization after prenatal hypoxia predicts persistent functional deficits in glutamatergic neurons

Cristancho A (Philadelphia, PA), Joseph D, Chauhan P, Gadra E, Gadra E, Zarrinnegar D, Rodriguez B, Marsh E

OBJECTIVE: Prenatal hypoxic injury affects over a million births annually, leading to neurodevelopmental disability in one-third of those children. We seek to understand the multifaceted, cell type-specific molecular consequences of hypoxia on the developing brain to develop novel therapeutic approaches.
METHODS: We performed joint single nucleus RNA-sequencing and assay for transposase-accessible chromatin sequencing from the cortex of mice immediately after a model of mild hypoxic injury (8 hours of 5% inspired oxygen at embryonic day 17.5). Over 140,000 nuclei were analyzed from 16 samples divided between normoxia and hypoxia. Golgi staining and whole-cell patch-clamp electrophysiology in juvenile mice were used to examine the structure and function of glutamatergic neurons.
RESULTS: We discovered that hypoxic glutamatergic neurons had a selective disassociation between global chromatin organization and gene expression. Glutamatergic neurons also demonstrated dysregulation of genes associated with neuron structure and synapse function after hypoxia. We found these neurons had decreased dendritic spine density and prolonged action potential hyperpolarization one month after hypoxia. Many of the potassium channels associated with hyperpolarization were not expressed in fetal neurons, but about 80% of these genes disruptions in nearby chromatin accessibility after hypoxia.
CONCLUSIONS: These findings suggest that hypoxia disrupts the organization of the epigenome and transcriptome in developing glutamatergic neurons, leading to their persistent disruption. Ongoing analyses will test (1) whether the shifts in the chromatin organization after hypoxia are persistent in juvenile mice and (2) which factors are regulating chromatin accessibility after hypoxia that may suggest new pharmacologic targets to improve neurodevelopmental outcomes.
KEYWORDS: Neonatal Neurology, Neurodevelopmental Disorders, Early Stage Investigator

GLOBAL NEUROLOGY

127. International virtual case-based learning program (VCBLP) in Pediatric Neurology between "Nicolae Testemitanu" State University of Medicine and Pharmacy of the Republic of Moldova, Atrium Health Wake Forest, NC and Monroe Carell Jr. Children's Hospital a

Railean A (Lewisville, NC), Grefe A, Railean G, Railean S, Hadjiu S, Postaru C, Cebanu E, Ghergheleglu E, Revenco N, Gavriliuc M, Gavriliuc O, Groppa S, Ciobanu M

OBJECTIVE: Although child neurology was recognized as a board-certified subspecialty in the United States 51 years ago, in the Republic of Moldova it is not recognized as a separate specialty. This has resulted in a lack of formal training, and subsequently a nationwide shortage of pediatric neurologists.

VCBLP, a collaboration between pediatric neurologists in the US and Moldova, provides educational support to trainees in Moldova. This study is designed to measure the program's effect on participants.

METHODS: We implemented a didactic curriculum using case-based learning of the most common conditions in pediatric neurology. 45 participants from host institution in Moldova (55% adult neurologist residents, 26% pediatric residents, 6 % fellows, and 6.5 % medical students or attendings with less than 10 years of experience). Pre-and post-program surveys are administered to all participants. Data collection for this study started in October 2022. We plan to complete it by October 2023.

RESULTS: With 3 of 10 sessions complete, 42 completed the survey (85%). 40 of the participants (82.6%) responded that VCBLP has increased their level of confidence in treating children with neurological conditions, 39 (81%) that VCBLP has changed their daily practice, 39 (81%) that the program helped them set new career goals, 38 (80%) that VCBLP is their only means of international exposure.

CONCLUSIONS: In countries with a profound lack of resources, VCBLP could be an extremely valuable educational resource for upcoming medical professionals. VCBLP is a powerful tool which provides mutual benefits to all parties, building local expertise and cross-cultural exchange.

KEYWORDS: Global Neurology, Diversity, Equity, Inclusion

128. Association between demographic and clinical factors and loss to follow-up in Malawian children with neurologic infections

Ramwell C (Washington, DC), Takle M, Liomba A, Barber J, Manda-Taylor L, Postels D

OBJECTIVE: Children surviving central nervous system (CNS) infections are at high risk of neurologic, behavioral, and cognitive sequalae. Early identification, characterization, and treatment of these sequelae may improve child and family health. In Africa, it is unclear if there are demographic or clinical factors that increase the risk of post-hospital loss to follow-up in children with CNS infections. If these factors exist, targeted educational efforts to increase rates of post-hospital retention could be focused on families at highest risk.

METHODS: We performed a case control study of Malawian children previously admitted with CNS infections to a specialized research unit in Queen Elizabeth Central Hospital in Blantyre, Malawi. Routine survivor post-hospital follow-up was scheduled for 1 month, 6 months, and 12 months. We compared demographic and clinical characteristic between 100 children who missed one or more of these post-hospital visits, to 200 children who attended all visits.

RESULTS: There were no statistically significant differences in demographic or clinical characteristics between children whose families returned for all follow-up visits, and those who did not. Specifically, when comparing these groups, we found no differences in age ($p = 00.646$), sex ($p=0.789$), duration of hospitalization ($p=0.903$), distance from home to hospital ($p=0.355$), type or severity of neurologic sequelae ($p=0.837$), or number of discharge medications ($p=0.464$).

CONCLUSIONS: There are no clear demographic or clinical factors that can identify Malawian child survivors of CNS infections at higher risk of loss to follow-up. During hospitalization, educational efforts to increase post-hospital retention should focus on all families.

KEYWORDS: Global Neurology, Neuroinfectious Disease

129. Neurodevelopmental outcomes of Colombian children with antenatal ZIKV exposure at age 4 years

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

OBJECTIVE: Assess neurodevelopmental outcomes of Zika virus (ZIKV)-exposed children without congenital Zika syndrome (CZS) and non-exposed controls at ages 4-5 in Colombia.

METHODS: We performed a prospective cohort study of in utero ZIKV-exposed children (cases) and unexposed children (controls) in Sabanalarga, Colombia. Cases were followed serially since the prenatal period. Controls were born prior to ZIKV entry to Colombia. The 51 cases and 70 controls were evaluated between 2020-2022 at ages 4-5. Neurodevelopment was assessed by parent questionnaire Behavior Rating Inventory of Executive Function (BRIEF), and child evaluations, Bracken School Readiness Assessment (BRSA), and Movement Assessment Battery for Children (MABC). Scores were compared between cohorts. P-values were adjusted using the Benjamini-Hochberg false discovery rate (FDR) (significance, $p<.1$).

RESULTS: Cases were evaluated at mean (SD) age 5.3(.4) years and controls at 4.7(.5) years. BRIEF scores for Shift and Emotional Control were higher in cases than in controls (FDR p-values = 0.06), leading to higher case emotional regulation factor (FDR p-value = 0.02), indicating lower function in emotional regulation skills. Cases and controls showed no differences on MABC. Across all BSRA sections except colors and composite score, ZIKV-exposed cases outperformed non-exposed controls (FDR p-value <0.0001), which may relate to the timing of pandemic exposure of the cases compared to controls.

CONCLUSIONS: Children with in utero ZIKV exposure may present risks to neurodevelopment in childhood for areas of emotional regulation. The COVID pandemic presented a challenge to early childhood research highlighting a need for continued follow-up of children with prenatal Zika exposure to determine any long-term effects.

KEYWORDS: Global Neurology, Neurodevelopmental Disorders, Neuroinfectious Disease

130. Feasibility and Success of an MRI training protocol in 7-year-old children from rural/semi-rural Colombian communities

Mulkey S (Washington, DC), Corn E, Williams M, Tarud R, Cure C, Berl M

OBJECTIVE: To assess low-cost MRI preparation activities to promote successful unsedated brain MRI in 7-year-old children in Colombia.

METHODS: Forty-two Colombian children in a neurodevelopment study (Mulkey et al. 2022) underwent MRI training in preparation for unsedated scans. All children resided in Colombia's lowest socioeconomic stratum in rural/semi-rural towns of Department of Atlántico. Researchers demonstrated the scanning process using a Playmobil radiology toy. A collapsible play tunnel simulated the scanning environment; children practiced lying still in the tunnel as a dishware container modeled a head coil and child-sized headphones familiarized them with MRI noises. Children received a customized book with photos of a child undergoing an MRI. Children participated in groups including being trained before and the actual scan day. On their MRI day, children traveled to the MRI site together, were provided lunch and waited in a more family friendly area separate from clinical patients. Hesitant children were permitted to watch peers. The 30-40 minute MRI protocol included resting state functional and structural images.
RESULTS: Children were a mean(SD) age of 7.3(.2) years at MRI. Training occurred between 6 and 122 days (mean[SD] =39[30]) before MRIs. Thirty-nine (93%) children successfully completed the MRI. The training supplies cost less than $100.
CONCLUSIONS: Children from a low-resource setting in Colombia demonstrated similar or greater success in unsedated MRIs after group training as compared to healthy similar-aged children in the United States (Woodword, et al. 2023, Barnea-Goraly et al. 2014). These methods, including peer-modeling, can promote unsedated MRI success in low resource and international settings.
KEYWORDS: Global Neurology, Neuroimaging

131. Neurologic Sequalae following Ebola Virus Disease in a Liberian Pediatric Population

Huff H (Washington, DC), Billioux J, Reilly C, Van Ryn C, Tarfeh-Burnette H, Bearden D

OBJECTIVE: To characterize the neurologic sequelae of Ebola Virus Disease (EVD) in children one year following infection.
METHODS: Under the Liberia-U.S. Partnership for Research on Vaccines and Infectious Diseases in Liberia (PREVAIL) III study, pediatric EVD survivors and their close contacts without EVD were enrolled in the neurology sub study of an Ebola natural history study. 79 pediatric participants (34 survivors and 45 close contact controls) ages 3 to 17 were seen approximately one year after acute EVD for full neurologic exam, neurologic history, and current symptoms assessment questionnaire. Survivors were compared to controls in terms of percentages and differences for categorical variables using Fisher's exact test.
RESULTS: On neurologic symptom questionnaire, 26.5% of survivors reported difficulty walking versus 8.9% of controls (p=0.045); 17.6% had fecal incontinence versus 0 controls (P=0.005). There were no statistically significant differences on neurologic exam in the survivors compared to controls. 8.8% of survivors met "slight disability" on Modified Rankin Scale (MRS) versus 0 controls (p=0.0012 across all observed categories of the MRS). On rater-determined executive function scoring, 41.2% of survivors had a minor issue and 17.6% a moderate-issue with executive function versus 35.6% and 2.2% respectively in controls (p=0.031 across all observed categories).
CONCLUSIONS: At one year following infection, pediatric EVD survivors had higher prevalence of neurologic symptoms including ambulation difficulties when compared to controls. On neurologic exam, there was no statistically significant difference in comparison with the control group, however, there were higher MRS scores and more executive function concerns in survivors.
KEYWORDS: Global Neurology, Neuroinfectious Disease

HEADACHE

132. A Pilot Study of Quality Care Improvement in Pediatric Migraine Management at School: The Migraine School Toolbox

McCracken E (Washington, DC), Gnanakumar A, Smith P, Strelzik J, DiSabella M, Langdon R

OBJECTIVE: Migraine is associated with functional impairment that uniquely impacts children at school. Challenges remain in effectively translating headache treatment strategies to the educational environment. This study aimed to provide adolescent migraineurs with a 'toolbox' encompassing individualized pain treatment and coping techniques to improve headache care at school.
METHODS: Over 2021-2022, 9 new patients aged 12-17 years meeting ICHD-3 criteria for migraine or daily persistent headache and HIT-6 score >50 were eligible to participate. Patients met monthly with a liaison to coordinate school medication and support plans. Pre and post-participation surveys were completed to determine headache frequency, school absences, HIT-6, and FDI scores.
RESULTS: Participants' disability due to headache improved over the study with a decrease in average HIT-6 score from 66.9 to 61.3 (p=0.008). Patients reported headaches were less likely to limit their ability to perform daily activities, they had less trouble being in school all day (p=0.031), and less trouble reading/doing homework. Additionally, patients reported increased control over migraine pain (p=0.04), life stress (p=0.008), an easily executed school plan (p=0.02), an improved understanding of their diagnosis (p=0.008), and how best to manage symptoms at school (p=0.004). Parents reported similar improvements in their child's management strategies (p=0.008).
CONCLUSIONS: This study indicates pediatric migraine patients benefit from comprehensive school-based management plans including a dedicated liaison to foster communication between the medical home and educational team with resultant improvements seen in overall disability, functioning, and self-efficacy. This suggests a role for educational advocates within the pediatric headache clinic model.
KEYWORDS: Headache, Education

133. Onabotulinumtoxin A in the Treatment of Pediatric Headache

Vilardo L (Washington, DC), McCracken E, DiSabella M, Strelzik J

OBJECTIVE: Migraine is a common neurological diagnosis that causes significant disability in adolescents. Onabotulinum toxin A (ONA) is an FDA-approved treatment for adults with chronic migraine; however, there is limited data on the efficacy of ONA in adolescents. This study aims to determine if ONA is effective in reducing headache disability in adolescents.

METHODS: Chronic migraine patients at the Children's National Hospital Headache Clinic were asked to report their headache frequency, abortive medications, and headache disability. Patients received ONA as part of the standard Phase II Research Evaluating Migraine Prophylaxis Therapy (PREEMPT) protocol of ONA injections for migraine prevention every three months. Participants completed questionnaires prior to each treatment, and post-treatment at 6 weeks, 3 months, 4.5, 6, 7.5, and 9 months from initiation of Botox. Demographics and baseline characteristics were obtained for all participants.

RESULTS: 134 baseline surveys and 50 six-week surveys were received between February 2022 and December 2022, totaling 45 patients. Baseline headache frequency was a median of 20 days per month (0-32 days, SD 10). After treatment with ONA, headache frequency reduced to 15 days per month (0-32 days, SD 10). Baseline frequency of abortive medications prior to treatment was 6.4 times per month on average (0-22 times, SD 9.8), and after treatment was reduced to 3.5 times per month (range 0-17, SD 4.2). 62% of patients (31/50) reported successful treatment with ONA, 28% (14/50) reported that treatments were unsuccessful, and 10% (5/50) were neutral.

CONCLUSIONS: The results suggest that ONA treatments may be effective for adolescents with chronic migraine.

KEYWORDS: Headache

134. Opening pressure and post-lumbar puncture headache in children undergoing intrathecal baclofen trial.

Wilson J (Portland, OR), Summers A

OBJECTIVE: Post-lumbar puncture (LP) headache occurs in 8-15% of children. The purpose of this study is to determine the frequency and predictors of post-LP headache in children with hypertonia undergoing LP with intrathecal baclofen injection (ITB trial).

METHODS: This was a retrospective single center chart review of all 43 children (<18 years) with hypertonia or dyskinesia undergoing ITB trial from 2013-2022. Predictors of post-LP headache were evaluated via one-way paired T-test and Fischer's exact test.

RESULTS: Subjects were a mean of 10.6 years (SD 4.3) and 34.9% female. Mean opening pressure (OP) was 24.0 cm H2O (SD 6.5, range 11-40). Five (11.6%) had elevated OP (>28 cm H2O). Seven (16.3%) developed post-LP headache. Three required emergency care or hospitalization and one needed a blood patch. One was misdiagnosed with constipation. Mean OP was higher for the post-LP headache group (28.6 vs 22.4 cm H2O, $p<0.001$). Sixty percent of those with elevated OP developed post-LP headache. Post-LP headache correlated with younger age ($p<0.001$). Baclofen pumps were placed in 4 (80%) of the patients with elevated OP and 6 (85.7%) with post-LP headaches without complications.

CONCLUSIONS: The frequency of post-LP headache after ITB trial was similar to that reported in the literature. Elevated OP occurred in 12% and predicted post-LP headache. Physicians may use OP to predict higher risk for post-LP headache and should educate families about symptoms. Elevated OP or post-LP headache may not preclude baclofen pump placement.

KEYWORDS: Headache, Cerebral Palsy, Experimental Therapeutics

135. Secrets and Migraines: A narrative medicine approach to unraveling the painful plot

Bacus P (Lexington, KY), Qaiser S

OBJECTIVE: A case series to illustrate that children provide better description of neurological complaints via narrative medicine than traditional history taking

METHODS: Informed consent was obtained from multiple patient's family for sharing of both historical and pictorial information. Literature review performed on PubMed and Cochrane review using terms "narrative medicine" and "headache".

RESULTS: Our patients presented to clinic with a history of migraine some with and without aura with fluctuating severities. Patients noted that headaches were associated with nausea, vomiting, photophobia, light-headedness and spinning sensation. Physical exam was unremarkable and imaging studies were within normal however PedMIDAS disability scores were correlated with increased number of components in pictures

CONCLUSIONS: Narrative medicine can play an essential role in the care of patients with neurological conditions ioncludoing migraine. By focusing on the patient's personal experience of their illness, narrative medicine can help physicians to better understand the true morbidity related to the neurological conditions. This approach can help physicians to develop more effective treatment plans, as well as to provide more personalized care that takes into account the unique needs and experiences of each patient. Moreover, by encouraging patients to share their stories and experiences, narrative medicine can also help to foster greater trust and communication between patients and physicians, which can lead to better health outcomes overall

KEYWORDS: Headache, Practice Parameters

136. Pediatric Cluster Headache Case Series: Symptomatic Cases and the Migraine Relationship

Eberhard S (Indianapolis, IN), Jackman C

OBJECTIVE: Current criteria help differentiate cluster headache from migraine. However, children with these disorders may have overlapping features making it difficult to

distinguish the two conditions, which may delay diagnosis into adulthood. Differentiating cluster headache from migraine is important regarding treatment as well as diagnostic workup for symptomatic causes.

METHODS: Cases from 2015 to 2023 with a cluster headache diagnosis given before the age of 19 at one institution were extracted. 25 cases met criteria for either chronic, episodic, or probable cluster headache.

RESULTS: 25 patients of 16 females and 9 males between ages 6 and 17 were given a diagnosis of cluster headache. Five cases were identified as symptomatic cluster headache, three cases as chronic cluster headache, seven cases as episodic cluster headache, and ten as probable cluster headache. Symptomatic etiologies include Graves' disease, optic neuritis, prolactinoma, hypothalamic pilocytic astrocytoma, and right eye congenital blindness. Migrainous features were common including 76% with nausea, 36% with vomiting, 68% with photophobia, and 56% with phonophobia. Cluster headache patients also had an independent diagnosis of migraine in 64%. Prolonged delay in diagnosis greater than one year was seen in 12 cases (48%).

CONCLUSIONS: Pediatric cluster headache has a high frequency of migraine symptoms and coincidental migraine diagnoses. A careful history should be obtained to identify cluster headache and evaluate and treat accordingly. Cluster headache and probable cluster headache should be screened for secondary causes with appropriate imaging and studies. Except for the prolactinoma, the symptomatic associations in this case series have not been reported before.

KEYWORDS: Headache

137. Headache Prevalence and Co-morbidities in Children with Autism Spectrum Disorder

Waldron L (Los Angeles, CA), Minota K, Grant Tejada M, Klomhaus A, Nwaobi S

OBJECTIVE: Migraine is among the most common and disabling conditions worldwide. Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental disorder. Both migraine and ASD are associated with abnormal sensory processing, including pain perception. Over 94% of individuals with autism experience hypo and/or hyper-reactivity to a variety of stimuli. Similarly, migraine is thought to represent a brain disorder of abnormal hypersensitivity with increased sensitivity to light, sound, and smell occurring both during and in between migraine attacks. In this study we aimed to examine the prevalence of headache in autism as well as delineate population characteristics of those with headache and autism.

METHODS: We collected summary statistics from the 2021 National Survey of Children's Health. We extracted relevant information on 3 groups: (1) ASD, (2) ASD with headache, and (3) non-ASD with headache.

RESULTS: Headache occurs more frequently in individuals with ASD compared to non-ASD and tends to be more severe. There are higher rates of headache in males compared to females, paralleling the known M:F (4:1) ratio in autism. Individuals with both ASD and headache demonstrate higher rates of anxiety, depression, ADD/ADHD, and behavioral issues compared to ASD without headache and non-ASD with headache.

CONCLUSIONS: Our study revealed that children with ASD and headaches are more likely to experience higher rates of psychiatric and developmental co-morbidities compared to children with ASD, but without headache. Our hope is to highlight the importance of recognizing headaches in this vulnerable pediatric population to provide adequate and timely interventions.

KEYWORDS: Headache, Behavioral Neurology

138. Medications Used During Improvement of Headache in Pediatric New Daily Persistent Headache

McCracken E (Washington, DC), Goucher O, Strelzik J, Langdon R, DiSabella M

OBJECTIVE: New Daily Persistent Headache (NDPH) is characterized as a constant, daily, and unremitting headache for at least three months. This retrospective study aims to describe the duration of headache in NDPH and the medications patients are taking during cessation of headache in pediatric patients.

METHODS: The participants in the current study were pediatric patients who attended the Headache Clinic at Children's National Medical Center between 2016 and 2021. All patients seen in the Headache Clinic were enrolled in an IRB-approved patient registry. The registry was queried for NDPH (ICD-10 G44.52) and these records were reviewed to examine their clinical presentation.

RESULTS: Between 2016 and 2021, there were a total of 327 patients diagnosed with NDPH. Ninety-three of those patients were analyzed at the time of review. During follow-up visits, 28 patients (30%) reported that their headaches were no longer constant and unremitting. Of the 28 patients who had remission of constant headache, 25 (89%) of those had resolution between 5.1 and 19.8 months from diagnosis. The medications patients were taking when their headaches were no longer constant included topiramate (n=27), riboflavin (n=13), frovatriptan (n=12), and amitriptyline (n=12).

CONCLUSIONS: Patients with NDPH who had cessation of constant headache reported headache for an average of 17 months from diagnosis. Patients with relief from NDPH were most often on topiramate, riboflavin, frovatriptan, and amitriptyline. Further studies including prospective randomized, placebo-based clinical trials are needed to understand if commonly used medications for migraine management can be effective in breaking the unremitting nature of NDPH.

KEYWORDS: Headache

139. Experience is illusory: how random variation in patient outcomes influence prescribers' perceptions

Henry C (Richmond, VA), Cannon II L

OBJECTIVE: Due to the relative paucity of randomized controlled trials, pediatric neurologists rely more heavily on personal clinical experience in pediatric migraine management.Therefore the objective of this study is to investigate the impact of random patient outcomes on the variability of

treatment choices among healthcare providers in the acute management of migraines.
METHODS: A web-based prescribing simulation was conducted with physicians, advanced practice providers, and medical students at VCU Medical Center. Participants were asked to choose one of three non-descript medications for treating acute migraines in the emergency department. They treated five patients at a time and then received immediate feedback on the patient outcomes. Two different scenarios were presented, where the treatments were either equally effective or differed by an absolute difference of 10-15%. Participants treated 100 patients in each scenario and were asked which medication was the most effective.
RESULTS: Of the participants who completed the simulation, only 21% were able to correctly identify the scenario where the medications had the same efficacy. Only 67% were able to correctly identify the most efficacious medication, while 9% chose the least efficacious medication as the most effective.
CONCLUSIONS: Despite immediate feedback on outcomes of 100 identical patients with the same condition, random variation in patient outcomes caused a significant amount of therapeutic variability. This grossly underestimates the problem as clinicians face longer times between prescribing and learning the outcome. This work can lead to interventions that help clinicians incorporate patient variability into their assessment of a treatment's efficacy, decrease therapeutic variability and improve outcomes.
KEYWORDS: Headache, Education, Early Stage Investigator

140. Determining the Role of TNFα in Sickle Cell Disease Pain using a Murine Model of Sickle Cell Disease

Konda M (Milwaukee, WI), Ehlers V, Zorn S, Brandow A, Stucky C

OBJECTIVE: We sought to determine the role of TNFα in Sickle Cell Disease (SCD) pain. SCD is the most common worldwide inherited blood disorder and is characterized by severe, chronic inflammatory pain beginning in childhood. Stress induces hemoglobin polymerization, distorting erythrocytes, which eventually leads to vaso-occlusive events (VOEs). Immune cells release cytokines following VOEs, including Tumor Necrosis Factor-alpha (TNFα), which is elevated in people with SCD and is linked to non-SCD allodynia following hypoxia.
METHODS: We used a transgenic mouse model of SCD that exhibits patient-reported sensitivity behaviors, such as cold and mechanical allodynia. 2–6-month-old mice with (n=12) and without (n=12) SCD received bi-weekly IP infliximab injections, an FDA-approved TNFα-inhibitor. All were exposed to (HR) hypoxia-reoxygenation (8% FiO2 for 2 hours), a validated VOE-induction method. Sensitivity was monitored by recording paw withdrawal to mechanical stimuli at baseline, pre-hypoxia, and up to 7 days post-hypoxia.
RESULTS: Infliximab-treated SCD mice had unchanged baseline mechanical sensitivity but improved at 24hr post-hypoxia to the level of healthy controls ($p=0.0030$). Infliximab-treated SCD mice retained improvement following multiple treatments and 3 rounds of HR, at 2 and 24 hours post-hypoxia, compared to vehicle-treated SCD mice ($p<0.001$ and $p=0.0028$).
CONCLUSIONS: These results suggest TNFα mediates acute SCD mechanical hypersensitivity. TNFα-inhibition following HR episode(s) alleviates SCD mechanical hypersensitivity. TNFα-inhibitors are readily translatable to people with SCD. TNFα likely promotes allodynia throughout the nervous system due to VOE-induced multisystem inflammation. Future directions include determining the effects of long-term TNFα inhibition on baseline SCD hypersensitivity and ascertaining mechanisms of TNFα's contribution to SCD hypersensitivity.
KEYWORDS: Headache, Lifespan Manifestations of Childhood Onset Conditions, Diversity, Equity, Inclusion

141. Opioids for Headache Treatment Among Youth in the Emergency Department: Who gets them and Why?

Zahir R (Charlottesville, VA), Gould O, Dave R, Kepplinger D, Lateef T

OBJECTIVE: Routine use of opioids for headache can lead to worsening headaches and may contribute to opioid dependence. The main objective of this study is to determine the prevalence and clinical factors associated with opioid used as abortive therapy, for adolescents presenting with headache, in a pediatric emergency room.
METHODS: We reviewed electronic medical records of youth aged 11 through 21 years presenting to a large suburban pediatric emergency department between January 2014 and December 2020 timeframe. Charts were reviewed for demographics and clinical characteristics.
RESULTS: 277 youth were seen in for headache in and received an opioid abortive medication for it. Among those 68 (25 %) received it for a procedure such as lumbar puncture. Among the remaining 209 patients – 151 received morphine, 27 - hydromorphone/hydrocodone, 16 - oxycodone, tramadol - 6, meperidine 4 4, codeine/fiorcet/fentanyl – 3. Among patients who received an opioid, over half (57%) were female, 19.1 % had a prior headache history, 13.4% had seen a neurologist and one in four had a comorbid mental health disorder. In terms of headache specific factors, only 20.6 % were on daily headache prophylaxis. Notably 42% had a history of prior opioid use and 6% had used an ergot medication in the past.
CONCLUSIONS: Youth receiving opioids for headache treatment were more likely to be female, have significant mental health comorbidity and lacked access to neurology. Our findings may help identify youth at risk for opioid use and highlight the need for early identification and referral to a neurologist.
KEYWORDS: Headache

142. Attention Please! ADD/ ADHD Symptoms in a Pediatric Headache Clinic

Candee D (Salt Lake City, UT), Caplin D

OBJECTIVE: Pediatric headache is often related to significant problems with physical, academic, and social

functioning. When they co-occur, difficulties with attention and concentration can complicate treatment and adherence to a headache management plan. However, the impact of ADD/ADHD on functional disability is not yet known, nor is it clear that parents are aware of these co-occurring concerns or their impact on one another.

METHODS: Data was collected from two samples of children, ages 4 to 17, with persistent headaches presenting to an interdisciplinary pediatric headache clinic at an academic medical center (1,059 from Dec 2017-March 2021; 139 inclusive of Jan-Dec 2022). 61% female and 37% male; mean age 12.37 years. Parents completed questionnaires screening for headache-related disability, functional disability, and mental health-associated behaviors (i.e. attention, externalizing and internalizing).

RESULTS: Analyses indicate that parent-reported youth attention problems were significantly predictive of greater headache disability and functional disability ($R2=0.27$, $p < 0.05$). In separate analyses, significantly more patients (31%) reported clinically significant problems with attention and concentration than reported having a diagnosis and/or treatment of ADD/ADHD (21%; $p< 0.01$).

CONCLUSIONS: Attentional difficulties are prevalent and critically influence functional disability for youth with headache. However, for a majority of patients presenting to headache clinic, these hurdles are unidentified and untreated. The findings highlight the importance of mental health assessment in the pediatric headache population in order to improve headache-related health outcomes and to facilitate collaborative interventions with educators/school administrators.

KEYWORDS: Headache, Behavioral Neurology, Education

LIFESPAN MANIFESTATIONS OF CHILDHOOD ONSET CONDITIONS

143. Detecting Opsoclonus Myoclonus Ataxia Syndrome (OMAS): Associations of Eye Tracking Metrics with Cognitive Outcomes

Wu S (Markham, ON, Canada), White B, Brien D, Coe B, Yea C, Munoz D, Yeh E

OBJECTIVE: To evaluate 1) differences in free-viewing (FV) eye tracking metrics between children with OMAS and healthy age- and sex-matched healthy controls (HC), and 2) correlations of cognitive metrics with FV eye tracking metrics in children with OMAS and HC.

METHODS: Youth (3-17 years) with a diagnosis of OMAS ($n=9$) and HC ($n=14$) completed a FV eye tracking task (EyeLink 1000 Plus) and cognitive testing (6 cognitive domains) (NIH Toolbox). Mean macro-saccade (≥2° in amplitude) rate (MMSR) (saccades/s) for clip-aligned analyses were dichotomized into early (100–150ms post clip change) and late epochs (150–400ms post clip change). Normalized probability of fixations (NPF) (count/viewing duration) were dichotomized into early (0– 180ms) and late epochs (180–640ms).

RESULTS: Mean early epoch MMSR was more suppressed in OMAS (0.417, IQR 0.863) vs. HC (1.118, IQR 1.448; $p=0.019$). Mean late epoch NPF was less in OMAS (0.039, IQR 0.024) vs. HC (0.055, IQR 0.023; $p=0.030$). Higher early epoch MMSR correlated with higher scores on the Dimensional Change Card Sort (DCCS) Task ($r=0.508$, $p=0.026$). Higher late epoch NPF correlated with higher scores on the DCCS Task ($r=0.639$, $p=0.003$) and the List Sorting Working Memory (LSWM) Task ($r=0.706$, $p=<0.001$).

CONCLUSIONS: Suppressed saccade rates in the early epoch and less probability of fixation durations in the later epoch were seen in OMAS children; both correlated with set shifting abnormalities on cognitive testing. Further research evaluating eye tracking metrics as a screen for cognitive deficits is needed.

KEYWORDS: Lifespan Manifestations of Childhood Onset Conditions

MOVEMENT DISORDERS

144. Deep Brain Stimulation for Refractory Status Dystonicus in Children: Multi-Centre Case Series and Systematic Review

Vogt L (Toronto, ON, Canada), Yan H, Santyr B, Breibart S, Anderson M, Germann J, Fasano A, Lizarraga K, Hewitt A, Ibrahim G, Gorodetsky C

OBJECTIVE: We sought to better understand the workflow, outcomes, and complications of deep brain stimulation (DBS) for pediatric status dystonicus (SD). We present a comprehensive systematic review, alongside a multi-center case series of pediatric patients with SD treated with DBS.

METHODS: We collected individual data regarding treatment, stimulation parameters, and dystonia severity for a multi-center case series ($n=8$) and previously published cases ($n=77$). Data for case series patients was used to create probabilistic voxel-wise maps of stimulated tissue associated with dystonia improvement.

RESULTS: In our case series, DBS was implanted a mean of 25 days post-SD onset. Programming began a mean of 1.6 days after surgery. All eight patients in our case series and 73/74 reported patients in the systematic review had resolution of their SD with DBS, most within 2-4 weeks of surgery. All patients in the case series and 68/77 in our systematic review had DBS implanted to the globus pallidus pars interna (GPi). In addition to reversing SD, there was a mean dystonia improvement of 32% and 51% in our case series and meta-analysis, respectively. Stimulation of the ventral-postero-lateral GPi was associated with improvement in dystonia our case series. Mortality was 4% in the meta-analysis, which is lower than what has been reported for those treated with pharmacotherapy alone (10-12.5%).

CONCLUSIONS: DBS is a safe, feasible intervention that can reverse pediatric SD and improve survival. More work is needed to increase awareness of DBS in this setting, so that it can be implemented in a timely manner.

KEYWORDS: Movement Disorders, Neurocritical Care

145. Tic Severity and Function in Youth with Tourette Syndrome and Coprophenomena

Myers S (Rochester, NY), Mink J, Vermilion J

OBJECTIVE: To determine associations among tic severity and function in youth with Tourette Syndrome (TS) and coprophenomena compared to those with TS without coprophenomena.

METHODS: The University of Rochester and University of South Florida jointly conducted a CDC-funded cross-sectional Tic Impact Study. Data were collected from youth with TS and their caregivers and teachers. Family impact was measured in domains of parent health-related quality of life (HRQOL), family functioning, and total family impact. We conducted analyses to compare global and family function in youth with TS with (TS+copro) and without (TS-copro) coprophenomena. Wilcoxon rank-sum tests were used to compare scores on individual function and family function measures.

RESULTS: Of 170 subjects, 17(10%) exhibited coprophenomena. Subjects with TS and coprophenomena had higher tic severity scores than those without coprophenomena (TS+copro mean(SD) = 36.9(7.5), TS-copro = 20.8(8.3), p<0.0001). Patients with coprophenomena had lower scores for global function (TS+copro median (IQR) = 51 (45,59), TS-copro = 60 (52,65), p = .0042), family functioning (TS +copro = 43.8 (25,62.5), TS-copro = 59.4 (46.9,84.4), p = .0007), parent HRQOL (TS+copro = 57.5 (38.1,61.3), TS-copro = 72.5 (56.3,86.3), p = .0003), and total family QOL (TS+copro = 50.7 (38.2,58.7), TS-copro = 65.3 (54.2,80.6), p = .0042).

CONCLUSIONS: Youth with TS and coprophenomena had lower individual function, family function, and parent HRQOL than youth without coprophenomena. Coprophenomena presence may represent a more severe phenotype of TS and may be an indicator for earlier intervention.

KEYWORDS: Movement Disorders

146. Treatment of Pediatric Movement Disorders with Deep Brain Stimulation

MacLean J (Orange, CA), Olaya J, Liker M, Sanger T

OBJECTIVE: While commonly utilized in adults, deep brain stimulation (DBS) is mainly utilized only for specific genetic dystonias in pediatrics. We present a variety of movement disorders including secondary dystonia, tremor, ataxia, and chorea noted to have positive response to DBS.

METHODS: Subjects were implanted utilizing a staged procedure to identify optimal stimulation targets. Location for permanent DBS was ascertained over 4-7 days based on clinical response to test stimulation. All nineteen subjects were implanted in globus pallidus internus (Gpi.) Fifteen secondary dystonia subjects were also implanted in various thalamic nuclei including ventral oralis complex (Vo), ventral intermediate (VIM), ventral anterior (VA), ventral posterolateral (VPL,) and ventral lateral (VL) nuclei of thalamus, and subthalamic nucleus depending on response during initial testing stage. The subject with ataxia was implanted in VA. The subject with tics was implanted in nucleus accumbens. One subject with chorea was implanted in Vo and the other in VIM.

RESULTS: Two subjects with chorea demonstrated a decrease in the Abnormal Involuntary Movement Scale by 33% and 65% respectively. The ataxia subject had a decrease in their Scale for Assessment and Rating of Ataxia of 29%. The tic subject had a decrease in Yale Tic Severity Score of 57%. The secondary dystonia subjects had an average of 36% decrease in the Burke-Fahn-Marsden Dystonia Rating Scale.

CONCLUSIONS: DBS may have possible benefit in various pediatric movement disorders with different symptomatology. Variable targets may be needed based on both symptoms and patient-specific considerations.

KEYWORDS: Movement Disorders, Cerebral Palsy

147. Anxiety and Functional Impairment in Chronic Tic Disorder

Sapozhnikov Y (Rochester, NY), Esposito E, Adams H, Ross A, Walsh N, Oakes L, Vermilion J

OBJECTIVE: We aimed to evaluate anxiety in youth with Chronic Tic Disorder (CTD) and to determine the contribution of anxiety symptoms to functional impairment.

METHODS: In this cross-sectional study, youth with CTD were evaluated for Anxiety Disorders (Anxiety and Related Disorders Interview Schedule), global functioning (Children's Global Assessment Scale) and severity of tics (Yale Global Tic Severity Scale) and anxiety symptoms (Pediatric Anxiety Rating Scale). Tic severity and global functioning were compared between youth with and without Anxiety Disorders using pooled t-tests.

RESULTS: We enrolled 33 youth (Mage = 11.5 years, SDage = 2.9; 66.7% male). Over half (54.5%) of participants reported clinically significant anxiety symptoms, and 78.8% of participants met DSM-5 diagnostic criteria for at least one Anxiety Disorder. Youth with social phobia and generalized anxiety disorder (GAD) had greater tic severity (p = 0.0076 and p = 0.0011, respectively) compared to youth without these diagnoses. Youth without any Anxiety Disorder diagnosis had overall lower tic severity and better global functioning compared to those with an Anxiety Disorder diagnosis (p = 0.0001 and p = 0.017, respectively).

CONCLUSIONS: Anxiety Disorders and clinically significant anxiety symptom severity are common among youth with CTD. Anxiety Disorders are associated with greater tic severity and worse global function. The association between tic severity and anxiety in this sample suggests that there may be a relationship between these symptoms in youth with CTD. This may have implications for treatment of anxious youth with CTD.

KEYWORDS: Movement Disorders, Behavioral Neurology

148. Remote Assessment of Abnormal Movements in TANGO2 Deficiency Disorder

Vermilion J (Rochester, NY), Hewitt A, Mink J, Hull M, Sandkuhler S, Yang P, Mackenzie S

OBJECTIVE: To characterize abnormal movements in a sample of children with TANGO2 Deficiency Disorder (TDD), a rare genetic disorder characterized by metabolic crises, seizures, developmental disability and cardiac arrhythmias.

METHODS: Participants were recruited through the TANGO2 Research Foundation website, social media sites, and TANGO2-related disease Natural History Study through Baylor College of Medicine. The parent/caregiver of each participant uploaded videos of the child having abnormal movements of concern onto a secure storage drive. Four movement disorders experts independently reviewed videos and classified the phenomenology of abnormal movements as primary and secondary movement disorders. The experts met to review all videos together to reach consensus. The frequency of primary movement disorders and inter-rater reliability (IRR) pre- and post-consensus meeting were assessed.
RESULTS: Thus far, 12 subjects (75% male) have been evaluated, with a median number of 5.5 videos submitted per subject (range 1-32). Primary movement disorders included dystonia (66.7%), ataxia (16.7%), and unknown (8.3%). We identified more than one type of movement disorder in 58.3% of subjects. There was 1 participant with abnormal movements that could not be categorized from the videos/data provided and 1 participant that did not have a movement disorder. The pre-consensus meeting IRR was 0.64. After the consensus meeting, IRR was 0.89.
CONCLUSIONS: Dystonia and ataxia may be common movement disorders in children with TDD. Accurate classification of movement disorders in TDD has the potential to improve rates of diagnosis of the disease, inform our pathophysiological understanding of the disease, and contribute to clinical trial readiness for future treatment trials.
KEYWORDS: Movement Disorders, Neurogenetics

149. Long-term safety and durability of effect of ecopipam in pediatric patients with Tourette Syndrome: Results of a 12-month open-label extension (OLE) study

Gilbert D (Cincinnati, OH), Kim D, Miller M, Horine S, Saljooqi K, Karkanias G, Wanaski S, Cunniff T

OBJECTIVE: Assess the safety and durability of effect of long-term treatment with ecopipam, a first-in-class dopamine 1 receptor antagonist, that significantly reduced tics in the preceding 12-week Phase 2b (D1AMOND) randomized, double-blind, placebo-controlled clinical trial in pediatric patients with Tourette syndrome (TS).
METHODS: Children and adolescents who completed the D1AMOND study were eligible to participate. Patients received ecopipam (2 mg/kg/day oral dose) nightly for up to 12 months. The primary outcome was incidence of treatment related adverse events. The primary efficacy endpoint was the Yale Global Tic Severity Scale-Total Tic Score (YGTSS-TTS).
RESULTS: The most frequent treatment related adverse events were anxiety (6.6%), insomnia (5.8%), somnolence (5.8%), and depression (4.1%). No clinically significant changes were observed in lab values, vital signs, ECG, physical exams, the Columbia Suicide Severity Rating Scale, Abnormal Involuntary Movement Scale, Barnes Akathisia Rating Scale, Children's Depression Rating Scale-Revised, or the Pediatric Anxiety Rating Scale. Median YGTSS-TTS was 30.0 at baseline (n=121). YGTSS-TTS scores were meaningfully improved at 3 months (-7.8 $\pm$ 8.1; n=106), 6 months (-11.0 $\pm$ 8.8; n=87), 9 months (-11.6 $\pm$ 8.5; n=85), and 12 months (-11.8 $\pm$ 9.6; n=77); all $p < 0.0001$ compared to baseline. The Clinical Global Impression of TS-Severity, the YGTSS-Global Score, and the Child & Adolescent Gilles De La Tourette Syndrome-Quality of Life Total Score each improved at all time points; all $p < 0.001$.
CONCLUSIONS: In this OLE study in children and adolescents with TS, ecopipam demonstrated an acceptable safety profile and continued or improved control of tics.
KEYWORDS: Movement Disorders

150. Associations between Deep Brain Stimulation Duration and Changes in Basal Ganglia Excitatory/Inhibitory Balance in Children and Young Adults with Dystonia

Larsh T (Cincinnati, OH), Vadivelu S, Gilbert D, Wu S

OBJECTIVE: We sought to explore associations between basal ganglia aperiodic signals and time since deep brain stimulation (DBS) implantation in children and young adults with dystonia.
METHODS: We collected local field potential (LFP) data from children and young adults with the Percept PC (Medtronic, USA) neurostimulator, noting time between DBS implantation and each clinic visit. LFP data was analyzed offline, using the Irregular-Resampling Auto-Spectral Analysis (IRASA) method to separate aperiodic and oscillatory components in the power spectrum of LFPs. We then quantified the spectral offset (intercept) and spectral exponent (negative slope magnitude). Linear regression modeling was used to assess effects of time since DBS implantation on aperiodic activity (spectral offset/exponent), considering within-subject effects.
RESULTS: Six subjects were included (mean age at implantation: 17.3, range: 7.9-27.7), with four receiving bilateral GPi, one with unilateral GPi, and one with bilateral STN and bilateral GPi DBS. There were 43 LFP recordings available for analysis (35 GPi, 8 STN). Mean time since DBS implantation was 16.3 months (range: 1.6-70.3). Overall, basal ganglia aperiodic activity decreased with time since DBS implantation (spectral offset: $p = 0.02$; spectral exponent: $p = 0.006$). However, this varied within individual subjects and appeared to differ between children and young adults.
CONCLUSIONS: We found basal ganglia aperiodic activity tended to decrease with time since DBS implantation, indicating more basal ganglia excitation. This was not universal across subjects and may differ between children and young adults. Factors that may have contributed to this finding include changes in plasticity induced by DBS, dystonia, and neurodevelopmental processes.
KEYWORDS: Movement Disorders, Early Stage Investigator, Cerebral Palsy

151. How Often Does Tourette Syndrome Require Intervention?

Trulove S (Birmingham, AL), Gantz E, Rowe J, Dure L

OBJECTIVE: Tics are normal movements that are considered abnormal due to their frequency and context.

Approximately 1% of school-aged children exhibit features consistent with Tourette syndrome (TS) or chronic tics (CTD), conditions chiefly defined by tic duration. A 2019 AAN practice parameter recommended education and cognitive behavioral interventions as first-line therapies. However, it is unknown what percentage of diagnosed individuals require intervention.
METHODS: Data from a single center with two dedicated pediatric movement disorder specialists from 2017-2022 have been abstracted to determine the natural history of TS/CTD regarding need for intervention. In this institution, a Cognitive Behavioral Intervention for Tics (CBIT) Clinic has provided first-line therapy for individuals warranting intervention since 2010, additionally receiving community referrals. Of individuals diagnosed with TS/CTD during this timeframe, the number referred to CBIT was determined. Patients referred to CBIT by pediatric movement disorder specialists were compared those referred by community providers.
RESULTS: Preliminary analysis indicates that 752 individuals were diagnosed with TS/CTD by movement disorder specialists. Of this group, only 14.4% warranted an intervention and were referred to CBIT. In contrast, outside providers referred twice as many patients to CBIT during this period. Analysis is ongoing regarding the relative efficacy of therapy and suitability of community referrals.
CONCLUSIONS: This is the first description of the likelihood of a child requiring an intervention for tics in a large, established movement disorder practice. This data supports that the majority of pediatric patients with TS/CTD do not require intervention and emphasizes the importance of education regarding the diagnosis and treatment indications.
KEYWORDS: Movement Disorders

152. Hearing and Vestibular Issues in Sickle Cell Disease Patients

Sriram S (Baltimore, MD), Andresen N, Alick A, Pecker L, Lanzkron S, McIntyre T, Kheradmand A, Nelson D, Ward B, Lance E

OBJECTIVE: Hearing and vestibular functions can be affected by sickle cell disease (SCD) but the associated dysfunctions are understudied. The objective of this study was to investigate the prevalence and risk factors for self-reported hearing loss and vestibular disorders in children and adults with SCD.
METHODS: A prospective survey was administered to adults and children with/without SCD from the hematology clinic and included standard hearing and balance inventories.
RESULTS: The survey was completed by 86 participants with SCD (66 adults, 20 children) and 16 control participants. Self-reported hearing problems, tinnitus, dizziness, and headaches were all more prevalent in adults with SCD compared to children with SCD ($p<0.02$ for all). Despite similar percentages of adults with SCD and control participants reporting an isolated hearing problem (26% vs 19%, non-significant), adults with SCD reported a dizziness and/or hearing problem much more frequently than controls (60% vs 25%, $p=0.005$) as well as dizziness or imbalance (53% vs 19%, $p=0.006$). SCD patients with dizziness were 74.5 times more likely to experience a fall than those with no dizziness. ($p<0.0001$).
CONCLUSIONS: Dizziness and imbalance symptoms are more common in SCD patients and may be associated with increased risk of falls. These results support the need for vestibular and audiological care for patients with SCD and further studies to understand the etiology of these dysfunctions.
KEYWORDS: Movement Disorders, Early Stage Investigator

153. Acquired Cerebellar Dystonia is Alleviated by Thalamic, but not Basal Ganglia, Deep Brain Stimulation

Nguyen M (Houston, TX), Sillitoe R, Gill J

OBJECTIVE: Acquired dystonias, resulting from damage to subcortical structures, are often refractory to treatments used in primary dystonias. The purpose of this study is to model acquired dystonia via electrolytic lesioning of the cerebellar outflow tracts in mice and, subsequently, to determine whether manipulation of upstream nodes in subcortical networks can improve dystonic symptoms.
METHODS: Bilateral electrolytic lesions of the cerebellar outflow tracts were produced using stereotactically targeted metal electrodes. Dystonia was assessed using the dystonia rating scale and nuchal electromyography. Bipolar electrodes were used to deliver 130Hz deep brain stimulation (DBS) to either the thalamus or the basal ganglia in lesion and sham lesion animals.
RESULTS: Compared to sham lesions, mice with electrolytic lesions to the bilateral cerebellar outflow tracts acquired an immediate, severe dystonia. DBS of the centrolateral thalamic nuclei led to significant improvement of the lesion associated dystonia. In contrast, DBS of the dorsolateral striatum did not significantly alter dystonic symptoms.
CONCLUSIONS: In clinical studies, dystonia is associated with dysfunction in the "dystonia network," comprised of the cerebellum, thalamus, basal ganglia, and sensorimotor cortex. This study finds that structural damage to the cerebellar outflow tracts produces a severe dystonia in mice. In addition, DBS of the thalamus, but not the basal ganglia, significantly reduces the dystonia. These findings point to the thalamus as a convergent site of the subcortical dystonia network. Furthermore, the current study indicates that cerebellar associated dystonias may be more amenable to thalamic DBS as compared to the more commonly targeted basal ganglia.
KEYWORDS: Movement Disorders, Cerebral Palsy, Early Stage Investigator

154. Deep brain stimulation outcomes in pediatric dystonia: the Phoenix Children's experience

Hadziahmetovic U (Phoenix, AZ), Kruer M

OBJECTIVE: Deep brain stimulation (DBS) has been used in adult patients for treatment of movement disorders for the past two decades and its popularity has grown in the pediatric population. Our aim was to determine the effect of DBS therapy on dystonia symptoms in children and adolescents.

METHODS: A retrospective chart review was performed using the Phoenix Children's electronic medical record, Sunrise Clinical Manager (Allscripts). Pediatric patients with dystonia-predominant presentations who had undergone DBS were included in the analysis. The Barry-Albright Dystonia (BAD) score was recorded for the following intervals: initial score (time 0), 3 months post-DBS placement, 6 months, 12 months, 18 months, and 24 months post-DBS placement. A repeated measures ANOVA [KM1] with multiple comparisons was performed to analyze the data.
RESULTS: BAD scores were reviewed for 10 patients. Although individual responses varied, overall there was a significant difference between pre-post implantation BAD scores (μpre=23.4, (μpost=19.8; range=9-32; p=0.0096). Differences became most apparent after surgery beginning at 12 months post-implantation (p=0.0209) and persisting at 18 months (p=0.0291) and 24 months (p=0.0416).
CONCLUSIONS: DBS significantly reduces dystonia severity in pediatric patients. The greatest benefits were noted 12 months or more after DBS placement, similar to prior findings in pediatric dystonia. Future work will assess DBS outcomes in other pediatric movement disorders, including chorea, myoclonus, and tremor. Multi-center studies accompanied by deep phenotyping are needed to determine predictors of DBS outcomes in order to identify the factors that best predict DBS response.
KEYWORDS: Movement Disorders

155. Highlighting a novel, stepwise pathway for the in-hospital management of children with acutely worsening dystonia

Vogt L (Toronto, ON, Canada), Yang K, Tse G, Gorodetsky C

OBJECTIVE: Dystonia is common in children with acquired and inherited neurological disorders. Status dystonicus (SD) is the most severe form of dystonia that can lead to life-threatening complications if not treated promptly. We identified a local provider knowledge gap in the acute management of dystonia, leading to uncertainty and delays in care. To our knowledge, no in-hospital clinical pathway exists for the ward-based management of acute dystonia. We hypothesized that a stepwise clinical pathway would standardize and improve comfort in managing hyperacute dystonia.
METHODS: We formed a multidisciplinary working group and developed a pathway based on literature review and expert consensus. Aims of the pathway included: reducing delays in recognition and treatment of acute dystonia, limiting variation in management, and decreasing progression to SD. A survey was administered to providers assessing knowledge and comfort post-implementation.
RESULTS: There has been high usability with 58% (18/31) of providers surveyed having used the pathway at least once. Provider comfort has improved, with 89% (25/28) of respondents reporting increased comfort managing SD due to the clarity of the pathway and stepwise directions.
CONCLUSIONS: The pathway fills a promising gap in the in-hospital management of dystonia and has led to increased provider comfort.
KEYWORDS: Movement Disorders

156. The rise and fall of functional tic-like behaviors in adolescent patients – a retrospective study

Tomczak K (Boston, MA), Worhach J, Rich M, Swearingen Ludolph O, Eppling S, Sideridis G, Katz T

OBJECTIVE: During the COVID-19 pandemic, an influx of adolescents presented to neurology and psychiatry clinics with acute onset functional tic-like movements. Multifactorial causes included stress related to the pandemic, increased anxiety and depression, increased social media use and exposure to online influencers. We sought to evaluate predisposing psychosocial factors and to examine outcomes after pandemic isolation protocols were lifted.
METHODS: A retrospective chart review of 56 patients seen at Boston Children's Hospital with a diagnosis of functional tics was completed. Psychosocial factors such as previous mental health diagnoses were recorded. To determine if patients improved, results from the Clinical Global Impression Improvement (CGI-I) and Severity (CGI-S) scales were obtained from follow-up visits August 2022 to December 2022. CGI-I assessed progression of functional tics and improvement or worsening over time; CGI-S assessed overall function.
RESULTS: The majority of patients (96%) were females assigned at birth; 45% identified as gender diverse. Sixty-eight percent had no prior history of tics. Most patients had preceding mental health struggles, including 93% with anxiety disorders and 71% with depressive disorders. On CGI-I scores, 79% of patients showed improvement in tic-like behaviors at follow-up. In terms of overall function, clinicians rated most patients as normal to mildly ill (71.4%) at follow-up; a subset developed other functional neurologic symptoms.
CONCLUSIONS: Increase in functional tics in adolescents during COVID-19 pandemic resolved for 79% of patients. A subset has received other neuropsychiatric diagnoses. Recognition of contributing psychosocial factors will allow optimal support for these patients.
KEYWORDS: Movement Disorders, Behavioral Neurology, Global Neurology

157. National Prescribing Practices for Dystonia Among Providers in the United States

Davis S (Kansas City, MO), Botteron H, Kane N, Gelineau-Morel R

OBJECTIVE: While multiple oral medications are used to treat dystonia, limited information exists on current prescribing practices. This study analyzes prescribing practices for dystonia in the United States, evaluating variations in dosing and impact of co-morbidities.
METHODS: Querying the Cerner Real World database from 2014 to 2019 for children age 0-18 with an ICD-10 diagnosis containing "dystonia" resulted in 11,300 inpatient and outpatient encounters. Information extracted included current dystonia medications (baclofen, clonidine, carbidopa-levodopa, gabapentin, tetrabenazine, trihexyphenidyl, and benzodiazepines including diazepam, clonazepam, midazolam, and lorazepam), medication dosing, and co-morbid diagnoses of cerebral palsy, epilepsy, or spasticity.

Encounters without current weight were excluded from medication dosage analysis.
RESULTS: Benzodiazepines were most commonly prescribed for dystonia (61.2%), then baclofen (12.0%) and clonidine (9.5%). Patients with cerebral palsy (n=5639) were prescribed baclofen more than clonidine (16.2% vs 7.0%), while patients without cerebral palsy (n=5731) were prescribed clonidine more frequently than baclofen (11.7% vs 7.6%). All medications showed decreased mean dosing in milligram per kilogram (mg/kg) as patient weight range increased. Mean weight-based dosing for baclofen varied by weight group from 0.162 mg/kg/dose (110-120 kg group, mean dose 18.3 mg) to 0.662 mg/kg/dose (0-20 kg group, mean dose 9.3 mg).
CONCLUSIONS: Benzodiazepines, baclofen, and clonidine are the most common medications prescribed for dystonia in the United States. Medication dosing is variable, with patients of higher weights receiving smaller weight-adjusted doses. There is a need for dystonia medication selection and dosing guidelines to standardize care and inform dosing recommendations for clinical trials.
KEYWORDS: Movement Disorders, Cerebral Palsy

NEUROCRITICAL CARE

158. Using interleukin-18, Eotaxin-1, and Eotaxin-3 to identify brain injury in neonates with congenital heart disease

Ghosh S (Brooklyn, NY), Candelario-Jalil E, Jacobs J

OBJECTIVE: Serum biomarkers for brain injury in neonates with congenital heart disease (CHD) would provide a bedside tool for early identification and intervention. In this preliminary study, we aim to evaluate potential inflammatory cytokines and chemokines as biomarkers for the detection of brain injury in neonates with CHD.
METHODS: We prospectively enrolled neonates diagnosed in-utero with congenital heart disease and obtained serum samples at various time points from birth, before and after surgery. Samples were analyzed using a human cytokine/chemokine multiplex assay. Brain injury was diagnosed on brain MRI before surgery.
RESULTS: Samples from seven neonates at four time points before surgery and three time points after surgery were analyzed. A significant difference was found in neonates with brain injury compared to CHD neonates without brain injury. Elevations in interleukin (IL)-18 pre- and post-operative ($p=0.007$), IL-18 pre-operative ($p = 0.046$), Eotaxin-1 pre-operative ($p= 0.011$), and Eotaxin-3 pre- and post-operative ($p=0.026$) were found in CHD neonates with brain injury.
CONCLUSIONS: This is the first novel use of IL-18, Eotaxin-1, and Eotaxin-3 in the detection of brain injury for neonates with congenital heart disease. These biomarkers may provide an actionable target for neuroprotection through immunomodulation. Larger cohorts are needed to determine the significance and clinical utility of these biomarkers.
KEYWORDS: Neurocritical Care, Neonatal Neurology, Neuroimmunology

159. A Comparison of Treatment Pathways for Seizures in Newborns Across Level II and III Neonatal Intensive Care Units

Dickman J (Madison, WI), Carrasco McCaul M

OBJECTIVE: Neonatal seizures represent a neurological emergency. Early recognition and treatment is essential to reduce morbidity and mortality. This study investigated the neonatal seizure treatment pathways employed by Level II/III neonatal intensive care units (NICUs) across the United States, in an effort to identify areas of consensus and variability.
METHODS: We surveyed personnel associated with Level II/III NICUs by reaching out to our professional network and the membership of the Newborn Brain Society and the Child Neurology Society. The electronic survey aimed to explore the varying institutional practices regarding evaluation and management of neonatal seizures. Access to anti-seizure medications and on-site EEG monitoring was also queried.
RESULTS: Only 26% of surveyed NICUs have an established clinical practice guideline or pathway available for treating neonatal seizures. Only 26% endorsed having a formal and specific definition for neonatal seizures, while 23% confirmed having no EEG monitoring available to them on-site. 11% of surveyed NICUs did not have access to anti-seizure medications within their unit at the time of survey and instead rely on pharmacy to send when needed.
CONCLUSIONS: Our research determined there is widespread variability in neonatal seizure detection and response from Level II and III NICUs, highlighting the lack of equitable access to neonatal seizure treatment. Specifically, our data suggests that areas of potential improvement include the implementation of a universal protocol, access to medications, and the need for education surrounding treatment pathway establishment. These developments may eventually provide earlier detection, evaluation, and treatment of seizures in newborns.
KEYWORDS: Neurocritical Care, Neonatal Neurology

160. Measurement Of Optic Nerve Sheath Diameter By Trans-Orbital Ultrasound To Detect Raised Intracranial Pressure In Children.

Bansal AB (Barnala, India), Tiwari LT, Kumar PK

OBJECTIVE: Raised Intracranial Pressure(ICP), a critical illness in children, can be appropriately managed by timely diagnosis. Optic nerve sheath diameter(ONSD) measurement by trans-orbital ultrasonogram(USG) is non-invasive point-of-care tool to recognize raised ICP however there are very limited studies globally in pediatric population. Our study aims to identify the difference in ONSD among pediatric patients with normal and raised-ICP and to achieve the cut-off value for diagnosing raised-ICP.
METHODS: A hospital based observational comparative study conducted in an institute of national importance in

India including patients aged 2-14 years admitted in pediatrics department using complete enumeration technique. Children with clinical features of raised-ICP(Muir's criteria) were included in raised-ICP group and compared with the patients without any signs of raised-ICP. ONSD was measured in both groups on Day-1 and Day-2 of admission. Final ONSD measurement was done on any day between day 4th-7th. On each day, average of the three readings taken from each eye and mean was used.

RESULTS: Out of 137 patients recruited, 34 had raised-ICP and 103 had normal ICP. Mean ONSD on day- 1 was found to be higher in the raised-ICP group(Mean=4.99±0.57) as compared to normal ICP group(Mean= 4.06±0.40) ($p<0.01$). Mean ONSD on day 2 also was higher in raised-ICP patients(Mean=4.94±0.55) in comparison to normal ICP patients(Mean=4.04±0.40) which was statistically significant($p<0.01$). The cut-off ONSD value for detecting raised-ICP was estimated to be 4.46 mm on ROC curve with area-under-curve 0.906(95% CI,0.844–0.968), 85.3% sensitivity and 86.4% specificity.

CONCLUSIONS: Measurement of ONSD by trans-orbital ultrasound was able to detect raised-ICP with excellent discriminatory performance.

KEYWORDS: Neurocritical Care

161. Accidental ingestion of marijuana in children 0 to 6 years of age: A single site retrospective cohort

Fonseca L (Dayton, OH), Dereci L, Ochoa P, Elliott J, Taylor M, Kumar G

OBJECTIVE: The legalization of medical marijuana has increased accidental exposure to marijuana in children under 6 years of age. In our study we explored the prevalence and clinical presentation of accidental ingestion of cannabis in children of this age group in Ohio.

METHODS: This was a retrospective cohort study from Dayton Children's Hospital (DCH). Children aged 0 to 6 years with a diagnosis of accidental ingestion of cannabinoids between 01/01/2010 through 09/01/2022 were included. We collected variables on age at ingestion, source and location of cannabis ingestion, parental use of drugs, and patient demographics.

RESULTS: 123 patients were included. Majority were female (63.4%), white (51.2%) and with Medicaid as their primary insurance (84.6%). The mean age at ingestion was 2.3 years (±1.6). 72.4% of patients were admitted to the hospital, with 14% admitted to the ICU. The most common product was cannabinoid edibles (58.6%). Prominent neurological symptom at onset included altered mental status (74%). A head CT scan was performed on 54.5% of patients, of which 88.6% were normal. There was a 14-fold increase in accidental marijuana cases pre-2017 (8 cases) versus post-2017 after the legalization of marijuana in Ohio (115 cases).

CONCLUSIONS: The number of patients presenting to the Emergency Department at DCH has increased 14-fold since the legalization of marijuana in Ohio. The most common presentation was altered mental status and majority of patients required admission and received a head CT scan. Accidental exposure to medical marijuana should be considered a common cause of altered mental status in young children.

KEYWORDS: Neurocritical Care, Neuroimaging, Education

162. Post-Intensive Care Syndrome in Pediatrics: Physical Symptom Burden following Neurocritical Care

Agbabian S (Houston, TX), Schultz R, Ramirez J, Ramirez B, Evans A, Risen S

OBJECTIVE: Advances in critical care medicine have shifted outcomes to increased morbidity, especially in children with neurological involvement. The primary aim was to describe the types and number of physical symptoms (physical symptom burden, PSB) in children following neurocritical illness. Secondarily, we explored the relationship between global functional outcomes and PSB.

METHODS: Retrospective analysis of 50 children (1 month – 18 years) admitted with neurocritical illness to the Pediatric Intensive Care Unit (PICU) of a large tertiary children's hospital, subsequently seen in the post-PICU clinic. Chart review obtained relevant clinical information including etiology, Functional Status Scale score (FSSs), EEG results, MRI findings, and the presence of physical symptoms.

RESULTS: Following neurocritical illness, most children (82%) report physical symptoms; the most common physical symptoms were motor deficits (50%), sleep issues (39%) and fatigue (31%). Physical symptom profiles varied by injury etiology, with the greatest PSB in infectious/inflammatory disorders. Brainstem, basal ganglia, and hypoxic brain injury on neuroimaging and seizures on EEG increased the PSB. While statistical evidence suggests a correlation between FSSs and PSB ($p<0.0158$), the data spread was large ($R2 = 0.11$).

CONCLUSIONS: Most children in our cohort experienced ongoing physical symptoms. Understanding risk factors for increased PSB and the relationship to etiology can help providers proactively monitor physical symptoms in this population. Importantly, the FSS, a global outcome measure, is inadequate to assess the PSB in the outpatient clinical setting. Measurement of specific physical symptoms is essential in outpatient care of children following neurocritical illness.

KEYWORDS: Neurocritical Care, Lifespan Manifestations of Childhood Onset Conditions

163. A Clinical Analysis of Parental Stress Following Neurocritical Illness in Children

Evans A (Houston, TX), Schultz R, Agbabian S, Edmondson E, Fisher K, Ramirez B, Lance E, Risen S

OBJECTIVE: While parents of children in the intensive care unit (ICU) report significant stress, less is known about clinical factors contributing to the degree of parental stress. The primary aims of this project were to evaluate the degree of parental stress in a post-PICU clinic and to explore the relationship between parental stress and their child's clinical course. We hypothesized that parental stress levels were independent of the child's injury severity or outcomes.

METHODS: Retrospective chart review of 73 child/parent dyads admitted with neurocritical illness to a tertiary

children's hospital, subsequently seen in the post-PICU clinic. Clinical information included demographics, etiology, Functional Status Scale scores (FSSs) at PICU discharge and first clinic visit, and ongoing clinical symptoms. Parental stress was measured using Impact of Event-Revised scale score (IoERss) collected at the first post-PICU clinic visit.
RESULTS: Over half (53%) of parents in the post-PICU clinic reported moderate–severe stress; only 2 parents denied any symptoms. Parental IoERss did not correlate with child's injury severity (duration of intubation, length of PICU and hospitalization) or FSSs. There was a significant association between maternal IoERss and child's ongoing physical symptoms but not behavioral or cognitive sequelae.
CONCLUSIONS: Parents experience significant stress following their child's critical illness, independent of the overall functional outcomes of the child. While ongoing physical symptoms appear to impact maternal stress levels, overall parental coping seems to be intrinsic to the parent. A better understanding of variables contributing to parental stress allows providers to optimize care for the whole family.
KEYWORDS: Neurocritical Care

164. Electroencephalography associations of cerebral injury in the pediatric intensive care unit

Sansevere A (Washington, DC), Keenan J, Conley C, Staso K, Harrar D

OBJECTIVE: To assess EEG background features, including epileptiform discharges (ED) and electrographic seizures (ES), as a marker of cerebral injury in the pediatric intensive care unit (PICU).
METHODS: Prospective study of patients admitted to the PICU from July 2021 to January 2023. We excluded patients with a known history of epilepsy and/or pre-existing cerebral injury. Clinical variables collected included age, sex, reason for admission, EEG background, electrographic seizures (ES), and neuroimaging findings. EEG background, epileptiform discharges (ED), and ES were defined in accordance with American Clinical Neurophysiology Society standardized critical care EEG terminology. Descriptive statistics were used to describe clinical variables. Specificity/sensitivity and odds ratio (OR) were applied to assess associations of EEG background metrics and cerebral injury.
RESULTS: We reviewed 197 patients with continuous EEG. Forty-two percent were female, and the median age was 3.5 years. The most common admission diagnosis was cardiac arrest (24%). 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%. EDs (Odds Ratio 7.11 (95% Confidence Interval 3.1-16.3), $p<0.0001$) and ES (OR 9.4 (2.7-32), $p=0.0004$) were associated with cerebral injury. A slow disorganized background without EDs or asymmetry was associated with the absence of cerebral injury (OR 0.096 (95 CI 0.05-0.2), $p<0.0001$).
CONCLUSIONS: EEG background features and ES may serve as a marker of cerebral injury when confirmatory imaging is delayed due to clinical instability or insensitive in early stages of injury.
KEYWORDS: Neurocritical Care

165. EEG Predictors of Neurologic Injury in Patients undergoing Extracorporeal Membrane Oxygenation

Ryan J (Washington, DC), Sansevere A, Keenan J, Staso K, Conley C, Harrar D

OBJECTIVE: To assess electrographic associations of brain injury in children undergoing extracorporeal membrane oxygenation (ECMO)
METHODS: Retrospective review of patients on ECMO in the pediatric and cardiac intensive care units (PICU/CICU) at a single center from August 2019 to December 2022. We included the first ECMO run and evaluated the first 24 hours of EEG. Patients with known cerebral injury were excluded. Clinical variables included age, sex, ECMO indication, presence or absence of congenital heart disease, duration on ECMO, ECMO type(veno-arterial (VA)/veno-venous (VV)), electrographic seizures(ES), and cerebral injury. A chi-squared test was used to assess the association of EEG features, ES, and cerebral injury.
RESULTS: We included 112 patients, median age 2.7 (Interquartile range(IQR) 0.4-31.2) months and 44% were female. The most common indication for ECMO was cardiopulmonary arrest (45%) and 84% had congenital heart disease. Nineteen percent were admitted to the PICU and 81% were admitted to the CICU with a median duration on ECMO of 85.3 hours (IQR 49.1-155.6). VA ECMO was the most common approach to cannulation (90%). A mildly abnormal EEG background was the most common finding (77%) and 38% had ES. Fifty-three percent had cerebral injury and the most common injury was anoxic (56%, 33/59). A severely abnormal EEG background ($p=0.028$) and presence of ES ($p<0.0001$) was associated with cerebral injury.
CONCLUSIONS: Severity of EEG background and presence of ES is associated with cerebral injury in patients on ECMO. The ability of these features to predict the type and degree of cerebral injury remains unclear.
KEYWORDS: Neurocritical Care

166. Impact of physiologic parameters on outcome after arteriovenous malformation rupture in pediatric patients

Yan F (Washington, DC), Keenan J, Staso K, Conley C, Sansevere A, Harrar D

OBJECTIVE: Arteriovenous malformations (AVMs) are the leading cause of intracranial hemorrhage (ICH) in children; however, little is known about the critical care management of pediatric ruptured AVMs. We evaluate the impact of critical care management on neurologic outcome after AVM rupture in children.
METHODS: Retrospective study of patients <18 years with ICH secondary to AVM rupture admitted to a single center from 2011-2023. Physiologic parameters were collected for the first 7 days after admission. Poor neurologic outcome was defined as Pediatric Stroke Outcome Measure score ≥1. Fisher's exact test was used to evaluate associations between physiologic parameters and outcome.

RESULTS: Forty-seven patients met inclusion criteria. The median age was 12.4 years (IQR 7.7-14.8), and 62% (29/47) had a poor outcome at discharge. Forty patients had hypertension (SBP ≥95th percentile), 20 had hyperthermia (T ≥38°C), 19 had increased intracranial pressure (ICP ≥20 mmHg), 16 had hypotension (SBP ≤5th percentile), 10 had decreased cerebral perfusion pressure (CPP <50 mmHg), and 7 had hyperglycemia (blood glucose ≥200 mg/dL) during the first week. Hyperthermia during the first 24 hours (37% vs. 0%; $p = 0.0037$), decreased CCP and hyperglycemia during the first 72 hours (63% vs. 0%, p=.0293; 25% vs. 0%, $p = 0.0429$, respectively), and hyperthermia any time during the first week (69% vs. 28%, $p = 0.0065$) were associated with poor outcome.
CONCLUSIONS: For children with ICH due to ruptured AVM, hyperthermia, decreased CPP, and hyperglycemia are associated with poor neurologic outcome – suggesting potential targets for improved critical care management in this population.
KEYWORDS: Neurocritical Care, Stroke

167. Ictal-Interictal Continuum in the Pediatric Intensive Care Unit

Sansevere A (Washington, DC), Pickup E, Keenan J, Conley C, Staso K, Harrar D

OBJECTIVE: To describe the incidence and imaging correlates of the Ictal Interictal Continuum (IIC) in the Pediatric Intensive Care Unit (PICU).
METHODS: Prospective study of patients admitted to the PICU at Children's National Hospital from July 2021 to January 2023. All patients with continuous EEG were screened for periodic and rhythmic patterns. We then applied the American Clinical Neurophysiology Society standardized critical care EEG terminology for the IIC to each pattern. We excluded patients with epilepsy and/or remote cerebral injury. Clinical variables included age, sex, reason for admission, EEG background, and neuroimaging findings. Descriptive statistics were used to describe clinical variables and IIC characteristics.
RESULTS: Of patients screened, 21% (39/189) had a rhythmic and/or periodic pattern, and 12% (22/189) met IIC criteria. The median age was 5.7 years (IQR 0.5-12), and cardiac arrest was the most common admission diagnosis (64%; 14/22) among patients with an IIC pattern. Sixty-eight percent (15/22) met a single IIC criterion, and the remainder met two. The most common criteria met was periodic discharges (PD) >1.0 Hz and ≤2.5Hz over 10 s,(criteria 1) (27%;6/22), and the most common combination was criteria 1 with criteria 2(PD >0.5 and but ≤1.0 over 10 s Hz with a plus modifier or fluctuation(18%;4/22). ES were identified in 82% (18/22) and cerebral injury in 91% (20/22). The most common neuroimaging finding was global anoxia (82%;9/22).
CONCLUSIONS: The IIC is a relatively common EEG pattern in the pediatric ICU and suggests cerebral injury. The approach to treatment of the IIC requires further study.
KEYWORDS: Neurocritical Care, Epilepsy

168. EEG stages of increased ICP after pediatric cardiac arrest

Horvat D (Washington, DC), Keenan J, Staso K, Conley C, Harrar D, Sansevere A

OBJECTIVE: Describe EEG findings of presumed increased intracranial pressure (ICP) after pediatric cardiac arrest.
METHODS: This is a prospective study of patients admitted to the pediatric intensive care unit (PICU) at a single center from July 2021 - January 2023. We screened patients on continuous EEG (cEEG) after cardiac arrest for clinical changes and/or neuroimaging suggestive of increased ICP post arrest. Patients requiring anti-seizure medications that could influence the EEG background were excluded. A board-certified epileptologist applied the American Clinical Neurophysiology Society standardized critical care EEG terminology at 6-hour intervals. We collected age, sex, EEG background, and neuroimaging findings. We described clinical variables with descriptive statistics.
RESULTS: We identified 5 patients, with median age 23 months (Interquartile range 37 months), 20% were female. We identified five stages: Stage 1 (burst suppression), 2 (discontinuous/continuous + multifocal or periodic discharges), 3 (burst suppression/discontinuous with periodic discharges), 4 (gradual voltage attenuation), and 5 (diffuse attenuation). Durations were Stage 1: 2-7 hours, 2: 2.5-33 hours, 3: 0.5-6.25 hours, 4: 0.5-7.5 hours. We could not accurately calculate the duration of Stage 5 given no uniform cEEG discontinuation pattern around brain death. Clinical change occurred in Stage 3 in two patients. Remaining patients presented without cranial nerve function. All patients had global anoxic brain injury.
CONCLUSIONS: EEG stages of increased ICP have not been systematically studied after pediatric cardiac arrest. Once established, these stages may offer a therapeutic target to prevent increased ICP in other populations at risk of cerebral edema and herniation.
KEYWORDS: Neurocritical Care

NEURO-CUTANEOUS DISORDERS

169. Presymptomatic Treatment in Children with Sturge-Weber Syndrome

Valery C (Baltimore, MD), Iannotti I, Ou Y, Pinto A, Comi A

OBJECTIVE: This retrospective review of clinical data aims to assess the impact of presymptomatic treatment in young children with Sturge-Weber syndrome. Seizure onset before the age of two is indicative of poorer neurologic outcome. Pre-symptomatic treatment during this critical period before seizure onset may delay seizure onset and improve outcome. Bilateral brain involvement is usually associated with early age of seizure onset and worse outcome.
METHODS: This two-centered, IRB approved, retrospective study (2009-2022) analyzed records from patients with Sturge-Weber Syndrome (SWS) brain involvement. Clinical data recorded (REDCap database) included demographics,

age of seizure onset (if present), brain involvement extent (unilateral versus bilateral) port wine birthmark (PWB) extent, family history of seizure, presymptomatic treatment (PS) if received, neuroscore, and seizure medication.
RESULTS: 80 patients were included (42 female) and 28 received presymptomatic treatment (5 aspirin only, 13 aspirin and levetiracetam; 8 aspirin and oxcarbazepine, 2 other). Presymptomatically treated patients were more likely to be seizure-free at 2 years of age (13 of 28; 46% versus 9 of 52; 17%; p=0.005). A greater percentage of PS patients had bilateral brain involvement (39% treated compared to 15% untreated; p=0.02). Median neuroscore at 2 years of age was better in presymptomatically treated patients but this was not statistically significant.
CONCLUSIONS: Presymptomatic treatment is a promising approach to young children diagnosed with Sturge-Weber syndrome prior to the onset of seizures. Further study is needed, including prospective drug trials and long term neurologic outcome, to further assess this approach and determine the best presymptomatic treatment.
KEYWORDS: Neuro-Cutaneous Disorders, Epilepsy, Neurodevelopmental Disorders

170. Preventative Treatment of Tuberous Sclerosis Complex with Sirolimus: Safety and Preliminary Efficacy

Ritter D (Cincinnati, OH), Capal J , Franz D, Griffith M, Bebin M, Northrup H, Koenig M, Mizuno T, Galndi S, Zhang W, Setchell K, Prada C, Holland K, Horn P, Krueger D

OBJECTIVE: Tuberous Sclerosis Complex (TSC) results from overactivity of the mechanistic target of rapamycin (mTOR). Sirolimus and everolimus are mTOR inhibitors that treat most facets of TSC disease but are understudied in infants. We sought to understand the safety and potential efficacy of preventative sirolimus in infants with TSC.
METHODS: We conducted a phase 1 clinical trial of precision-dosed sirolimus treating five patients until 12 months of age based on their current age, size, predicted growth, and sirolimus blood levels measured by mass spectrometry. Enrolled infants had to be less than six months of age, not have had a prior seizure, and not have a clinical indication for sirolimus treatment. Adverse events (AEs), tolerability, seizure characteristics, and developmental profiles were tracked through 24 months of age.
RESULTS: There were 92 AEs, with 34 possibly, probably, or definitely related to treatment. Of those, only two were Grade 3 (both elevated lipids) and all AEs were resolved by the age of 24 months. During the trial, 94% of sirolimus levels were in the expected range, and 2700 out of 2941 (92%) doses were given. Of the five patients, four had normal development, one had possible autism spectrum disorder, and three developed seizures (but were well-controlled on medications).
CONCLUSIONS: These results show that sirolimus is both safe and tolerated when treating infants with TSC preventatively in the first year of life. Additionally, the preliminary work suggests a favorable efficacy profile which will be studied further in a phase 2 clinical trial.
KEYWORDS: Neuro-Cutaneous Disorders, Epilepsy, Experimental Therapeutics

171. Sturge Weber Syndrome Neurologic Symptoms, Quality of Life, and Potential Biomarkers

Comi A (Baltimore, MD), Kimbrell B, Hammill A, Pinto A, Yeom S

OBJECTIVE: Sturge Weber Syndrome (SWS) is a rare neurocutaneous disorder with abnormal vasculature affecting the leptomeninges, eye, and facial skin. These dilated blood vessels lead to symptoms including seizures, hemiparesis, visual deficits, pain, cognitive problems, and social stigma across the lifespan. Longitudinal analysis of clinical factors and biomarkers is needed for prognostication.
METHODS: Sixty one individuals with SWS aged 0.4-55 years were assessed annually for 3 years gathering neurologic symptoms, quality of life (QOL), and urine angiogenic factors. Nonparametric statistical tests and modeling with generalized estimating equations (GEE) were used to explore associations between clinical and laboratory data.
RESULTS: Beta Fibroblast Growth Factor (bFGF) was elevated in SWS children compared to controls. Abnormally elevated bFGF was associated with better mean seizure score, but not with longitudinal change in seizure score. Abnormally elevated bFGF was associated with poorer mean QOL in upper and lower extremity function in adults and with better fatigue symptoms in children, but was not associated with change in QOL over time. Worse total neuroscore was associated with worse QOL ratings for depression, sleep disturbance, and emotional and behavioral dyscontrol in adults with SWS. Higher seizure score was associated with worse QOL rating in children for depression, anger, fatigue, and pain and better QOL rating for stigma.
CONCLUSIONS: Elevated bFGF is associated with SWS. This study does not support the use of urine vascular growth factors for prognostic biomarkers. Neuroscore is associated with quality of life rating in Sturge Weber Syndrome.
KEYWORDS: Neuro-Cutaneous Disorders, Lifespan Manifestations of Childhood Onset Conditions, Epilepsy

NEURODEVELOPMENTAL DISORDERS

172. Natural history, brain imaging, and human cell modeling for NAA10-related neurodevelopmental syndrome

Lyon G (Staten Island, NY), Rusielewicz T, Wesely J, Chen Y, Sapar M, Ramnarine K, Marchi E, Harpell R, Monsma F, Gropman A, Whitehead M

OBJECTIVE: This is a natural history study being conducted for development of a gene therapy for an ultra-rare severe human neurodevelopmental disorder involving pathogenic variants in NAA10 and NAA15, which encode the N-terminal acetyltransferase A complex.
METHODS: One clinician interviewed 56 and 19 families with NAA10 or NAA15 variants, respectively, among known cases (N=106 NAA10; N=66 NAA15). Induced pluripotent

stem cells (iPSCs) were made from skin fibroblasts or PBMCs.

RESULTS: This natural history study shows severe impairment with progressive declines in functioning, measured by ABC global score. For females with p.Arg83Cys variant, there is substantial variability (mean 36.6 ± 14.3 SD, ABC standard score), which is similar to females with other variants (mean 41.6 ± 16.9 SD). Brain MR imaging (n=14 NAA10, n=6 NAA15 patients) showed variable brain volume reduction (n=16), macrophthalmia and/or globe dysmorphia (n=7), globus pallidus signal T2WI hyperintensity (n=6), brain malformations (n=4) and myelin deficiency (n=3). Repeat scanning in 5 NAA10 cases and 2 NAA15 cases showed later onset cerebellar hypoplasia in 3 NAA10 cases; cerebral and brainstem volume remained stable. From a resource of 34 iPSC patient-specific lines, there are no cell-autonomous defects in three male lines, with isogenic controls, for iPSC-derived astrocytes and excitatory and inhibitory neurons.

CONCLUSIONS: NAA10-related neurodevelopmental syndrome is a very severe neurodevelopment disorder, with reduced brain volume, but with no cell-autonomous defects in iPSC-derived brain cells. Together, brain volume reduction, enlarged and/or misshapen ocular globes, and globus pallidus hyperintensity are neuroimaging features that may raise the possibility of or add specificity to a suspected diagnosis.

KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Lifespan Manifestations of Childhood Onset Conditions

173. Risk factors in children with optic nerve hypoplasia and septo-optic dysplasia

Salman M (Winnipeg, MB, Canada), Ruth C, Yogendran M, Rozovsky K, Lix L

OBJECTIVE: To identify optic nerve hypoplasia (ONH) and septo-optic dysplasia (SOD) risk factors.

METHODS: A retrospective population-based study with case-control design was undertaken using the Population Research Data Repository at the Manitoba Center for Health Policy in Canada. Cases were 111 patients with ONH/SOD diagnosed during 1990-2019, matched to 555 unrelated population-based controls on year of birth, sex, and area of residence. Additionally, 75 ONH/SOD cases were matched 1-on-1 with sibling controls (the rest had no siblings). Several antenatal maternal risk factors (alcohol, smoking, & illicit drugs use during pregnancy; parity; antidepressant, anticonvulsant, & mood stabilizers use during pregnancy; vaginal bleeding, psychological distress, & income assistance during pregnancy; prematurity; gestational & pre-gestational diabetes mellitus [types 1&2]; gestational & pre-existing maternal hypertension; maternal age at conception, & gestational age) associated with ONH/SOD were tested for their association with case/control group membership using adjusted odds ratios (OR) and 95% confidence intervals (CI) from a multivariable conditional logistic regression model. Outcome was risk of developing ONH/SOD.

RESULTS: Maternal age at conception (OR:0.91, 95% CI:0.86-0.96), primigravida (OR: 3.39, 95% CI:1.92-6.01), and smoking (OR:2.86, 95% CI:1.61-5.05) were independently associated with ONH/SOD in the cohort matched to unrelated controls (p<0.001). In the sibling cohort, smoking was an important risk factor (OR:3.65, (95% CI:1.2-11.1, p=0.02).

CONCLUSIONS: Non-modifiable and modifiable antenatal maternal risk factors are associated with ONH/SOD. Our investigation suggests that several risk factors reported in prior studies may have been due to confounding bias and that maternal smoking during pregnancy is the main modifiable risk factor associated with ONH/SOD.

KEYWORDS: Neurodevelopmental Disorders

174. Eladocagene exuparvovec gene therapy increases Bayley-III cognitive and language raw scores in patients with aromatic L-amino acid decarboxylase deficiency

Hwu P (Taipei, Taiwan), Lee N-C, Chien Y-H, Krolick A, Sierra R, Wang A, Tai C-H

OBJECTIVE: Aromatic L-amino acid decarboxylase (AADC) deficiency is a rare, autosomal recessive disorder that causes impaired neurodevelopment. The impact on cognitive and language development in children with AADC deficiency was assessed following gene therapy with eladocagene exuparvovec, which is approved for use in the EU and UK.

METHODS: Eladocagene exuparvovec was infused bilaterally into the putamina of 22 children with AADC deficiency in two single-arm, open-label clinical trials (AADC-010 [n=10] and AADC-011 [n=12]). The Bayley Scales of Infant and Toddler Development 3rd Edition (Bayley-III) was used to measure cognitive and language (receptive and expressive) scores. Patients were assessed every 3 months for 1-year post-gene therapy, then every 6 months for 5 years and then annually up to 7 years. A repeated measures model was employed to calculate the least squares (LS) mean for change from baseline (CFB) in Bayley-III scores.

RESULTS: Baseline mean (95% confidence interval [CI]) cognitive score was 12.4 (10.6-14.2) for the 22 patients, who had a mean age of 40.9 months (standard deviation [SD]: 25.6). This corresponds to a developmental age equivalent of a 3.0-month-old infant (SD: 1.0). The LS mean for CFB in cognitive score at 60 months was 22.7 (95% CI: 19.5-25.9; p<0.0001). Increases in LS mean for CFB were also observed for expressive language score (6.5 [95% CI: 4.7-8.2; p<0.0001]) and receptive language score (7.3 [95% CI: 6.3-8.3; p<0.0001]) at 60 months.

CONCLUSIONS: Gradual and sustained increases were observed for LS means for CFB in Bayley-III cognitive and language scores following treatment with eladocagene exuparvovec for 5 years.

KEYWORDS: Neurodevelopmental Disorders

175. Visual acuity outcomes in children with optic nerve hypoplasia and septo-optic dysplasia

Salman M (Winnipeg, MB, Canada), Hossain S, Carson E, Ruth C, Clark I

OBJECTIVE: To investigate best-corrected visual acuity (BCVA) outcomes in patients with optic nerve hypoplasia (ONH) and septo-optic dysplasia (SOD). Our primary

hypothesis was that BCVA in patients with ONH/SOD does not change significantly over time.
METHODS: This relatively large longitudinal observational study on this rare disorder was performed through a chart review undertaken in patients with a confirmed diagnosis of ONH/SOD. Demographic and clinical ophthalmological data were extracted. Quantitative BCVA data were investigated across clinic visits after converting visual acuities to the logarithm of the minimum angle of resolution (logMAR) to facilitate analysis.
RESULTS: There were 102 patients (56 males). Median age at study end was 12.7 years. Median duration of follow-up was 4.5 years. The total number of clinic visits for the whole cohort was 571. BCVA worsened slightly in the most affected eyes (0.056 average increase in logMAR/year, 95%CI: 0.037-0.075) and improved mildly in the lesser or equally affected eyes (0.014 average decrease in logMAR/year, 95% CI: 0.009-0.019) ($p<0.0001$).
CONCLUSIONS: Although the overall BCVA data showed a statistically significant change with time, the actual changes were small and are of doubtful meaningful clinical significance (less than one line change on a Snellen chart). Our data suggests that ONH/SOD are non-progressive neurodevelopmental disorders. The mild worsening of BCVA in the most affected eyes may be caused by amblyopia, whilst the small improvement in the lesser or equally affected eyes may be caused by developmental maturation. In addition, the changes in BCVA may also be due to increasing reliability of visual assessments with increasing age.
KEYWORDS: Neurodevelopmental Disorders

176. Impact of Seizures on Cognitive Outcome in a Cohort of 44 Individuals with KBG Syndrome

Sarino K (Chicago, IL), Guo L, Yi E, Park J, Kierzkowska O, Carter D, Marchi E, Lyon G

OBJECTIVE: This study aimed to determine the impact of seizures on neurocognitive outcomes in KBG syndrome, a rare genetic neurodevelopmental disorder characterized by pathogenic variants in the gene ANKRD11 or deletion of 16q24.3 including ANKRD11.
METHODS: A single clinician interviewed forty-four participants with confirmed KBG diagnoses. The cohort was further subdivided into individuals with epilepsy and individuals without epilepsy. Trained evaluators conducted the Vineland Adaptive Behavior Scales (Vineland-3). Comparisons were made using seizure history, medical records, and Vineland-3 scores.
RESULTS: The cohort demonstrated impairment in adaptive functioning compared to the general population ($n = 44$, mean 70.80 ± 22.56 SD vs. population mean 100 ± 15.00 SD). The epilepsy group ($n = 11$, mean 59.82 ± 23.39 SD) exhibited cognitive adaptive function deficiency compared to the group without seizures ($n = 25$, mean 76.80 ± 20.88) ($p = 0.037$). Impairments were observed in the communication ($p = 0.016$) and daily living skills (DLS) ($p = 0.040$) domains of the epilepsy group (mean 54.91 ± 23.76 SD communication, mean 63.27 ± 25.87 SD DLS) versus the non-seizure group (mean 76.04 ± 22.55 SD communication, mean 81.84 ± 23.19 SD DLS). Nine participants who did not fit epilepsy criteria were excluded from analysis.
CONCLUSIONS: Individuals with KBG syndrome and epilepsy demonstrated impaired adaptive behavior compared to those without seizures, with emphasis on communication and daily living skills. These results can inform epilepsy screening upon KBG syndrome diagnosis and further guide treatment recommendations.
KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Epilepsy

177. Trends in Diagnosis and Management of ADHD in Children and Adolescents – A 5 Year Overview

VanZant J (Pittsburgh, PA), Adenaiye O, Houtrow A

OBJECTIVE: Attention Deficit Hyperactivity Disorder (ADHD) is the mostly commonly diagnosed neurodevelopmental condition in the United States. Many children and families seek care from pediatric neurologists and neurodevelopmental specialists. Disparities in recommended treatments have been previously shown. This study aims to evaluate current patterns in diagnosis and treatment to determine which factors independently correlate with receipt of an ADHD diagnosis, as well as guideline-based treatment.
METHODS: Data from the National Survey on Children's Health (NCHS) from 2016-2020 were analyzed for children aged 4-17 years. Odds ratios were calculated for various subgroups and treatment groups of interest. In addition, logistic regression models were created to determine the individual significance of variables on receipt of diagnosis and treatment.
RESULTS: The weighted sample totaled 52,333,015 with 4,765,817 reporting a current diagnosis of ADHD (prevalence of 9.1% [8.79-9.42]). Multiple logistic regression models showed that male gender, older age, non-Hispanic black and white cultural background, higher household income, public insurance, and presence of a medical home are significantly associated with receiving an ADHD diagnosis (p-values <0.05). Regarding receiving guideline-based treatment, male gender, older age, Hispanic ethnicity, insurance status, and presence of a medical home were individually significant factors (p-values <0.05).
CONCLUSIONS: ADHD is the most diagnosed pediatric neurodevelopmental condition. There are significant sociodemographic disparities in being diagnosed with ADHD and receiving guideline-based care. As more children and families present to neurologists and developmental neurologists, awareness of these trends, and knowledge to ensure the most appropriate treatment is essential.
KEYWORDS: Neurodevelopmental Disorders, Behavioral Neurology, Diversity, Equity, Inclusion

178. Trofinetide for the Treatment of Rett Syndrome: Results From the Open-Label LILAC Study

Percy A (Birmingham, AL), Neul J, Benke T, Berry-Kravis E, Glaze D, Marsh E, An D, Bishop K, Youakim J

OBJECTIVE: Trofinetide, a synthetic analog of glycine-proline-glutamate, significantly improved core symptoms of Rett

syndrome (RTT) and had an acceptable safety profile in the 12-week, randomized, placebo-controlled, phase 3 LAVENDER study (NCT04181723). Here, we report the efficacy and safety results of LILAC (NCT04279314), an open-label extension of LAVENDER.

METHODS: Females with RTT, 5–21 years of age, who completed the LAVENDER study received open-label treatment with twice-daily, oral trofinetide for 40 weeks. Safety assessments included the incidence of adverse events (AEs). Efficacy endpoints included the caregiver-assessed Rett Syndrome Behaviour Questionnaire (RSBQ) and the clinician-assessed Clinical Global Impression–Improvement (CGI-I) scale.

RESULTS: Overall, 154 patients were enrolled and treated with open-label trofinetide following the LAVENDER double-blind treatment of trofinetide (n = 69) or placebo (n = 85). In total, 54.5% of patients completed the study. The most common AEs were diarrhea (74.7%) and vomiting (28.6%). Diarrhea (21.4%) was the most common AE leading to treatment withdrawal. The mean (standard error [SE]) change from the LAVENDER baseline to Week 40 in the LILAC study in RSBQ was −7.3 (1.62) for patients treated with trofinetide in LAVENDER and −7.0 (1.61) for patients treated with placebo in LAVENDER. Mean (SE) CGI-I scores compared with the LILAC baseline at Week 40 were 3.1 (0.11) and 3.2 (0.14) for patients treated with trofinetide and placebo in LAVENDER, respectively.

CONCLUSIONS: In LILAC, open-label treatment with trofinetide continued to improve symptoms of RTT. Consistent with the LAVENDER study, diarrhea and vomiting were the most commonly reported AEs.

KEYWORDS: Neurodevelopmental Disorders

179. A randomized placebo controlled crossover trial of cannabidiol to treat severe behavior problems in Autism: Effects on behavior as measured by the Vineland Adaptive Behavioral Scales, Third Edition (VABS-3)

Oppenheim H (San Diego, CA), Knight C, Grant I, Trauner D

OBJECTIVE: Children with severe forms of autism often have associated behavioral problems (e.g., aggression, self-injurious behaviors) that impair functioning. They also exhibit difficulties with activities of daily living and social communication. Cannabidiol (CBD) has emerged as a potential candidate for treating some of the difficult behaviors. Initial studies based on parental reports of unregulated forms have shown promising results. Our objective was to determine whether CBD improved adaptive behaviors using a randomized placebo- controlled crossover study design.

METHODS: Participants were children and adolescents (7-14 years old) with an autism diagnosis and substantial behavioral problems based on parental assessment and clinician agreement. Participants were randomly assigned to either CBD or placebo treatment for 8 weeks, followed by a washout period of four weeks and then crossing over to whichever treatment they had not received in the first phase. Parents completed the VABS-3 prior to and after each intervention arm.

RESULTS: 37 male participants (mean age 10 years) were included in this report. 71% were nonverbal. We noted a significant improvement in the motor skills subdomain in the CBD treated group but not in the placebo group.

CONCLUSIONS: This is the first placebo-controlled trial using an FDA regulated CBD product (Epidiolex) in children with autism. We found that CBD treatment improved adaptive motor skills in children with severe autism. More detailed analyses are being performed to further examine the effects of CBD in this group of children.

KEYWORDS: Neurodevelopmental Disorders

180. Validation of STARx for Assessing Healthcare Transition Readiness in Young Adults with ASD

Ferrell A (Durham, NC), Cejas D, Cheak-Zamora N, Ferris M

OBJECTIVE: This study outlines the validation of the Self-management and Transition to Adulthood with Rx=Treatment (STARx) caregiver questionnaire as a tool to assess YA-ASD's readiness to transition to adult care.

METHODS: Secondary analysis was completed on data collected from caregivers (n=484) at five Autism Treatment Network sites. Caregivers completed a demographics battery, STARx parent questionnaire, AIR self-determination scale, and Health-Related Independence (HRI) scale. Concurrent validity was assessed through Pearson correlations between STARx total scores and scores on the AIR and HRI scales. Predictive validity was evaluated through a one-sided independent samples t-test comparing STARx scores between YA-ASD that had and had not transitioned, as well as linear regressions with demographic variables likely to be associated with healthcare transition readiness.

RESULTS: STARx scores showed strong concurrent validity with the AIR Self-determination scale and Health-Related Independence (HRI) scale. Relevant demographic variables predicted STARx scores, and there were significant differences in STARx scores among YA-ASD who had already transitioned to adult care and those that had not.

CONCLUSIONS: he STARx questionnaire is a validated gold-standard for readiness assessment in many chronically ill populations and can serve an important role in helping clinicians support YA-ASD as they transition care.

KEYWORDS: Neurodevelopmental Disorders, Practice Parameters

181. High-Likelihood ASD Infant Profiles: Enhancing Data Quality and Retention in Multi-site Early EEG Biomarker Studies

Booth M (Los Angeles, CA), Dickinson A, Lee A, Zempel J, Piven J, Pruett J, Jeste S

OBJECTIVE: The multisite Infant Brain Imaging Study (IBIS) was established to identify early clinical and neurobiological markers of ASD. To enhance early detection and interventions, we examined pre-symptomatic markers of atypical development in infants who are at a higher likelihood of developing ASD (~20%; based on the presence of an older diagnosed sibling). To ensure clinical reliability, multisite biomarker studies require rigorous standardization of data collection, quality control, and signal processing. Here, we describe our standardization process and its impact on data quality.

METHODS: At 6-months of age, all infants were scored on 1) the Vineland Adaptive Behavior Scale-III (VABS-III) and 2) completed three EEG paradigms (task-free, visual, and auditory evoked potentials). EEGs were standardized through rigorous behavioral management training, regimented recording procedures, and detailed post-processing data quality checks. EEG data was visually inspected for artifact free time periods and the proportion of data retained per infant for each paradigm was calculated.
RESULTS: 6-month-old infants presented with variable degrees of adaptive skills based on parent reports. Despite early developmental differences, data retention rates were on average over 60% across all infants and all EEG paradigms.
CONCLUSIONS: Previous studies report retaining infant EEG data from less than 50% of all participants and often do not report on quality of the data that are preserved (Cuevas et al., 2014). High quality EEG recordings are essential for understanding the relationship between progression of adaptive capabilities, clinical outcomes, and underlying neurodevelopmental biomarkers, all essential components in the establishment of early interventions.
KEYWORDS: Neurodevelopmental Disorders, Neuroimaging, Neurogenetics

182. Population Pharmacokinetic Modelling to Confirm Weight-Based Banded Dosing and Exposure-Response Efficacy Analyses to Support Trofinetide Treatment in Rett Syndrome

Darwish M (San Diego, CA), Passarell J, Maxwell K, Youakim J, Bradley H, DeKarske D, Bishop K, Stankovic S

OBJECTIVE: Trofinetide is the first approved treatment for Rett syndrome (RTT) and was recently shown to be efficacious and well tolerated in the phase 3 LAVENDER study (NCT04181723). Weight-based dosing to achieve target exposure in LAVENDER was based on population pharmacokinetic (popPK) modeling using data from 13 studies. These exposure-response (E-R) analyses of LAVENDER results explored the relationship between exposure and efficacy endpoints.
METHODS: A previous popPK model was refined using pooled PK data from 13 studies (N=442) including LAVENDER. E-R models were developed using data from LAVENDER and two phase 2 studies and included the coprimary (Rett Syndrome Behaviour Questionnaire [RSBQ], Clinical Global Impression-Improvement [CGI-I]) and key secondary (Communication and Symbolic Behaviour Scales-Developmental Profile™ Infant-Toddler Checklist [CSBS-DP-IT] Social Composite score) efficacy endpoints, and a secondary efficacy endpoint related to nonverbal communication (RTT-Clinician Rating of Ability to Communicate Choices [RTT-COMC] scores) from LAVENDER that demonstrated benefit with trofinetide versus placebo.
RESULTS: After weight-based banded dosing in LAVENDER, median and individual area under the concentration-time curve from 0–12 hours at steady-state fell within the target exposure range (800–1200 μg*h/mL). The E-R relationship was significant and higher trofinetide exposure was associated with improved RSBQ, CSBS-DP-IT Social Composite and RTT-COMC scores.
CONCLUSIONS: The proposed weight-based banded dosing regimen in the LAVENDER study achieved the targeted trofinetide exposure range. The E-R relationship was significant and demonstrated that higher trofinetide exposures are associated with improved efficacy outcomes.
KEYWORDS: Neurodevelopmental Disorders

183. Human motor cortex single-cell transcriptome depicts high TSC1 expression in parvalbumin-positive inhibitory neurons

Jakkamsetti V (Dallas, TX), Pascual J, Evans P

OBJECTIVE: Humans with tuberous sclerosis complex (TSC1/2) deficiency have an increased risk for autism and seizures. Tsc mouse-model studies exploring the mechanistic basis for seizures indicate deficits in cortical inhibition leading to unbalanced excitation. However, it is unknown if this proposed pathophysiology for seizures is translatable to the human disorder. We theorized that the proclivity of TSC1/2 expression in single cells in the human cortex could offer clues regarding cell-types more vulnerable to deficits. We further hypothesized that the expression profile of TSC1/2 in inhibitory neurons compared to excitatory neurons could provide a basis for seizures in patients with gene deficits.
METHODS: Single-cell RNA-seq data was acquired from the 10x genomics single-cell RNA database at Allen's Brain Map. RNA expression within each cell was normalized to tubulin within the same cell. Statistical testing involved a two-way ANOVA with Tukey's test for multiple comparisons.
RESULTS: Same-cell tubulin-normalized human TSC1 expression was remarkably high in parvalbumin-positive interneurons (4.8 ± 0.3, $n=15$) and significantly higher than that in excitatory pyramidal cells ($3.\pm 0.1$, $n=44$, $p<0.0001$) or somatostatin-positive inhibitory neurons (3.8 ± 0.3, $p<0.01$). In contrast, TSC2 expression was relatively low across all M1 cortical cells compared to TSC1. There was no difference in TSC2 expression between parvalbumin-positive (1 ± 0.14, $n=15$) and excitatory (1.1 ± 0.05, $p>0.05$) or somatostatin-positive inhibitory neurons (0.45 ± 0.09, $p>0.05$). Somatostatin-positive inhibitory neurons had lower TSC2 expression than excitatory cells ($p<0.01$).
CONCLUSIONS: Our results indicate that parvalbumin-positive inhibitory neuron function could be especially vulnerable to deficits of TSC1, thus suggesting it's failure as contributing to seizures in human TSC1 deficiency.
KEYWORDS: Neurodevelopmental Disorders, Epilepsy, Neurometabolic

184. Population Pharmacokinetic Modelling to Predict Trofinetide Exposure and Exposure-Response Safety Analyses in Girls With Rett Syndrome Aged 2–4 Years

Darwish M (San Diego, CA), Maxwell K, Barcomb H, Bradley H, DeKarske D, Bishop K, Stankovic S

OBJECTIVE: Trofinetide is the first approved treatment for Rett syndrome (RTT). Previous trofinetide population pharmacokinetic (popPK) modeling confirmed weight-based banded dosing in the phase 3 placebo-controlled LAVENDER study in females with RTT aged 5-20 years would

achieve target therapeutic exposure range (area under curve 0-12 hours at steady-state [AUC0-12,ss] = 800−1200 μg*h/mL). This study aims to confirm weight-based banded dosing in girls with RTT aged 2–4 years.
METHODS: A previous popPK model (n=13 studies) was updated with the phase 2/3 DAFFODIL study (NCT04988867) in females with RTT aged 2-4 years receiving weight-based open-label trofinetide dosing (≥9-12 kg = 5 g BID; ≥12-20 kg = 6 g BID). Individual trofinetide exposure parameters were estimated to confirm target exposure achievement in DAFFODIL. Exposure values versus select treatment-emergent adverse events (TEAEs) in DAFFODIL were compared with two phase 2 studies and LAVENDER.
RESULTS: Exposure parameters (AUC0-12,ss) in DAFFODIL were within target range and similar to LAVENDER. TEAEs of diarrhea and vomiting were exposure dependent in LAVENDER. Exposure ranges with TEAEs in DAFFODIL were within those observed in the previous studies.
CONCLUSIONS: Weight-based banded trofinetide dosing for females with RTT aged 2–4 years achieved targeted exposure as evaluated in LAVENDER and there were no additional safety concerns.
KEYWORDS: Neurodevelopmental Disorders

185. Bridging the Quality Care Gap in ASD Diagnosis and Management: The Role of Education, Training, and EMR Integration

Wells D (Houston, TX), Guzman Karlsson M, Massrey C, Newell M, Risen S, Lazar S, Dicarlo S, Fisher K, Emrick L, Bala T

OBJECTIVE: To increase the amount of formal autism spectrum disorder (ASD) diagnoses made by pediatric neurology providers through education, training, and electronic medical record (EMR) integration of the Child Autism Rating Scale-2 (CARS-2) diagnostic tool.
METHODS: Semi-structured interviews and surveys were utilized to evaluate local pediatric neurologists' experiences and barriers in making, disclosing, and counseling on ASD diagnoses, recommending therapeutic interventions, and providing secondary diagnostic referrals. We then created a comprehensive educational curriculum covering diagnostic criteria, CARS-2 administration, billing for developmental testing, post-diagnosis counseling, therapy referrals, and EMR workflow optimization.
RESULTS: Primary outcomes examined the extent of CARS-2 utilization, frequency of ASD diagnoses, and changes in secondary referral patterns to other subspecialty providers (e.g., developmental-behavioral pediatricians, (neuro) psychologists, psychiatrists).
CONCLUSIONS: Our quality improvement initiative aims to equip pediatric neurology providers with the essential knowledge and skills to diagnose, counsel, and manage patients with a clear ASD diagnosis. By incorporating education, training, and EMR integration of the CARS-2 diagnostic tool, providers can bridge the quality care gap and make ASD diagnosis and management more efficient, timely, equitable, and patient-centered.
KEYWORDS: Neurodevelopmental Disorders, Education, Behavioral Neurology

186. Identifying atypical motor development in infants at genetic risk for Autism Spectrum Disorder

Abdullahi S (Los Angeles, CA), Ly R, Wilson R

OBJECTIVE: Motor impairments may be the first sign of atypical development in infants at genetic risk for ASD. 1,2 Yet, little is known about when these impairments first present and whether they are related to later diagnosis of ASD. Here we evaluate motor development of infants at high familial risk for ASD (one older sibling with ASD, "HR") and infants with TSC and whether motor deficits are related to severity of ASD symptoms.
METHODS: Participants included 39 HR infants, 8 with TSC and 15 low-risk (LR) with no family history of ASD. Motor skills were assessed using Alberta Infant Motor Scale (AIMS) at 3, 6, 9 and 12 months. ASD outcome was measured using Brief Observation of symptoms of autism (BOSA) at 36 months.
RESULTS: HR infants scored significantly lower than LR infants and the TSC infants scored significantly lower than both LR and HR groups on AIMS subscales and Total percentile scores ($p<0.05$). AIMS percentile score was inversely correlated to BOSA score and significantly so at 6 months ($r=-0.31$, $p<0.05$).
CONCLUSIONS: HR and TSC infants show deficits in gross motor skills including being prone, supine, siting and standing. TSC infants show more motor delays compared to HR infants. Motor deficits as early as 3 months of age were correlated with more severe ASD symptoms at 36 months. Motor deficits in infancy could be used as markers for early surveillance of high risk infants and potentially as targets for therapy to improve neurodevelopmental outcomes.
KEYWORDS: Neurodevelopmental Disorders

187. Insights into the Natural History and Clinical Spectrum of GNAO1-Neurodevelopmental Disorder: Findings from a Prospective, Longitudinal Study spanning 4 Years

Robichaux-Viehoever A (St. Louis, MO), Cheung S, Balk K, Patterson J, Smith E, Bell E, Fox A, Garris J, Axeen E

OBJECTIVE: To define the natural history of GNAO1-Neurodevelopmental Disorder (GNAO1-NDD) in a prospective manner.
METHODS: A multi-disciplinary team evaluated 50 subjects from 2019-2022 using a range of qualitative and quantitative measures, including full neurological history and exam, movement disorder rating scales, communication and quality of life measures. Data was collected for 4 consecutive years in 10 subjects, with 2020 and 2021 data collection conducted remotely.
RESULTS: All subjects had hypotonia as infants and some degree of motor developmental delay, with a range of severity. Abnormal movements did not correlate with overall motor disability, but those with a history of seizures were more likely to have severe hypokinetic motor disability. Previously unknown symptoms including GI dysmotility, dysautonomia, and light sensitivity were discovered with detailed histories. Two subjects died due to complications of hypotonia and abnormal movements.

CONCLUSIONS: GNAO1-NDD is an emerging cause of previously undiagnosed hypotonia, movement disorder, and epilepsy, sometimes resulting in fatal outcomes. Further understanding of the natural history of this disorder disease and a disease specific rating scale is needed before quality clinical trials can be conducted. This study sheds light on the potential complications and diverse clinical manifestations associated with GNAO1-NDD.

KEYWORDS: Neurodevelopmental Disorders, Movement Disorders, Epilepsy

188. Personalized treatment of behavioral symptoms with memantine in a child with a suspected gain of function variant in GRIN2A

Kuerbitz J (Houston, TX), Kannan V, Emrick L

OBJECTIVE: The GRIN2A gene encodes one of four glutamate binding GluN2 subunits of the heterotetrametric NMDA receptor. Variants in GRIN2A have been associated with a spectrum of neurodevelopmental and epilepsy phenotypes. GRIN2A protein consists of several distinct functional domains, and disruption of particular domains has been shown to predict phenotype severity. We present a case of a patient affected with severe self-injurious behavior found to have a variant disrupting the M2 pore domain who showed an encouraging response following treatment with the NMDA antagonist memantine.

METHODS: Retrospective study of one subject

RESULTS: A two-year-old female was seen in neurology clinic for evaluation of developmental delay, autism, and hypotonia. Of particular concern to parents was frequent episodes of head banging occurring up to 400 times per day. Prior workup was notable for a de novo missense variant (c.1844A>T, p.Asn615Ile) within the M2 loop of GRIN2A. Based on published functional assays of nearby variants, we hypothesized that her variant would lead to a gain of function effect via disruption of magnesium-mediated voltage-gating. Based on previous reports demonstrating safety and tolerability in children with autism, we began empiric treatment with the NMDA antagonist memantine. Following memantine treatment, her parents and ABA therapist noted a dramatic improvement in volume of self-injurious behaviors.

CONCLUSIONS: Our case demonstrates successful symptomatic treatment of a GRIN2A-associated neurodevelopmental disorder using extrapolated functional validation data of similar variants from the same protein domain. Domain-specific functional phenotyping may facilitate delivery of early precision treatments to patients affected by neurodevelopmental channelopathies.

KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Experimental Therapeutics

189. Autism Spectrum Disorder (ASD) in a Conflict-Affected Area

Askalan R (Jerusalem, Israel), Alerawi A, Yacoub R, Mikki N

OBJECTIVE: Studies on ASD are very scarce in conflict-affected areas with compromised health care and limited support for patients and their families. This study describes the presentation, diagnosis, intervention and outcome of ASD in the Palestinian Territories.

METHODS: A retrospective cohort study was conducted in children aged 1-14 years presented to our institution with speech delay between Jan 2021-Dec 2022. Diagnosis of ASD was established using ADOS and ADIR. Patients were offered personalized treatment plans that included behaviour, speech and sensory integration therapies.

RESULTS: In this study, 72 (73%) of 99 children with speech delay had ASD with an average time lag between presentation and diagnosis of 1.81 years. Most affected children (53) received at least one treatment modality but only 39 children (73%) remained in therapy for more than 6 months. The two most common causes of noncompliance were parental denial of the diagnosis (45%) and inaccessibility to treatment center (48%). Surprisingly, finances were the cause of noncompliance for 18% of patients only despite lack of health insurance. Most families who had difficulty accepting the diagnosis (80%) had one parent at least with university education. Of the children who remained in therapy for at least 6 months, 16 children were integrated in regular schools. Consanguinity in the ASD cases (37%) was comparable to known population rate.

CONCLUSIONS: results of this study should help designing a national comprehensive care for children with autism that focuses on increasing awareness, unified diagnostic protocol, accessibility of intervention and integration in the school system.

KEYWORDS: Neurodevelopmental Disorders, Global Neurology

190. Evaluation of Theta Burst Transcranial Magnetic Stimulation as an adjunct to standard therapy in improving core function deficits in children 5 to 15year age with Autism Spectrum Disorder- A randomized, double blind, sham controlled trial

Gulati S (New Delhi, India), Tiwari R, Kamila G, Sondhi V, Jauhari P, Chakrabarty B, Sharma R, Bhatia R, Pandey S, Pandey RM

OBJECTIVE: Our objective was to assess changes in core function deficits in children with Autism Spectrum Disorder(ASD) aged 5-15 years, after Theta Burst Transcranial Magnetic Stimulation(TBS) as an adjunct to standard therapy.

METHODS: Sixty-one children were randomized into intervention-arm(n=31); sham-arm(n-30). Children with syndromic causes of ASD, uncontrolled epilepsy, contraindications for TBS therapy were excluded. Intervention arm received TBS-5 trains; 40 second-on; 20 second-off at 100% of resting motor threshold at dorsolateral prefrontal cortex of non-dominant side. Change in core function deficits was measured as mean-difference in RBS-R(Repetitive Behaviour Scale Revised), CY-BOCS(Children's Yale-Brown Obsessive Compulsive scale), SRS2(Social Responsiveness Scale-2), CARS-2 (Childhood Autism Rating Scale-2), PedsQL(Paediatric Quality of life). Executive and cognitive skills were assessed by time to Stroop and Wisconsin card sorting test. Quantitative-EEG (qEEG) was explored pre-and post-TBS in a subset of patients.

RESULTS: Mean difference in intervention and sham arm in RBS-R at 4 weeks- 8.35(4.65) and 3.84(2.39)[p<0.001], at 12 weeks- 10.71(5.49) and 6.37(2.39)[p<0.001]. Peds-QL at

4 weeks showed mean difference of 6.35(2.37) and 2.97(1.12) and at 12 weeks 8.19(2.87) and 4.67(1.47) in intervention and sham arms with p<0.001. CY-BOCS, CARS-2 and SRS-2, Time to Stroop and Wisconsin card sorting, did not show significant changes. qEEG spectral coherence demonstrated increased beta band coherence between limbic and frontal lobes but spectral power remained unchanged post-TBS.
CONCLUSIONS: TBS may be used as an upcoming modality in therapy of children with ASD, especially with significant repetitive behaviors. Parent reported quality-of-life of child shows improvements post TMS therapy. Role of qEEG to detect changes post-TBS may need further exploration.
KEYWORDS: Neurodevelopmental Disorders, Behavioral Neurology

NEUROGENETICS

191. Carbamazepine responsive Episodic Dystonia and Hallucination due to Pyruvate Dehydrogenase E2 (DLAT) gene mutation

Policherla J (Detroit, MI), Serajee F, Huq A

OBJECTIVE: PDH E2 deficiency due to DLAT mutations is a very rare condition with only 4 reported cases to date.
METHODS: We describe a 15-year-old girl with mild intellectual disability, paroxysmal dystonia and bilateral basal ganglia signal abnormalities on brain MRI. Additional neurophysiological, imaging, metabolic and exome sequencing studies were performed.
RESULTS: Routine metabolite testing, and GLUT1 and PRRT2 mutation analysis were negative. A repeat brain MRI revealed "Eye-of-the-tiger-sign". Exome sequencing identified homozygous valine to glycine alteration at amino acid position 157 in the DLAT gene. Bioinformatic and family analyses indicated that the alteration was likely pathogenic. Patients 's dystonia was responsive to low dose carbamazepine. On weaning carbamazepine, patient developed hallucinations which resolved after carbamazepine was restarted.
CONCLUSIONS: PDH E2 deficiency due to DLAT mutation has a more benign course compared to common forms of PDH E1 deficiency due to X-linked PDHA1 mutations. All known cases of PDH E2 deficiency due to DLAT mutations share the features of episodic dystonia and intellectual disability. Our patient's dystonia and hallucinations responded well to low dose carbamazepine.
KEYWORDS: Neurogenetics, Neurometabolic

192. Expanding the Spectrum of Aicardi Goutieres Syndrome due to IFIH1 gene disorders

Obeid R (Royal Oak, MI), Nolan D, Beaudry-Rodgers K, Berger J

OBJECTIVE: Pathogenic variants in the IFIH1 gene are associated with autosomal dominant Aicardi-Goutières syndrome (AGS). AGS is classically characterized by severe encephalopathy within the first year of life including developmental regression. Neuroimaging often demonstrates leukodystrophy and calcification. In recent years the spectrum for clinical findings in IFIH1-related disorders has expanded.
METHODS: We report cases from our neurogenetic and neurodevelopment clinics that were found to have missense variants of unknown significant (VUS) in the IFIH1 gene.
RESULTS: Three cases presented to our clinics at Beaumont Children's Hospital in Royal Oak MI between 2020 – 2023. These cases reported acquired diplegic cerebral palsy after a previous period of normal development without symptoms of severe infantile encephalopathy. Genetic testing identified missense VUS in the IFIH1 gene. Patient-1 had a paternally inherited heterozygous c.2941 T>C (p.C981R) variant. Patient-2 had a heterozygous c.2622G>C (p. L874F) variant (parental testing not obtained). Patient-3 was identified to have a heterozygous c.2321T>A (p.V774D) variant. All had different degrees of diffuse increased FLAIR signal intensity in the white matter centrum semiovale both posteriorly and anteriorly on brain MRI, and no involvement of the grey matter. Notably they did not exhibit hepatomegaly, thrombocytopenia, or microcephaly described in typical AGS.
CONCLUSIONS: We found reasonable clinical, imaging, and laboratory evidence to suggest that these variants of uncertain significance in the IFIH1 gene can be associated with neurologic symptoms of AGS without evidence cortical calcifications or systemic concerns. Further expansion of genetic testing may help with the identifying others with similar IFIH1 variants and expansion of genotype-phenotype recognition.
KEYWORDS: Neurogenetics, Cerebral Palsy, Neurodevelopmental Disorders

193. Heightened cerebral blood oxygenation changes during a cognitive task in Glut1 deficiency syndrome (G1D)

Khaksari K (Washington, DC), Chen W, Primeaux S, Avila A, Pascual J, Gropman A

OBJECTIVE: We previously postulated that decreased brain glycogen in G1D renders neural activity abnormally susceptible to changes in blood glucose: Inhibitory neurons exhibit elevated metabolism and their glucose-dependent failure provides a mechanism for how blood glucose reduction enhances brain regional activity as measured by fMRI and EEG during seizures. Cognition is similarly susceptible to red blood cell Glut1 abundance . Both seizures and cognition are intimately coupled to blood oxygen extraction. However, no measurement of blood oxygenation during cognition is available. Thus, we tested the hypothesis that cerebral blood oxygenation is abnormal during a passive cognitive task.
METHODS: Standard, 16-channel fNIRS averaged over the prefrontal cortex at wavelengths 730 and 850 nm provided a measure of the change in blood hemoglobin via a modified Beer-Lambert law. Six age-matched controls and six G1D individuals ranging from children to adults manifesting varying disease severity were thus studied while observing a 15-minute video of Timmy Time cartoon likely to induce brain activation.
RESULTS: The procedures were completed by all participants. Relative to control, there were rapid, significantly greater average signal amplitudes and signal oscillation excursions in G1D during the task.

CONCLUSIONS: It is unlikely that molecular hemoglobin properties or cytochrome C levels account for the results. Rather, the augmented and oscillating pattern of hemodynamics that represent changes in regional blood flow and or in cerebral oxygen extraction from hemoglobin during cognitive activity, thus uncovering a novel facet to G1D.
KEYWORDS: Neurogenetics, Neuroimaging, Neurometabolic

194. Identifying Neuroimaging Patterns in Mitochondrial Leukoencephalopathies

Sharma S (Philadelphia, PA), Peterson J, Alves C, Goldstein A

OBJECTIVE: Primary mitochondrial diseases (PMD) have been estimated to affect 1 in 4300 individuals and can present at any age with an average of 16 multi-systemic symptoms per patient. Neurological system is often involved due to its high metabolic demand. In this study, we reviewed patterns of white matter involvement on MRI in patients with PMD.
METHODS: Retrospective chart review of 186 patients with genetically confirmed PMD was conducted. MRI studies available for 153 patients were analyzed to identify presence of white matter involvement. Patterns were delineated based on location, type of involvement, T1/T2 appearance, volume loss, atrophy, restricted diffusion, contrast enhancement and associated brain structure involvement. Information was also collected regarding CSF protein, plasma lactate and lactate peak on magnetic resonance spectroscopy.
RESULTS: White matter involvement was observed in 61 out of 153 patients. Genetic diagnosis included genes involved in mitochondrial translation (C12ORF65, MRPS34, RMND1, EARS2, CARS2, FARS2, VARS2), mtDNA depletion (FBXL4), oxidative phosphorylation (AIFM1), complex I function (NDUFS1, NUBPL), complex II function (SDHB), complex IV function (SURF1), single large scale mtDNA deletion, mt-tRNAs (MT-TL1), pyruvate metabolism (PDHA1), valine catabolism (ECHS1) and thiamine transport (SLC19A3). Leukodystrophy pattern was seen in 14 while hypomyelination was observed in 16 patients. Location was periventricular in 23, diffuse in 15 and involving corpus callosum in 25 patients. Restricted diffusion was observed in 18, volume loss in 14 and associated cerebral/cerebellar atrophy in 11 patients.
CONCLUSIONS: Leukoencephalopathy with specific imaging patterns in neurologically complex patients with multisystemic presentation should warrant detailed evaluation for mitochondrial disease.
KEYWORDS: Neurogenetics, Neuroimaging, Neurometabolic

195. Whole Exome/Genome Sequencing in Cyclic Vomiting Syndrome, a Migraine Variant, Reveals Multiple Candidate Genes, Suggesting a Model of Elevated Intracellular Cations and Mitochondrial Dysfunction

Bar O (Cherry Hill, NJ), Mintz M, Boles R

OBJECTIVE: To utilize whole exome/genome sequencing and the literature for identifying candidate genes for cyclic vomiting syndrome (CVS), an idiopathic migraine variant.
METHODS: A retrospective chart review of 80 unrelated participants was conducted. The literature was queried for genes associated with dominant cases of paroxysmal vomiting or both discomfort and disability; among which the raw genetic sequence was analyzed for "Qualifying" variants conferring a high risk for disease association. A point system identified candidate gene associations to CVS.
RESULTS: Thirty-five paroxysmal genes were identified. Among these, 13 genes were scored as "Highly likely" (SCN4A, CACNA1A, CACNA1S, RYR2, TRAP1, MEFV, mtDNA) or "Likely" (SCN9A, TNFRSF1A, POLG, SCN10A, POGZ, TRPA1) CVS related. Nine additional genes (OTC, ATP1A3, ATP1A2, GFAP, SLC2A1, TUBB3, PPM1D, CHAMP1, HMBS) had sufficient evidence in the literature but not from our study participants. Among these 22 CVS candidate genes, a Qualifying variant was identified in 61/80 (76%) of participants. These findings were highly statistically significant ($P<0.004$) compared to a control group regarding neurotransmitter receptor genes. Additionally, a post-analysis less-intensive review of all genes (exome) identified 13 additional genes as "Possibly" CVS related.
CONCLUSIONS: All 22 CVS candidate genes are associated with either cation transport or energy metabolism (14 directly, 8 indirectly). Our findings suggest a cellular model in which aberrant ion gradients lead to mitochondrial dysfunction, or vice versa, in a pathogenic vicious cycle of cellular hyperexcitability. Among the post-analysis genes identified, 5 are known causes of peripheral neuropathy. Our model is consistent with multiple current hypotheses of CVS.
KEYWORDS: Neurogenetics, Early Stage Investigator

196. GATAD2B-associated Neurodevelopmental Disorder (GAND): Modeling of Corticogenesis and the NuRD Complex with patient-derived IPSCs and Mice

Pierson TM (Los Angeles, CA), Abad C, Otero MG, Robayo MC, Muñiz-Moreno MdM, Freeman C, Babros M, Bernardi MT, Walz K, Young JI

OBJECTIVE: GATAD2B-associated Neurodevelopmental Disorder (GAND) is the result of dominant variants in GATAD2B and is characterized by macrocephaly, distinct facies, apraxia of speech, motor delays, and intellectual disability. Our work seeks to determine the role of GATAD2B and GAND in neurodevelopment and corticogenesis using patient-derived IPSCs and mouse models.
METHODS: Five patient-derived GAND-IPSC lines were generated and compared with control- (CTL) IPSC lines during differentiation along a neuronal pathway and then evaluated with immunochemistry and transcriptomics. Gatad2b-heterozygous (GAND) and -null mice were studied in parallel to determine cognitive ability, cortical structure, and single cell transcriptomic gene expression profiles.
RESULTS: GAND-IPSCs were capable of differentiating into neuro-progenitor cells (NPCs) and cortical neurons (CNs). GAND cells with loss-of-function variants had haploinsufficient expression of GATAD2B mRNA and protein. Transcriptomic analysis of GAND-IPSCs and -NPCs indicated GAND-NPCs had altered expression of ~650 DEGs involved in gene ontogeny groups associated with

neural cell proliferation, migration, and differentiation. 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. GAND and Null mice had altered cortical morphology and abnormal patterning of cortical laminar markers. Single-nucleus transcriptomics of mouse cortices at E16.5 showed abnormal co-expression of cortical laminar markers in both excitatory and inhibitory NPCs and CNs along with altered signaling pathways important for corticogenesis.

CONCLUSIONS: GATAD2B-possessing NuRD complexes are important regulators of gene expression during neuronogenesis and corticogenesis. Changes in gene expression associated with GAND affect neuronal identity and projections.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

197. Neurodegeneration and failure of autophagy in an Atp13a2 knockout mouse model of Kufor-Rakeb Syndrome

Magee H (Phoenix, AZ), McBeth L, SAhir N, Doorn J, Madeo M, Jepperson T, Lewis S, White K, Weimer J, Padilla-Lopez S, Chan C, Pearce D, Kruer M

OBJECTIVE: Mutations in ATP13A2, a transmembrane P-type ATPase transporter, have been shown to lead to Kufor-Rakeb Syndrome (KRS: MIM #606693), a childhood neurodegenerative disease associated with juvenile Parkinsonism and neuronal ceroid lipofuscinosis. This study aimed to characterize a novel Atp13a2 knockout mouse model of KRS and evaluate how well this model recapitulates human disease phenotypes to model disease mechanisms and treatment.

METHODS: A novel KRS mouse model was generated by deleting exons 21-29 of Atp13a2. Motor function was evaluated at several ages using the open field (N = 7-11), force plate actimeter (N = 7-11) and rotorod tests (N = 6-33). Cognitive function was assessed with the Barnes Maze task (N = 4-17). To assess Parkinson and NCL disease pathology, immunohistochemistry experiments were performed to evaluate accumulation of autoflouroscent material, neuroimmunological activation, and neurodegeneration of dopaminergic neurons (N = 5-6). Lysosomal function was evaluated by measuring autophagy (N = 4-8).

RESULTS: We found that the novel Atp13a2 knockout mouse model exhibits decreased motor function and coordination, and decreased survival, compared to control animals. Pathologically, the knockout animals exhibit increased accumulation of autofluorescent storage material, glial activity and neurodegeneration of dopaminergic neurons. Autophagic flux was decreased in embryonic fibroblasts derived from knockout animals.

CONCLUSIONS: Compared to existing Atp13a2 mouse models, our model shows an earlier onset motor phenotype, diminished survival, and recapitulates neuropathological hallmarks of Parkinsonism and neuronal ceroid lipofuscinosis.

KEYWORDS: Neurogenetics, Movement Disorders, Neuroimmunology

198. Neuro-ophthalmologic Features of the Neurodevelopmental Disorder NGLY1 Deficiency from a Prospective Longitudinal Cohort

Levy R (Palo Alto, CA), Frater C, Beres S, Alcorn D, Shue A

OBJECTIVE: NGLY1 Deficiency is a rare recessive neurodevelopmental disorder causing developmental delay, hyperkinetic movement symptoms, polyneuropathy, liver enzyme abnormalities, and hypo- or alacrima. We characterize the full spectrum of the neuro-ophthalmologic phenotype in NGLY1 Deficiency.

METHODS: We completed a prospective natural history study for 29 participants with a confirmed molecular diagnosis of NGLY1 Deficiency. 15 participants were evaluated on-site, the remainder were followed remotely. Detailed clinical data was obtained via standardized medical history and medical record review. Serial on-site clinical evaluations included an ophthalmological exam with Schirmer testing to measure tear production. Outcome measures included Schirmer testing, standardized questions regarding ocular symptoms, and ophthalmologic exam findings.

RESULTS: Of 29 individuals, 90% (26/29) reported at least one neuro-ophthalmologic finding, most commonly hypolacrima, refractive error, and chronic ocular infection. 62% (18/29) utilized eye medication including artificial tears drops, ointment, and/or topical antibiotics. Of the 15 participants with on-site exams, 93% had a refractive error, 80% had low visual acuity, and 73% exhibited corneal abnormalities. Extraocular movement and retinal abnormalities were very rare.

CONCLUSIONS: Neurologists can accelerate diagnosis and optimize overall health in rare disorders by identifying associated symptoms. Given nearly universal hypo/alacrima and prominent neuro-ophthalmologic findings in NGLY1 Deficiency, an ocular history and ophthalmology examination may facilitate diagnosis in individuals with neurodevelopmental delay and hyperkinetic movement disorder. For individuals diagnosed with NGLY1 Deficiency, early initiation of preventive eye care can preserve vision and overall ocular health. Schirmer testing and a standardized questionnaire may be useful for future clinical trials in NGLY1 Deficiency.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders, Neurometabolic

199. Moyamoya Syndrome in a child with an unbalanced rearrangement of 6p: Building evidence of a new genotype-phenotype association

Abd Allah A (Madison, WI), Pardo K, Wallace A

OBJECTIVE: Moyamoya disease is a progressive vascular angiopathy of cerebral arteries with development of compensatory capillary collaterals. The major neurological sequelae are hemorrhagic and ischemic stroke. The genetics of Moyamoya angiopathy are not well understood. Two known case reports have demonstrated a possible association between Moyamoya angiopathy and complex rearrangement of chromosome 6p. This study aims to highlight this genetic association and enhance the understanding of Moyamoya syndrome.

METHODS: We identified a patient with Moyamoya disease and Chromosome 6p25.3 Duplication Syndrome. The patient's chart was reviewed for relevant clinical, imaging and genetic data. A literature review of Moyamoya syndrome and chromosome 6p duplication was performed.
RESULTS: A 3-year-old-girl with a history of intrauterine growth restriction, prematurity, developmental delay, facial dysmorphism, hearing impairment, cardiac, and renal congenital anomalies presented with acute left-sided hemiparesis. MRI revealed bilateral restricted diffusion in the frontal lobe white matter consistent with acute ischemic stroke.
The diagnosis of Moyamoya disease was made based on computed tomography angiography demonstrating bilateral internal carotid artery tapering with prominent lenticulostriate arteries. Management included Aspirin and surgical revascularization. Illumina microarray analysis revealed an unbalanced rearrangement resulting in a 13.3-Megabase gain of the short arm of chromosome 6, from band 6p23 to 6pter. The gain of 6p includes 66 protein coding genes. These genes have not been previously linked to Moyamoya angiopathy.
CONCLUSIONS: This case report strengthens the association between complex genetic rearrangement of chromosome 6p and Moyamoya angiopathy. This study begins to define the genetic mechanisms involved in vascular angiopathies in patients with chromosome 6 rearrangement.
KEYWORDS: Neurogenetics, Stroke, Neuroimaging

200. Acute Necrotizing Encephalitis in patient with NUP214 variant

Sun F (Indianapolis, IN), McLaughlin A, Eberhard S, Kenfield-Kelleher T, Ozkir M, Walsh L

OBJECTIVE: Acute necrotizing encephalitis (ANE) occurs in about 10% of cases of influenza-associated encephalitis and is associated with increased mortality and morbidity. Treatment involves immunomodulation with steroids and intravenous immune globulin (IVIG). Nucleoporin gene NUP214 has been associated with febrile encephalopathies, but not specifically with ANE. We report a case of ANE in a 17-year-old woman who was found to have NUP214 variant.
METHODS: An unvaccinated-to-influenza 17-year-old female with a history of influenza-associated encephalitis 6 years previously, presented with altered mental status one week after she tested positive for influenza A. She developed worsening confusion, incomprehensible speech, visual hallucinations, unsteady gait, and a prolonged focal seizure.
RESULTS: Initial brain and spine MRI revealed symmetrical diffusion restriction in the deep gray nuclei. A repeated MRI brain showed worsening swelling and signs consistent with ANE. Whole genome sequencing revealed a likely pathogenic variant in the NUP214 gene. She was treated with IV methylprednisolone, high dose oseltamivir, IVIG, and a mitochondrial cocktail (riboflavin, thiamine, Coenzyme Q10, and IV levocarnitine). On discharge, she was alert and oriented with hypophonia, decreased grip strength, coordination challenges, and required assistance with ambulation.
CONCLUSIONS: To our knowledge, there are no effective therapies yet described for those with NUP214-associated encephalopathy presenting as ANE. This case showed that a combination of mitochondrial cocktail and immunomodulation is possibly associated with an overall symptomatic improvement.
KEYWORDS: Neurogenetics, Neuroimmunology

201. High Sensitivity for Monogenic Causal Diagnoses in Autism, Including De Novo Variants Representing Several Novel Disorders, with Trio Whole Genome Sequencing and Data Reanalysis

Bar O (Cherry Hill, NJ), Vahey E, Mintz M, Boles R

OBJECTIVE: To determine the current sensitivity of trio whole genome sequencing (trio-WGS) in autism, as the last decade has seen dramatic improvements in the proportion of the genome clinically sequenced (e.g., < 1% to > 99%), accuracy, bioinformatic tools, and variant databases. Additionally, the current literature is almost entirely from academic research centers.
METHODS: NeurAbilities Healthcare® is an independent organization specializing in neurodevelopmental disorders. As part of our routine clinical practice, we analyzed the raw DNA sequencing files on the Variantyx® (Framingham, MA) bioinformatics platform for the last 50 autism patients with trio-WGS.
RESULTS: Monogenic causal diagnoses (MCD) were provided in 31/50 (62%) of cases, including 24 heterozygous de novo, 3 X-linked, 3 autosomal recessive, and 1 autosomal dominant/affected parent. All variants considered for MCD were "Qualified", defined as coding, rare, and evolutionarily conserved; in addition to identifying published data linking that gene to autism. De novo variants in genes associated with autism were far more likely to be Qualified than non-Qualified (control group, P=0.002). Only 17/31 (52%) of MCD cases had the variant listed on the laboratory report. The "missed" cases predominately included genes with few to no prior case reports. Many cases without an MCD had inherited Qualifying variants in autism-associated genes, suggesting polygenic inheritance. Over 60% of cases had treatment recommendation(s) based on DNA analyses.
CONCLUSIONS: Our results demonstrate high yield of trio-WGS for revealing molecular diagnoses in autism that is greatly enhanced by re-analyzing DNA sequencing files. Many are de novo and represent un/under-published conditions.
KEYWORDS: Neurogenetics, Early Stage Investigator, Neurodevelopmental Disorders

202. Pontocerebellar Hypoplasia: A Systematic Review from 1912 to 2022

Kukulka N (Washington, DC), Whitehead M, du Plessis A, Chang T, Kousa Y

OBJECTIVE: The diagnosis of pontocerebellar hypoplasia (PCH) usually portends severe developmental delay, epilepsy, and/or neurodegeneration in childhood. Our objective was to review and evaluate published evidence addressing the clinical, genetic, and neurodiagnostic features of PCH by type and subtype and provide recommendations in diagnosis, prognosis, and management for the neurologist.

METHODS: We performed a systematic review of published literature between 1912 and 2022. By combining search results from PubMed, OMIM, and bibliography cross-referencing we identified 191 publications relevant to PCH. Publications on developmental neuroanatomy, not pertaining to PCH, or published in a foreign language were excluded. We performed both qualitative (1912-1993) and quantitative (1992-2022) systematic analyses to identify the clinical, genetic, and neurodiagnostic features of PCH by type and subtype.

RESULTS: The most reported forms of PCH are 1, 2, and 6; less frequently described cases are 3, 4, and 9. Very few cases are described for other types of PCH (12-16). The most frequently reported genetic mutations are found in TSEN54, RARS2, EXOSC3, and AMPD2 genes, which regulate RNA processing and basic cellular metabolism. Neuroradiographic features of PCH are complex and evolve over time, affecting the pons, cerebellum, vermis, cortex, and cerebral white matter.

CONCLUSIONS: PCH is a rare neurodevelopmental disorder, often the result of genetic dysfunction in basic neural metabolism. The diagnosis conveys significant implications on the affected individual and their family. A combination of clinical, neuroradiographic, and genetic testing informs type/subtype categorization, which is best made through ongoing clinical evaluation, genetic testing, and follow-up diagnostic imaging.

KEYWORDS: Neurogenetics, Neuroimaging, Fetal Neurology

203. Consider the Net You Cast: Multigene Panel Testing Misses 15% of Diagnostic Results Compared to Exome Sequencing

Schultz C (Aliso Viejo, CA), Stolar D, Holman M, Horton C, Towne M

OBJECTIVE: Exome sequencing (ES) is recommended as a first-tier test for patients with a neurodevelopmental disorder (NDD), autism spectrum disorder (ASD), intellectual disability (ID), and epilepsy by professional organizations; however, multigene panel testing (MGPT) is still widely used. We assessed the probability that pathogenic/likely pathogenic (P/LP) variants reported in an ES cohort would be detected on MGPT.

METHODS: We analyzed data from individuals under 21 years who underwent ES at a diagnostic laboratory between 2016-2021 for an indication of NDD, ASD, ID, or epilepsy. Report outcomes (positive, uncertain, negative) were assessed. For positive cases, genes with P/LP variants were compared to the laboratory's current MGPT offerings. Fisher's exact test was used for statistical analysis.

RESULTS: Overall ES diagnostic yield was 25% (1046/4205). Trios comprised 77% of orders and resulted in a 30% increase in diagnostic yield (26% vs. 20%) and a 40% decrease in uncertain results (15% vs. 25%) compared to non-trio ES. Of positive cases, 15% (161/1046) would have had at least 1 P/LP variants missed if only MGPT was ordered. Overall, 29 patients had two diagnoses reported on ES, and 59% (17/29) would have had one (n=13) or both (n=4) variants missed on MGPT alone. Individuals were more likely to have a variant missed by MGPT if they were male (p=0.026) or had a primary indication of ASD (p=0.006).

CONCLUSIONS: We found 15% of ES patients would have had one or more P/LP missed by MGPT alone. Trios provide additional clarity for interpreting results and improve diagnostic yield while decreasing uncertain results.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders, Epilepsy

204. Clinical actionability of genetic findings in cerebral palsy

Lewis S (Phoenix, AZ), Chopra M, Cohen J, Bain J, Aravamuthan B, Carmel J, Fahey M, Wintle R, Zech M, Segel R, Haque N, May H, Fehlings D, Srivastava S, Kruer M

OBJECTIVE: Single gene variants are increasingly recognized as a cause of cerebral palsy (CP), although the potential clinical actionability of these findings is less well explored. We assessed how identification of a monogenic disorder could prompt changes to clinical care in CP.

METHODS: A working group of genetic counselors, neurologists, developmental pediatricians, and clinical and research geneticists reviewed published cohorts of patients with CP who had undergone exome sequencing (n=1841). 491/1841 patients (26.7%) had a genetic etiology, or pathogenic/likely pathogenic variant in a CP-associated gene. Clinically actionable genetic findings that potentially change clinical management through prevention or treatment were identified via standardized literature assessment. We adopted the ClinGen actionability framework to assess total utility, including potential outcome severity, intervention efficacy and intervention risk/burden on a 0-3 scale.

RESULTS: For 243 CP-associated genes, interventions are available for 61 (25.1%) and under development for another 8 (3.3%). Evidence was limited to a single patient or small cohort clinical reports for 35 genes (57%). 7.7% (142/1841) of patients in published CP cohorts had a genetic diagnosis that may directly alter clinical management, with another 8 having treatments in clinical trials. Scores indicated moderate utility of findings with an average rating of 6.0 (5.8-6.2 CI) in a 0-9 scale.

CONCLUSIONS: The clinical actionability of genomic findings indicates that genetic testing should be strongly considered as part of the CP diagnostic evaluation to personalize care and improve patient outcomes. As more etiologies and treatments are identified, the impact of genetic testing will continue to improve.

KEYWORDS: Neurogenetics, Cerebral Palsy, Neurodevelopmental Disorders

205. A de novo pathogenic CSF1R variant implicates microglial dysfunction in FIRES pathogenesis

Levine J (Houston, TX), Ankar A, Duan R, Fatih J, Risen S, Trandafir C, Fisher K, Posey J, Tsai P-C, Lupski J, Calame D

OBJECTIVE: To describe a likely genetic etiology of febrile infection-related epilepsy syndrome (FIRES) and propose a role for microglia dysfunction in the development of FIRES.

METHODS: Clinical trio whole genome sequencing (WGS) was performed. 3D protein modeling was studied using Mol* Viewer. CSF1-induced autophosphorylation of CSF1R was examined in vitro to assess CSF1R variant effects and implicate pathogenicity.
RESULTS: A previously healthy 16-year-old male presented with super refractory status epilepticus and was diagnosed with FIRES. His diagnostic workup demonstrated elevated CSF WBC, protein, neopterin, IL-13, IL-2 receptor, and IL-6. WGS identified a de novo CSF1R variant of uncertain significance, (NM_001288705.3): c.1772G>A; p.(Gly591Glu). The variant is absent from gnomAD and is predicted damaging by in silico analytic tools (CADD 24.6, REVEL 0.96). CSF1R encodes colony stimulating factor 1 receptor, a regulator of microglial development and homeostasis. Pathogenic variation in CSF1R results in microgliopathies including diffuse hereditary leukoencephalopathy with spheroids 1 (HDLS1) and brain abnormalities, neurodegeneration, and dysosteosclerosis (BANDDOS). 3D protein modeling of CSF1R p.Gly591Glu showed it lies in the receptor ATP-binding domain in close proximity to a known pathogenic variant, and in vitro functional studies confirmed defective autophosphorylation like observed in other pathogenic variant alleles.
CONCLUSIONS: FIRES is a poorly understood severe epilepsy syndrome attributed to immune dysregulation. Although FIRES is suspected to have a genetic underpinning, genomic studies have failed to identify disease-causing variants in known epilepsy genes in patients with FIRES. The identification of a pathogenic CSF1R variant implicates a potential role for microglia in FIRES pathogenesis and may support interventions targeting microglia.
KEYWORDS: Neurogenetics, Neuroimmunology, Epilepsy

206. Beyond the First Result: A Case Report of Siblings with Two Rare Genetic Disorders

Varnet M (Dallas, TX), Goodspeed K

OBJECTIVE: To report opsoclonus in an infant leading to diagnosis of two rare genetic disorders in siblings.
METHODS: We completed a retrospective chart review.
RESULTS: Abnormal eye movements and visual deterioration were incidentally found in a 6-month-old male. Opsoclonus with hypotonia and delayed developmental milestones were noted. Paraneoplastic, autoimmune, and metabolic etiologies were not found. The 11-year-old sister presented similarly at 3 months old with opsoclonus and delayed milestones. She `developed blindness, hearing loss, intellectual disability, and menstrual dysregulation among other symptoms. Both children had 22q11.2 microduplication identified on chromosomal microarray. Due to medical complexity, additional genetic testing was completed for the infant and identified variants consistent with Alström syndrome. Subsequent testing of his sister revealed the same variants.
CONCLUSIONS: The siblings presented here were diagnosed with 22q11.2 Duplication Syndrome and Alström Syndrome. 22q11.2 Duplication Syndrome can feature developmental delay and hypotonia. Alström Syndrome affects multiple systems including hearing, vision, metabolic and endocrine; culminating in organ failure. Although earliest symptoms may present in infancy, diagnosis is frequently delayed due to variable expression of symptoms. This case demonstrates the need for targeted genetic testing, sometimes beyond an established diagnosis. Opsoclonus is unlikely to occur in 22q11.2 microduplication; considering this led to further testing to fully understand symptoms. Early diagnosis of Alström Syndrome will allow for earlier intervention and monitoring, thus slowing organ dysfunction. This dual diagnosis carries great implications for the older sibling, as she would not yet have been diagnosed with Alström Syndrome. Maternal reproductive planning was also significantly impacted by these findings.
KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

207. The choline transporter FLVCR1 causes severe neurodevelopmental disabilities and epilepsy

Calame D (Houston, TX), Wong J, Panda P, Dat N, Fatih J, Dardas Z, Du H, Coban-Akdemir Z, Ammouri F, Rezich B, Herman I, Rodan L, Posey J, Gibbs R, Pehlivan D

OBJECTIVE: Choline is an essential nutrient involved in metabolism and neurotransmitter synthesis. Its cellular uptake is mediated by transmembrane proteins including FLVCR1. Flvcr1 knockout mice exhibit embryonic lethality, anemia, and craniofacial and limb deformities. In humans, FLVCR1 causes an ultra-rare recessive disease, posterior column ataxia with retinitis pigmentosa (PCARP), characterized by childhood-onset retinitis pigmentosa and adult-onset gait ataxia. Here we demonstrate FLVCR1 variants also cause severe neurodevelopmental disabilities (NDD) and epilepsy.
METHODS: We analyzed sequencing data from >30,000 individuals in genomic datasets to identify patients with biallelic FLVCR1 variants. FLVCR1 variant impact on choline transport was assessed in an in vitro assay.
RESULTS: Genomic analysis identified 12 unrelated families with biallelic ultra-rare FLVCR1 missense or loss-of-function (LoF) variants. Affected individuals had microcephaly, severe developmental delay, epilepsy, hypotonia, and brain atrophy. Some individuals exhibited features seen in Flvcr1 null mice including macrocytic anemia, craniofacial and limb deformities, and hepatosplenomegaly. FLVCR1 missense variants reduced choline transport activity, and loss-of-function variants associated with severe NDD phenotypes. Plasma and urine metabolomics demonstrated consistently low dopamine metabolite levels in one patient, and CSF HVA and 5-HIAA were low in another patient.
CONCLUSIONS: These data demonstrate a broad FLVCR1 phenotypic spectrum encompassing severe NDD with epilepsy. The phenotypic gradient from PCARP to severe NDD is likely explained by the degree of residual FLVCR1 transport activity. Further studies are needed to determine whether low neurotransmitter levels are a biomarker, if maternal genotype or dietary choline intake influences phenotypic severity, and if choline supplementation may be therapeutic as in other transporter disorders.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders, Early Stage Investigator

208. Flexible strategies to improve access to genetic testing for neurological disorders

Mura C (New York City, NY), Abreu N, Steigerwald C

OBJECTIVE: Genetic testing in pediatric and adult neurology clinics has been vital for early diagnosis of rare disease, risk recurrence counseling, and medical decision-making. Healthcare professionals trained in comprehensive counseling, test selection/ordering, and variant interpretation are essential when offering genetic testing services. However, access and availability remain limited for most neurological patients. The NYU Langone Health Division of Neurogenetics sought to define current models of genetic consultations for baseline performance and develop updated models to improve access.

METHODS: Retrospective chart review of 55 clinic visits from February to March 2022 was conducted. During this time, the care model included combined physician and genetic counselor (GC) visits in which clinical roles and responsibilities were determined at weekly clinical care conferences (GC/MD flex).

RESULTS: During this period, 70.9% of presenting clinic patients had no known genetic syndrome, while 21.9% were previously diagnosed. 67.3% of visits resulted in test orders (i.e. panels, exome sequencing, mitochondrial genome sequencing, and microarrays); 37.8% of evaluations resulted in a genetic diagnosis. After review, GC-only visits and MD-then-GC (stacked) visits were incorporated into the clinic workflow structure to address the needs of patients both with and without diagnoses.

CONCLUSIONS: Improvements to genetic consultation workflows allowing for GC-only and stacked visits may be utilized to improve access to genetic testing services for the neurological patient. Future research is needed to assess outcomes of referral wait times, patient/family satisfaction and referring providers' experience of these alternate models.

KEYWORDS: Neurogenetics

209. A novel pathogenic synonymous TRAPPC2L variant causing aberrant splicing and phenotypic expansion.

Guzman-Karlsson M (Houston, TX), Li S, Faith J, Dardas Z, Levine J, Edmondson E, Sudheendra M, Mizerik E, Scott D, Parnes M, Owen N, Posey J, Lupski J, Liu P, Calame D

OBJECTIVE: To describe two patients with severe neurodevelopmental disorders (NDD) due to a homozygous synonymous TRAPPC2L variant and demonstrate the clinical utility of RNA sequencing (RNA-seq) for evaluating pathogenicity of variants of uncertain significance (VUS).

METHODS: Exome sequencing and RNA sequencing were performed using established sequencing and bioinformatic protocols.

RESULTS: A 2-year-old male presented with microcephaly, developmental delay, spasticity, and epileptiform EEG, but without rhabdomyolysis, hyperCKemia, or clinical decompensation with infections. His MRI revealed cerebral and cerebellar atrophy and delayed myelination. Clinical genetic evaluations revealed absence of heterozygosity totaling 334 Mb across several chromosomes consistent with known historical account of parental consanguinity and a homozygous, synonymous VUS in exon 1 of TRAPPC2L (NM_016209.5:c.33G>A, p.E11=). The nucleotide is highly conserved (phyloP100 7.898) and in silico analysis suggested a deleterious effect (CADD 32). RNA-seq confirmed pathogenicity due to aberrant intron 1 retention. Finally, we identified an additional unrelated individual with the same homozygous variant and phenotype, further supporting variant pathogenicity.

CONCLUSIONS: TRAPPopathies are a group of rare genetic disorders caused by pathogenic variants in genes encoding proteins in TRAPP (TRAfficking Protein Particle) complexes, which are involved in vesicle-mediated transport of proteins and lipids. Pathogenic variants in TRAPPC2L have been identified in four families with progressive early onset encephalopathy with episodic rhabdomyolysis (PEERB, MIM #618331). We demonstrate that not all individuals with PEERB exhibit rhabdomyolysis or decompensation with illness. RNA-seq can improve NDD molecular diagnostic rates by successfully detecting abnormal mRNA splicing or expression outliers due to pathogenic variant alleles.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders, Movement Disorders

210. Aicardi–Goutières syndrome secondary to ADAR mutation masquerading as athetoid cerebral palsy

Deborah L (Dayton, OH), Chikkannaiah M, Fonseca L, Goenka A, Kumar G

OBJECTIVE: This case report describes a 4-year-old boy diagnosed as athetoid cerebral palsy secondary to kernicterus but subsequently found to have Aicardi–Goutières syndrome (AGS) secondary to ADAR mutation.

METHODS: The patient had abnormal MRI brain with bilateral basal ganglia signal changes that were attributed to kernicterus at the initial hospital of care. He was seen for second opinion at our institution and underwent testing with whole exome sequencing (WES), mitochondrial DNA testing, and genetic testing for neurotransmitter disorders.

RESULTS: WES was positive with compound heterozygous mutation in the ADAR gene, which is associated with type 6 Aicardi–Goutières syndrome. He was started on Baricitinib, a Janus kinase (JAK) inhibitor, which resulted in improvement in his speech with expansion of his vocabulary, better language and physical development, and most importantly, no further significant developmental regression.

CONCLUSIONS: This case highlights the importance of considering Aicardi–Goutières syndrome as part of differential diagnoses in patients with bilateral basal ganglia signal abnormalities on MRI brain. With novel treatment options becoming available for AGS, early and accurate diagnosis is imperative and perhaps, if treated early enough, we may be able to prevent severe dystonia that is characteristic of ADAR mutation positive AGS.

KEYWORDS: Neurogenetics, Cerebral Palsy, Neuroimaging

211. Exploring the Landscape of Genetic Testing Orders from Pediatric Neurologists: Utility of CMA With Reflex to WES to Inform Upon Future Guidelines

Stevens A (Salt Lake City, UT), Bilancia C, Serrano M, Al-Sweel N, Baxter A

OBJECTIVE: The American Academy of Neurology and Child Neurology Society previously published guidelines recommending chromosomal microarray (CMA) in children with developmental delay (DD), stating a diagnostic yield of 7.8%1,2. As these guidelines were retired with no published follow-up, we present the experience of one laboratory with genetic testing orders from pediatric neurologists demonstrating the importance of CMA with reflex to whole exome sequencing (WES) for children with DD as well as other clinical indications.

METHODS: A retrospective review was completed on all CMA and reflex WES orders from pediatric neurologists at our laboratory between January 2018 - March 2023. Diagnostic rates were calculated for the following groups: CMA with DD as an indication (n=1,709), CMA without DD as an indication (n=4,479), and reflex WES for any indication (n=42).

RESULTS: Our diagnostic rates for CMA in the DD and non-DD populations were comparable. Patients who received CMA with reflex to WES had 9.52% diagnostic yield compared to 8% with CMA alone.

CONCLUSIONS: CMA identifies structural variations (deletions and duplications) while WES detects sequence variants. Thus, a patient with DD or other clinical indications would benefit from CMA with reflex to WES testing, resulting in a combined diagnostic yield of ~17% in our lab's experience. Strict adherence to these previous guidelines for use of CMA only in patients with DD will miss an appreciable proportion of diagnoses. This data supports the need for updated genetic testing guidelines for child neurologists including CMA with reflex to WES for a wide range of clinical indications.

KEYWORDS: Neurogenetics, Neurodevelopmental Disorders, Practice Parameters

212. Large vessel vasculopathy in a previously healthy school-aged child: expansion of COL4A1 phenotype?

Camperchioli D (Salt Lake City, UT), Coletti M, Fleming E, Pabst L

OBJECTIVE: Describe a case of recurrent arterial ischemic strokes in a previously healthy school-aged child as a novel presentation of a COL4A1 spectrum disorder, which is typically associated with small vessel vasculopathy.

METHODS: Chart Review.

RESULTS: A healthy 10-year-old girl presented after a mild trampoline fall progressed to stuttering right hemiparesis and aphasia. MRI revealed a left middle cerebral artery internal borderzone infarct. CT angiogram demonstrated long segmental narrowing from the left internal carotid artery (ICA) bifurcation through the cavernous segment, suggesting dissection. Treatment included anticoagulation. Follow-up vessel imaging showed stable critical stenosis of the left supraclinoid ICA. She subsequently developed transient dysarthria secondary to a new left anterior cerebral artery infarct. Diagnostic catheter angiogram demonstrated diminutive caliber of the left ICA with critical supraclinoid stenosis, occlusion of the left A1 segment and short segment moderate right supraclinoid ICA stenosis without evidence of moyamoya vasculopathy. Workup for vasculitis was unremarkable and rapid genome testing identified a de novo pathogenic COL4A1 mutation. Secondary stroke prevention was changed to aspirin and the patient has no residual deficits. Screening evaluation was negative for ophthalmologic, cardiac, or renal defects.

CONCLUSIONS: COL4A1 disorders in children cause small vessel white matter disease, intracerebral hemorrhage, porencephaly, epilepsy, and developmental delay. Other than in a recent report of familial cervical arterial dissection, COL4A1 large vessel arteriopathies have not been described. This child's case may represent an expansion of the COL4A1 phenotype to large vessel arteriopathy precipitated by minor trauma in neurotypical children. Further study is needed.

KEYWORDS: Neurogenetics, Stroke

213. Reconstructing the longitudinal history of SYNGAP1-related disorders through data integration across healthcare resources

McKee J (Philadelphia, PA), Xian J, Cohen S, Toib J, Brimble E, Fitter N, Helbig I

OBJECTIVE: SYNGAP1-related neurodevelopmental disorder is one of the more common monogenic causes of generalized epilepsy, including myoclonic-astatic epilepsy, intellectual disability, and autism spectrum disorder. The clinical variation in individuals with SYNGAP1-related disorder is poorly understood, and no clear genotype-phenotype relationship has been established.

METHODS: We assessed clinical data in 155 individuals with SYNGAP1-related neurodevelopmental disorder across >1180 patient years, mapping clinical annotations onto the human phenotype ontology (HPO) in individuals with protein-truncating (PTV, n=133) vs. missense (n=20) variants. We reconstructed the seizure histories of 114 individuals across 1,622 patient months and retrieved 2,564 anti-seizure medication (ASM) prescriptions from the electronic medical records in addition to 850 medications targeting behavioral symptoms. Furthermore, we used a novel comparative effectiveness framework to assess seizure patterns and ASM response.

RESULTS: The overall phenotypic landscape in SYNGAP1-related neurodevelopmental disorder is characterized by developmental delays or intellectual disability in 97% and seizures in 76% of individuals. Seizures are usually generalized, including absence (27%), myoclonic (23%) and atonic (30%). The most effective ASMs were lamotrigine and valproate. Autism spectrum disorder is prevalent (59%) and behavioral concerns were present in 94% of individuals, including aggression (51%), ADHD (12%), and sleep disturbances (71%).

CONCLUSIONS: We utilized a data-driven approach to assess phenotypic patterns, identify clinically significant genotype-phenotype correlations, and demonstrate the

dynamic pattern of seizures and drug response in individuals with SYNGAP1-related disorder. Elucidating the full clinical spectrum in SYNGAP1-related disorder will be critically important for understanding the disease mechanism, developing disease-specific outcome measures and guiding future precision medicine efforts.

KEYWORDS: Neurogenetics, Epilepsy, Early Stage Investigator

214. Genetic Modifiers of Disease Severity in Tuberous Sclerosis Complex

Sanchez-Castillo M (Phoenix, AZ), Rangasamy S, Ramsey K, Sekar S, Adkins J, Cuyugan L, Monheim-Janss C, Sankaramoorthy A, Kaneshamoorthy S, Swaminathan P, Aziz A-M, Narayanan V

OBJECTIVE: In Tuberous Sclerosis Complex (TSC), phenotypic variability has been observed within a single family (intrafamilial phenotypic variability-IPV), where all the affected individuals have the same TSC1 or TSC2 mutation. This IPV indicates the possibility that other factors could be contributing to a mild or severe phenotype.

We hypothesized that this variation could be due to (1) other variants found in genes (other than TSC1 and TSC2), or (2) differential expression of mTOR network genes.

METHODS: We enrolled 15 parent-child pairs with TSC where the child was severely affected but the parent was mildly affected. We aimed to identify genetic modifiers that could account for this variability though comprehensive exome and transcriptome sequencing analysis focused on mTOR pathway genes.

RESULTS: RNA sequencing data showed 18 differentially expressed genes between the mildly affected parents (RPTOR, LAMTOR4, LRP5, ULK1) and the severely affected children (PIK3C2A, EIF4G1, SREBF1, and PIK3R3). Of these differentially expressed genes, 6 were upregulated and 12 were downregulated relative to the severe phenotype. In a family with a TSC2 deletion, we identified a RPTOR variant (p. R997C) in a mildly affected parent which indicates that RPTOR variants could reduce mTOR pathway activity in TSC patients. Thus p. R.997C can be considered a protective variant in mildly affected parents with a TSC mutation.

CONCLUSIONS: Our research aimed to define a comprehensive set of modifier genes that could be used as genetic biomarkers to predict disease severity. Such a test may allow us to select patients for early initiation of disease modifying therapies.

KEYWORDS: Neurogenetics, Neuro-Cutaneous Disorders, Epilepsy

215. GATORopathy with a twist: A novel partial gene deletion in NPRL3 with variable expressivity

Guzman-Karlsson M (Houston, TX), Fisher K

OBJECTIVE: To describe a novel heterozygous partial gene deletion in NPRL3 and highlight the associated variable expressivity in focal epilepsy and malformations of cortical development.

METHODS: This case report involves two related patients, specifically a brother and sister, who underwent whole exome sequencing (WES) and were found to have a maternally-inherited, heterozygous, 4kb deletion of chromosome 16p13.3, including exon 9 of NPRL3, predicted to result in loss of function and presumed haploinsufficiency.

RESULTS: The affected brother is a 19-year-old male with left hemimegalencephaly, intellectual disability, quadriplegic spastic cerebral palsy, and medically refractory epilepsy characterized by focal motor epilepsy with secondary generalization, currently managed on oxcarbazepine and zonisamide. The affected sister is a developmentally typical 14-year-old female with chronic tension headaches and non-lesional, focal motor/sensory seizures with intact awareness of childhood-onset, currently managed on oxcarbazepine monotherapy.

CONCLUSIONS: GATORopathies are a group of rare genetic disorders caused by pathogenic variants in genes encoding subunits of the GATOR1 complex (DEPDC5, NPRL2, and NPRL3), resulting in hyperactivation of mTOR complex I (mTORC1) pathway. NPRL3-related disorders exhibit a variable phenotypic spectrum characterized by autosomal dominant focal epilepsies, malformations of cortical development (focal cortical dysplasia, hemimegalencephaly, and megalencephaly), and neurodevelopmental features.

KEYWORDS: Neurogenetics, Epilepsy, Neuroimaging

216. Multigene panel testing results in patients with clinical suspicion of leukodystrophy and correlation by race/ethnicity and potential for therapeutic impact

Bonkowsky J (Salt Lake City, UT), Morales A, Chen E, McKnight D, Agre K, Esplin E

OBJECTIVE: To determine the prevalence of genetic findings in patients with clinical suspicion of leukodystrophy, the association with self-reported ancestry, and their potential clinical implications.

METHODS: A retrospective analysis of individuals presenting with clinical concerns for leukodystrophy who had a multigene panel test for leukodystrophies between 9/17/2020 – 02/10/2023. Chi-squared test was used to analyze positive rate differences.

RESULTS: 7,581 individuals had testing; 7,439 (98%) were the proband. The cohort had a mean age at testing of 15.9 years; 3,392 (45%) were female; 191 (3%) Asian, 236 (3%) Black/African-American, 2320 (31%) Hispanic, and 3358 (44%) White. A molecular diagnosis was identified in 1,117 (15%) probands. The highest molecular diagnoses rates were in 23% and 20% of Asian and Hispanic individuals, respectively ($p < 0.001$). Among the 1,117 patients with a molecular diagnosis, medical management implications were identified in 605 (54%), including interventions for drug therapy (n=358; 59%), prognosis (n=292; 48%), medical intervention (n=179; 30%), and lifestyle (n=27; 4%). The most common leukodystrophies identified in decreasing order of prevalence were Adrenoleukodystrophy, Metachromatic Leukodystrophy, Pelizaeus-Merzbacher disease, and Alexander disease; 234 different leukodystrophies had at least one patient identified.

CONCLUSIONS: Our results show a broad distribution of different genetic leukodystrophies across and ethnicities. 54% of patients with a molecular diagnosis had genetic findings

with clinical actionability. Our analysis suggests that the higher positivity rates in Asian and Hispanic individuals is unlikely to result from a founder effect. The reason for the higher positivity rates in these groups is unknown and requires more research.

KEYWORDS: Neurogenetics, Neurometabolic, Pediatric Demyelinating Disease

NEUROIMAGING

217. Texture features obtained using 3D MRI reveal abnormalities in brain regions associated with cognitive impairment in obese children with OSA

Sare D (Toronto, ON, Canada), Brocke A B, Kassner A K

OBJECTIVE: The aim of this study was to characterize brain abnormalities on T2-weighted MRI using texture analysis on specified subcortical brain regions of interest (ROIs) impacted by cognitive impairment in obese children with and without obstructive sleep apnea (OSA).

METHODS: T1- and T2-weighted MR images of 43 obese subjects (19 with moderate to severe OSA and 24 with no OSA) acquired using a 3T MRI system were used for analysis. Polysomnography confirmed OSA presence and severity. Preprocessing included co-registration, brain extraction, and automatic segmentation of subcortical regions from T1 anatomical images using FreeSurfer. Texture analysis using LIFEx software was applied within these regions on T2-weighted data to generate 164 texture features per subcortical region. Features were analyzed within 8 subcortical ROIs known to be associated with cognitive impairment in children with OSA. Student's t-test was used to compare the features between groups, and classification performance was evaluated using receiver operating characteristic (ROC) analysis

RESULTS: Five out of the eight subcortical regions (left thalamus, left and right hippocampus, and left and right amygdala) contained texture features that showed significant differences ($p < 0.05$) between the two groups.

CONCLUSIONS: By applying 3D MRI texture analysis on data in obese children with and without OSA, we were able to show that the presence of OSA is associated with microscopic changes in normal-appearing white matter in regions impacted by cognitive impairment. These findings are also associated with lower tissue homogeneity and a decrease in cortical density and thickness previously reported in children with OSA.

KEYWORDS: Neuroimaging, Sleep

218. Effect of Propofol Dosing on EEG Fast Activity in Pediatric Patients

Asato BH (Honolulu, HI), Shin Y, Gragas K, Abe K, Yamamoto G

OBJECTIVE: For patients with seizures, electroencephalograms (EEG) in parallel with the referral to neurology can expedite initial evaluation. Patients may require sedation, resulting in EEG artifact "fast activity" (FA), making the EEG more difficult to read. The purpose of this study is to investigate propofol dosing and its relationship to FA artifact.

METHODS: This study involved retrospective chart reviews at a children's hospital for sedated EEG encounters. Data was collected from a total of 43 charts. Total doses of propofol (mg/kg/hr) were calculated for the first half (start time of sedation to the midpoint of EEG) and the second half (midpoint of EEG to end of EEG). The EEGs were reviewed by a pediatric neurologist study investigator (who was blinded to the propofol dosing), to classify the degree of FA: none, mild, moderate, severe. Using linear regression and ordinal logistic regression, we examined whether total doses of propofol given during the EEG halves affected the severity of FA.

RESULTS: Propofol doses (paired T-test, $p<0.001$) and EEG FA (Bowker's test of symmetry, $p=0.002$) were higher in the first half compared to the second half of the sedated EEG procedures, allowing us to treat each half as separate samples. Linear and ordinal logistic regression shows a positive relationship between propofol dosing and FA severity ($p=0.0007$, OR=1.22, 95% CI=1.09-1.38, respectively).

CONCLUSIONS: Fast activity due to propofol appears to be dose-dependent. Lower doses of propofol resulted in less FA on EEG, suggesting that reducing the propofol dose can reduce the FA artifact, improving interpretations of these studies.

KEYWORDS: Neuroimaging, Epilepsy

219. Divided by a thin line: a case report of Marchiafava-Bignami in a child with severe malnutrition.

Bacus P (Lexington, KY), Toupin N, Haghighat Z

OBJECTIVE: We review a 5-year-old patient who came to our institution with symptoms of severe dehydration secondary to gastrointestinal illness, severe malnutrition and concern for abuse/neglect. The patient was diagnosed with Marchiafava-Bignami syndrome based off MRI brain findings. This report adds to the sparse number of documented cases and a review of the relevant literature.

METHODS: Literature review performed on PubMed and Cochrane review using terms "Marchiafava- Biganami disease" and "MBD"

RESULTS: The patient is a 6-year-old female with nonverbal autism spectrum disorder who had not received care in five years. She was born intrauterine growth restriction (IUGR) and did not receive prenatal care until late 2nd or 3rd trimester. The patient presented to the hospital with a two-day history of a gastrointestinal illness, was found to have severe dehydration, needing resuscitation with fluids in the pediatric intensive care unit. Due to her presentation and concern for abuse/neglect brain MRI was obtained which showed significant demyelination/necrosis of the corpus callosum and T2 hyperintensities of the right frontal lobe. A repeat MRI after 10 days showed less pronounced abnormal signal in the corpus callosum after improvement in her nutrition.

CONCLUSIONS: MBD has significant impact in teenagers and adults however due to its rarity is it is difficult to say

what the significance is in infancy and early childhood. More case reports and studies are necessary to determine if and what long-term impact MBD may have.
KEYWORDS: Neuroimaging, Pediatric Demyelinating Disease, Neurodevelopmental Disorders

220. The presence of OSA increases cerebral blood flow and decreases gray matter volume in obese youth: an MRI study

Sherwood S (Toronto, ON, Canada), Sare D, Kassner A

OBJECTIVE: The purpose was to assess MRI measures of cerebral blood flow (CBF) and gray matter (GM) volume in obese youth ± moderate/severe obstructive sleep apnea (OSA). OSA is associated with periods of intermittent hypoxia and is a common comorbidity in obese youth which may impact brain development; we hypothesize that obese youth with OSA have altered CBF and GM volumes.
METHODS: 23 obese children (aged 13.9 ± 2.7) underwent polysomnography and were classified into two groups: No OSA (n = 13), and Moderate/Severe OSA (n = 10). 3T MRI data were acquired - arterial spin labeling (ASL) and a 3D T1-weighted sequence. CBF maps and GM volumes were extracted using ExploreASL. A Linear Mixed Effects model was used to compare both groups in relation to sex, BMI, and age with a threshold of significance of $p = 0.05$.
RESULTS: Obese Moderate/Severe OSA subjects had significantly higher GM CBF than subjects without OSA, both between groups alone ($p = 0.046$), and when considering the effects of sex and BMI ($p = 0.050$). Moderate/Severe OSA subjects showed increased CBF with age, while No OSA subjects showed a decrease. No significant relationships in GM volume emerged between the groups alone, however, Moderate/Severe OSA subjects showed a significant age-related GM volume decrease when compared to No OSA subjects ($p = 0.0014$).
CONCLUSIONS: The CBF increase could be a compensatory response to the hypoxia associated with OSA even at wakefulness, while the GM decrease may be associated with neuronal damage. Further research is needed to investigate this.
KEYWORDS: Neuroimaging, Sleep

221. An Altered Teenager, Pouncing on the Diagnosis

Wright J (Winston-Salem, NC), Lapid D

OBJECTIVE: To describe the clinical and radiographic features of a rare condition.
METHODS: A 16 year-old female presented with altered mental status and electrolyte derangements after multiple days of vomiting, poor oral intake, and lethargy. Family reported a history of regular illicit Percocet use. On her initial exam, she was obtunded but followed some commands. She had mutism versus expressive aphasia, upward gaze preference, proximal weakness, and low tone. She was ultimately intubated on day 2 of admission for disordered breathing.
RESULTS: Brain MRI demonstrated areas of restricted diffusion in the bilateral cerebellar dentate nuclei, adjacent cerebellar white matter, and middle cerebellar peduncles with faint edema without intracranial mass effect, and a cytotoxic lesion of the corpus callosum. Over the course of 3-4 weeks, her exam evolved to scanning speech, bilateral dysmetria, and truncal titubation. Repeat brain MRI one month after initial imaging demonstrated mild cerebellar volume loss with interval resolution of previously seen restricted diffusion. Metabolic, nutrition, infectious, and autoimmune workup were also pursued which was largely negative, except for low B6 (2.6).
CONCLUSIONS: Her presentation and clinical course is consistent with Pediatric Opioid Use-associated Neurotoxicity with Cerebellar Edema (POUNCE) syndrome. POUNCE syndrome is a rare condition postulated to be caused by a direct neurotoxic effect to cerebellar opioid receptors leading to cytotoxic edema. Most commonly presents with bilateral cerebellar edema and diffusion restriction. The clinical course may be complicated by herniation, compression, or hydrocephalus. Clinicoradiological monitoring is required and surgical intervention has been required in severe cases.
KEYWORDS: Neuroimaging, Neurocritical Care

222. Leigh syndrome masquerading as a leukodystrophy: A Case Report

Hogue B (New York City, NY), Garcia M, Steigerwald C, Borja M, Abreu N

OBJECTIVE: Leigh syndrome is typically associated with basal ganglia and brainstem involvement, though cases of confluent white matter disease have been well-described with certain genetic variants, specifically NDUFS8-related disorders. This case report demonstrates a novel variant in NDUFS8 initially presenting with imaging suggestive of a leukodystrophy.
METHODS: Case Report.
RESULTS: A 6-month old of non-consanguineous Honduran parents presented with hypotonia and MRI suggestive of a leukodystrophy. She developed progressive encephalopathy, dysphagia and spastic quadriparesis in the setting of illness. Additional evaluation showed lactic acidosis, hyperCKemia and progressive signal abnormalities on neuroimaging two months later. She expired at 15 months in the setting of sepsis and respiratory failure. A novel homozygous variant in NDUFS8 (c.307 C>T p.(R103W)) was identified, consistent with Leigh syndrome in this clinical setting. Parents were found to be heterozygous.
CONCLUSIONS: Biallelic variants in NDUFS8, which encodes a complex I subunit of the mitochondrial electron transport chain, have been associated with Leigh syndrome. While Leigh syndrome is typically associated with basal ganglia and brainstem involvement, cases of confluent white matter disease have been well-described with NDUFS8-related disorders. This case demonstrates a novel variant in NDUFS8 associated with Leigh syndrome and highlights that mitochondrial disorders should be considered in the differential for confluent cerebral white matter disease in early childhood.
KEYWORDS: Neuroimaging, Neurogenetics

NEUROIMMUNOLOGY & NEUROINFECTIOUS DISEASE

223. Antibody response to SARS-CoV-2 vaccination or infection in a prospective cohort of children with neuroinflammatory diseases

Gombolay G (Atlanta, GA), Kaufmann C, Morris M

OBJECTIVE: Antibody responses to SARS-CoV-2 vaccination are altered by immune medications in adults with neuroinflammatory disorders, but little is known about antibody responses in children with neuroinflammation and on immune treatments. Here we measure antibody levels post-SARS-CoV-2 vaccination or infection in children by disease modifying therapy (DMT).

METHODS: Children under 21 years of age with pediatric-onset neuroinflammatory disorders who received at least two mRNA vaccines were included. Plasma samples were assayed for SARS-CoV-2 antibodies (spike, spike receptor binding domain-RBD, nucleocapsid) and neutralization antibodies using an electrochemilumenscence assay (MesoScale Discovery).

RESULTS: Twenty-one participants with pediatric onset neuroinflammatory diseases were included: 16 multiple sclerosis, one neuromyelitis optica spectrum disorder, two MOG-associated disease, and two autoimmune encephalitis. Eighteen were on medications (12 on CD20 monoclonal antibodies-mAbs, four on fingolimod, one on steroids, one on intravenous immunoglobulin) and three were untreated. Thirteen patients also had pre-vaccination samples available. All participants had seropositivity to spike or spike RBD antibodies except for those receiving CD20 mAbs. However, this proportion was higher in children than in an adult MS patient cohort. The most significant contributor to negative antibody levels was a longer duration of DMT.

CONCLUSIONS: SARS-CoV-2 antibodies are decreased in children on CD20 monoclonal antibodies than on other treatments. Treatment duration associated with vaccination responses. Further studies should also investigate T cell responses to SARS-CoV-2 vaccination and clinical implications of post-SARS-CoV-2 vaccination immune responses.

KEYWORDS: Neuroimmunology, Neuroinfectious Disease

224. Approach to new-onset neuropsychiatric symptoms in children: a multidisciplinary consensus for inpatient evaluation and treatment of suspected autoimmune encephalitis at a single-center institution

Nguyen L (Dallas, TX), Abdel A, Odom C, Remster E, Diederich A, Lee J, Wang C

OBJECTIVE: Autoimmune encephalitis (AE) is an inflammatory brain disease with varied clinical features, including cognitive and psychiatric changes, movement disorders, and seizures. Diagnosis of AE can be challenging, particularly when a patient presents with predominantly psychiatric symptoms, has normal paraclinical studies, and is antibody negative. Workup offered to pediatric patients can be highly variable. We present an inpatient clinical pathway and weighted scoring approach to a child presenting with new-onset neuropsychiatric symptoms concerning for AE.

METHODS: A multidisciplinary team consisting of hospitalist medicine, psychiatry, neurology, neuroimmunology, and emergency medicine physicians, nurses and ancillary staff convened to create and implement a standardized approach and scoring model for assessment and management of acute to subacute onset of neuropsychiatric symptoms concerning for AE. A retrospective chart review was also conducted to assess the performance of our scoring model for predicting likelihood of AE.

RESULTS: Our scoring model and guidelines draw from current practice guidelines and review of limited published evidence specific to the pediatric population. The scoring model considers multiple factors, including clinical presentation, CSF, serological, MRI and EEG findings. We also report on the validation of our scoring model using a retrospective cohort who underwent AE workup at our institution.

CONCLUSIONS: We present an evidence-based approach for evaluating the likelihood of AE as the primary cause of new-onset neuropsychiatric symptoms in children. This objective scoring system reduces subjectivity in interpretation of individual scored factors and helps provide a rational basis whether or not to administer empirical immunotherapy. Future directions include prospective studies to validate this approach.

KEYWORDS: Neuroimmunology, Practice Parameters

225. A novel presentation of pediatric N-methyl D-aspartate receptor encephalitis (NMDARE) and possible neurosarcoidosis overlap syndrome

Alaqla N (Washington, DC), Redmond C, Sherman M, Sule S, Wells E, Kornbluh A

OBJECTIVE: Describe a complex pediatric case of anti-N-methyl-d-aspartate receptor encephalitis (NMDARE) and possible neurosarcoidosis with excellent therapeutic response to interleukin-6 (IL-6) receptor blockade.

METHODS: Chart review

RESULTS: A 9-year-old boy presented with new right-sided focal motor seizures and encephalopathy. Seizures remained refractory despite escalation of three medications. EEG showed left-sided slowing with epileptiform discharges, and MRI showed right > left frontal convexity leptomeningeal and cranial nerve 7/8 complex enhancement. CSF infectious evaluation was negative but oligoclonal bands were positive.

After presenting in status epilepticus, he was treated with empiric IVIg and pulse IV methylprednisolone. Expanded inflammatory workup revealed elevated serum and CSF IL-6, so IV tocilizumab was given. Neuropsychological testing revealed hypophonic, poorly articulated speech and deficits in temporal orientation, memory, and response speed. Tocilizumab treatment led to seizure resolution as well as improved speech and mental status. Further workup revealed elevated serum and CSF angiotensin converting enzyme (ACE) and positive CSF NMDA titers (1:4). Post-steroid meningeal biopsy showed nonspecific perivascular

inflammation but no granulomas. The patient was discharged with plan to continue IVIg and subcutaneous tocilizumab. At 1 month follow-up he remained seizure-free with ongoing cognitive improvements.
CONCLUSIONS: There are few reports of NMDARE overlapping with neurosarcoidosis, and none previously described in children. Elements in favor of NMDARE include the clinical presentation and CSF NMDA antibodies; aspects aligned with neurosarcoidosis include MRI findings and positive serum/CSF ACE. Our patient responded well to treatment with IL-6 receptor blockade, highlighting the benefits of utilizing cytokines to guide empiric immunotherapy in children presenting with neuroinflammatory disease.
KEYWORDS: Neuroimmunology

226. MRI of the optic pathway as a preliminary pathway to timely diagnosis of MOG spectrum disorder in children

Saini L (Jodhpur, India), Kumar A, Laxmi V, Manjunathan S, Gunasekaran P K, Tiwari S, Varshney J S

OBJECTIVE: MOG (Myelin oligodendrocyte glycoprotein) associated disorders are a relatively recent expanding group of diseases increasingly recognized with the emerging advancement in the Pediatric acquired demyelination syndromes. The myriad of clinical presentations is ever-expanding, and thus, Early identification of emerging phenotypes can play a pivotal role in achieving this target.
METHODS: All pediatric patients with MOG antibody-positive children in 2022 were identified from the hospital records. A retrospective chart review was done to find an early radiographic pointer toward early and specific diagnosis.
RESULTS: Sixteen patients with MOG antibody positive were identified. Out of these 16, 2 presented with visual disturbances and features suggestive of optic neuritis, 6 presented with encephalopathy and altered sensorium, 3 presented with lower limb weakness, 2 presented with ataxia, and 3 presented with features of meningoencephalitis. On neuroimaging, 13 patients (excluding the ones with clinical features of transverse myelitis alone) had involvement in the anterior segments of the optic nerve. 8 out of these 13 patients with MOG antibody positive had a distinctive optic nerve head enhancement visible on MRI, however clinically, papilledema was visible only in 5/8.
CONCLUSIONS: Radiological optic nerve head edema on MRI visible as a distinctive rim-like enhancement post-contrast bulging through the orbit, even in the absence of clinical papillitis or papilledema, can serve as an early and specific marker of MOG encephalitis, prior to the evolution of specific clinical signs suggesting blown clinical disease spectrum.
KEYWORDS: Neuroimmunology, Neurocritical Care

227. Acute immune-mediated sensory polyneuropathy with anti-ganglioside antibody pan-positivity in a pediatric patient

Runco A (Houston, TX), Guzman-Karlsson M, Yarimi J, Gill J

OBJECTIVE: To describe a rare pediatric presentation of a pure sensory Guillain-Barré syndrome variant.
METHODS: Descriptive Case Report
RESULTS: A 13-year-old male presented with a 3-day history of intermittent diplopia, progressive difficulty with walking, and bilateral numbness of hands, feet, and lower trunk in the setting of an antecedent non-bloody diarrheal illness. His exam was remarkable for sensory ataxia with preserved cranial nerve function, strength, and reflexes. MRI brain and complete spine with and without contrast revealed enhancement of thoracic and lumbar dorsal nerve roots. CSF analysis showed cyto-albuminologic dissociation with a mild pleocytosis (WBC 8, RBC 2, protein 95, glucose 64). Confirmational testing revealed positive serology for anti-GD1b, anti-GD1a, and anti-GQ1b antibodies. Furthermore, 11 days after symptom onset, an EMG/NCS showed reduced sensory nerve amplitudes and latencies, confirming a sensory polyneuropathy with motor sparing. While hospitalized, the patient received immunotherapy consisting of a 3-day course of IVIG with subsequent symptomatic improvement, allowing for discharge home with outpatient physical and occupational therapies. By 3-month outpatient neurology follow-up, the patient had complete symptom resolution and intact activities of daily living, not requiring additional immunotherapy or rehabilitative therapies.
CONCLUSIONS: Pure sensory variants of GBS are rare, atypical, and often misdiagnosed presentations of sensory loss and ataxia. A complete neurological evaluation that utilizes CSF analysis, diagnostic imaging, electrodiagnostic studies, and autoantibody testing can provide diagnostic certainty, improved prognostication, and may improve time to recovery, especially in rare variants.
KEYWORDS: Neuroimmunology, Neuromuscular, Pediatric Demyelinating Disease

228. Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) secondary to norovirus infection.

Parekh A (Dayton, OH), Chikkannaiah M, Fonseca L, Agarwal A, Kumar G

OBJECTIVE: This article illustrates the case of a previously healthy boy diagnosed with Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) secondary to norovirus infection.
METHODS: We describe a 2-year-old boy who presented with febrile status epilepticus and was diagnosed with AESD. Investigations included a continuous EEG monitoring, neuroimaging studies, cerebrospinal fluid (CSF) evaluation, metabolic, autoimmune, and infectious work-up. A review of literature of AESD secondary to norovirus and other etiology was performed.
RESULTS: Head CT completed in the emergency department (ED) was negative. Initial MRI brain at 24 hours of presentation, showed large confluent areas of T2 signal abnormality with restricted diffusion throughout the cerebellum and similar, smaller areas in the subcortical white matter of occipital lobes, parietal lobes, and to a lesser extent in the frontal lobes. Continuous EEG showed left > right generalized slowing and bilateral, independent, left > right frontally predominant diffuse epileptiform activity. Extensive work up was negative except for Gastrointestinal Infectious Disease Panel, which was positive for Norovirus. Follow up MRI brain completed 5 days after initial presentation due to

persistent encephalopathy showed near diffuse, abnormal T2 prolongation and restricted diffusion throughout the subcortical white matter and cortex of the cerebral and cerebellar hemispheres bilaterally and he was diagnosed with AESD.
CONCLUSIONS: Acute encephalopathy with biphasic seizures and late reduced diffusion is often caused by viral infection, however other etiologies like bacterial infection and trauma have also been reported. Outside of Asian countries, especially Japan, AESD is rare, indicating that genetic background may play a role.
KEYWORDS: Neuroimmunology, Neuroimaging, Neuroinfectious Disease

229. Neuroinflammatory Disease of the Neuroaxis and ROHHAD: Casting A Wide NET

Sudheendra M (Houston, TX), Guzman-Karlsson M, Pareek A, Kannan V, Shukla N, Lotze T, Hardwick V

OBJECTIVE: To describe clinical, imaging, and laboratory features of a neuroinflammatory syndrome affecting the central and peripheral nervous system in a patient with rapid-onset obesity with hypothalamic dysfunction, hypoventilation, autonomic dysregulation, and neuroendocrine tumor (ROHHAD-NET).
METHODS: This case report was created through retrospective chart review.
RESULTS: A seven-year-old boy with a known diagnosis of ROHHAD and cardiomyopathy presented with subacute-onset of catatonic stupor in association with dystonia characterized by leftward head version and left arm tonic flexion as well as bilateral leg weakness. Brain MRI revealed restricted diffusion and hyperintense T2 signal involving the globi palidi, thalami, and cerebellar cortices. EEG demonstrated diffuse slowing. Body MRI identified a presacral mass suggestive of an NET. CSF showed albuminocytologic dissociation (WBC 5, Protein 224) and oligoclonal bands. Serologic antibody testing (GM1, GQ1b, paraneoplastic) was negative. Electrodiagnostic studies revealed acute demyelinating motor neuropathy. He received five days of high-dose intravenous methylprednisolone and 2 gm/kg of IVIG, with subsequent improvement in his leg strength, prompting continuation of monthly IVIG treatments. Wakefulness and dystonia improved with lorazepam and memantine. Due to his cardiomyopathy and high surgical risks, excision of the presacral mass was not attempted.
CONCLUSIONS: In addition to classic symptoms of ROHHAD-NET, our patient had diffuse involvement of the neuroaxis, including the brain and peripheral nervous system, with features suggestive of a neuroinflammatory etiology. This supports emerging evidence for paraneoplastic immune-mediated disease mechanisms in ROHHAD-NET.
KEYWORDS: Neuroimmunology

230. Metabotropic glutamate receptor 1 (mGluR1) antibody positivity in a child presenting with acute cerebellar ataxia

Abdel A (Dallas, TX), Geraldino-Castillo E, Wang C

OBJECTIVE: Metabotropic glutamate receptor 1 (mGluR1) antibody autoimmune encephalitis is a rare condition that can present as ataxia, primarily in adults. It is characterized by three phases: a prodromal phase (headache, fatigue, nausea, and myalgias), a cerebellar phase (dysarthria, gait and trunk instability, nystagmus, and limb ataxia) and a neuropsychiatric phase (altered mental status, memory deficits, and mood changes). We present a case that highlights the importance of considering this entity as a cause for cerebellar ataxia in a young child.
METHODS: Case report featuring clinical presentation, laboratory and neuroimaging results, with discussion of differential diagnosis and medical decision making.
RESULTS: Patient CI is a 6-year-old female who presented with five days of dizziness, vertigo, and gait instability without any apparent antecedent event. She was discharged with a diagnosis of acute cerebellar ataxia with a recommendation of supportive care and physical therapy. She returned twelve days later with persistent cerebellar dysfunction and development of cognitive slowing, emotional blunting, and overall fatigue. MRI Brain showed several tiny foci of non-specific T2 hyperintensities. Spine imaging and CSF profile were normal. Symptoms had persisted for a month without improvement when results returned with positivity for metabotropic glutamate receptor 1 (mGluR1) antibody.
CONCLUSIONS: While the incidence of antibody-mediated cerebellar ataxia is unclear, it is likely that early treatment is beneficial. Delays in immunotherapy may result in neuronal cell death, cerebellar atrophy, and persistent neurological deficits. We argue autoimmune encephalitis testing should be considered in children with persistent ataxia and neuropsychiatric symptoms.
KEYWORDS: Neuroimmunology

231. Anti-NMDA receptor (NMDAR) encephalitis manifesting with auditory agnosia, a case report

Salazar K (Houston, TX), Guzman-Karlsson M, Wells D, Fisher K

OBJECTIVE: Often confused for schizophrenia, pediatric NMDAR encephalitis is an increasing cause of new-onset psychosis. Here we present a case of medically refractory NMDAR encephalitis characterized by encephalopathy, seizures, and dystonia, along with the uncommon manifestation of verbal auditory agnosia.
METHODS: Case Report
RESULTS: A previously healthy neurotypical 17-year-old male was transferred from an inpatient psychiatric center where he presented with a 1-month history of increasing agitation, forgetfulness, manic behaviors, and hallucinations. On exam, he was noticeably agitated and disoriented, with non-fluent speech and inability to follow commands.
Workup was positive for serum and CSF anti-NMDAR antibodies (1:320). EEG showed diffuse slowing with rhythmic theta activity in bifrontal regions. Initial MRI notable for signal abnormality on diffusion-weighted and T2 imaging along parasagittal frontal and cingulate convexities, but subsequent imaging normalized. While hospitalized, he received intravenous methylprednisolone, Rituximab, and ultimately escalation to tocilizumab for refractory symptoms. During inpatient rehabilitation, he made significant gains in motor

and occupational functionality compared to his speech and language abilities. Although able to read, follow written commands, and understand non-verbal gestures, he exhibited marked difficulty with understanding and following verbal commands. Audiological evaluation revealed intact sensorineural hearing, confirming likely verbal auditory agnosia. Thirteen months after initial presentation, he began to show improvement in understanding of spoken language.
CONCLUSIONS: Auditory agnosia is a rare neurologic manifestation resulting from numerous etiologies, including structural, cerebrovascular, and genetic. This case highlights NMDAR encephalitis as a rare cause of verbal auditory agnosia, postulated to be secondary to NMDA-receptor hypofunction.
KEYWORDS: Neuroimmunology

232. A case of Parechovirus Meningoencephalitis with Absent Pleocytosis

Al-Robaidi K (Birmingham, AL), Rashid S

OBJECTIVE: The presence of pleocytosis in the cerebrospinal fluid (CSF) can be an essential marker aiding in the timely diagnosis of a central nervous system infection in pediatrics. We present a case of Parechovirus meningoencephalitis with an absent CSF pleocytosis.
METHODS: A case report.
RESULTS: A 17 days old male infant presented to our emergency department with fever. The infant was born at term after an uncomplicated pregnancy and delivery. Shortly after presentation, the patient started having clinical seizures with unresponsiveness, gaze deviation, and upper extremity shaking that were later captured on electroencephalogram monitoring. His initial cerebrospinal fluid (CSF) indices were unremarkable with 3 white blood cells, normal protein and glucose for age. Magnetic Resonance Imaging (MRI) of the Brain revealed extensive bilateral diffusion restriction in the white matter and meningeal enhancement. The brain MRI findings triggered discussions on the potential differential diagnoses, including infectious, metabolic, or hypoxic-ischemic etiologies. However, the lack of involvement of the basal ganglia pointed away from a likely metabolic or hypoxic-ischemic cause. Subsequently, the CSF Biofire Meningitis Encephalitis Panel returned positive for Human Parecho Virus (HPeV).
CONCLUSIONS: The absence of pleocytosis on CSF analysis can be misleading when meningoencephalitis is clinically suspected in a neonate, especially in cases of Parechovirus encephalitis. Brain MR imaging and PCR analysis are tools that can help make the diagnosis when clinically suspected.
KEYWORDS: Neuroinfectious Disease, Neuroimaging

233. A Severe Case of Streptococcus pneumonia Meningoencephalitis in a 6-month-old Resulting in Fatal Strokes

Goodman M (New York City, NY), Garcia M, Wang H, Miller C, Borja M, Segal D

OBJECTIVE: Not applicable
METHODS: Not applicable
RESULTS: A previously healthy 6-month-old presented to the hospital with altered mental status and whole body shaking with right gaze deviation after a week of upper respiratory symptoms. Brain MRI revealed multiple infarcts in the bilateral basal ganglia, thalami, and brainstem with diffuse leptomeningeal enhancement concerning for infection. CSF and blood cultures grew Streptococcus pneumoniae and he was treated with Ceftriaxone and Vancomycin. Initial EEG demonstrated left sided cerebral dysfunction and epileptic discharges, without seizure activity. Days later, a fast T2 brain MRI demonstrated increased infarcts in the bilateral cerebral hemispheres, gangliocapsular regions, thalami, upper brainstem, and cerebellar regions. The patient subsequently developed hypercarbic respiratory failure, prompting intubation. Repeat brain MRI demonstrated new large bilateral cerebellar infarctions resulting in obstructive hydrocephalus and cerebellar tonsillar herniation. Given the patient's clinical status and poor neurological prognosis, the family opted for palliative extubation.
CONCLUSIONS: While the advent of vaccines has greatly diminished the rates of pneumococcal disease, there are still cases, like this one, due to non-vaccine serotypes. Notably, this patient's serotype, serotype 34, which commonly colonizes children and causes respiratory tract infections, is not included in any current pneumococcal vaccines including the PCV15.
KEYWORDS: Neuroinfectious Disease, Stroke

234. Spectrum of Central Nervous System Disease Caused by Streptococcus Anginosus Group: A Single Center Experience

Meylor J (Milwaukee, WI), Farias-Moeller R, Mehta N, Sawdy R, Patel N-D

OBJECTIVE: Streptococcus Anginosus Group (SAG) is known to cause focal central nervous system (CNS) infections in children. Prior case series of CNS SAG infections lack electrophysiologic and outcome data. We present a single center case series describing CNS SAG infections including clinical, electrophysiologic, radiographic and long-term outcome data.
METHODS: Data was obtained via retrospective chart review of 14 patients aged 0-18 years hospitalized for SAG CNS infections between 2013-2023.
RESULTS: All patients had preceding infections: sinusitis (n=10) and orbital disease (n=4). Neuroimaging revealed subdural (n=10) and epidural (n=2) empyema. There were no patients with intracranial hemorrhage. Surgical intervention included craniectomy (n=9), burr hole (n=2), or orbitotomy (n=2) with washout. Continuous EEG was initiated for postoperative monitoring and/or clinical seizure concerns (n=8). Average EEG duration was four days. Common electrophysiologic findings included severe generalized background slowing, focal slowing usually consistent with area of infection/intervention, and epileptiform discharges (rare multifocal sharps to lateralized periodic discharges). Acute symptomatic seizures manifested as clinical (n=4) and electrographic (n=2), treated with short-term course of anti-seizure medication. One patient developed refractory epilepsy. There were no patient deaths, no new tracheostomy or g-tube dependence. Common acquired deficits included motor weakness (n=2), executive dysfunction (n=3), and memory impairment (n=3).

CONCLUSIONS: Our case series demonstrates that SAG CNS infections presented acutely with preceding orofacial infection. Neuroimaging identified focal intracranial infections that commonly correlated with focal slowing on post-operative EEG. Many required invasive surgical interventions. Though we noted low rates of epilepsy, lasting focal and neuropsychological sequelae were more common.
KEYWORDS: Neuroinfectious Disease, Neurocritical Care, Epilepsy

235. Five Versus Fourteen Days Oral Dexamethasone in Children and Adolescents (aged 2-18 years) with viable parenchymal Neurocysticercosis (up to 5 lesions): An Open Labelled Clustered Randomized Superiority Trial

Chakrabarty B (New Delhi, India), Choudhary P K, Gulati S, Kumar A, Jauhari P, Pandey R M

OBJECTIVE: To evaluate optimal duration of steroids for management of NCC (neurocysticercosis)
METHODS: An open-labelled clustered randomized superiority trial (TRI/2021/04/032691) in 2-18-year-olds with up to five viable parenchymal NCC was conducted at a tertiary-care-teaching-hospital in north-India. All children received albendazole for 7 days along with anti-seizure medications and were randomised to receive dexamethasone for either 14 (long arm) or 7 (short arm) days. At 2-3week post-steroid therapy, an MRI brain evaluated T2-relaxation-time and perilesional edema. At 6 months follow-up, a contrast-enhanced CT head looked for resolution of NCC.
RESULTS: Forty-nine children with 67 cysts were randomized (long arm: 24 children and 36 cysts; short arm: 25 children and 31 cysts). At 6 months follow up, calcification was less in long compared to short arm (intention-to-treat: 25% versus 51.6%, p=0.03; per-protocol: 33% versus 50%, p= 0.1). Resolution (complete and partial {reduction in cyst size<1cm}) was more in long compared to short arm (intention-to-treat: 55.6% versus 41.9%, p=0.2; per-protocol: 63% versus 43.3%, p= 0.1). Breakthrough seizures over 6 months was comparable (37.5% versus 36%). The T2-relaxation-time of the perilesional edema and cyst size on MRI brain at 2-3 weeks post therapy and baseline cyst size were significantly less in completely or near completely resolved (<5mm) cysts compared to calcified or partially resolved (>=5mm) cysts at 6 months follow-up.
CONCLUSIONS: Increased duration of steroid is associated with reduced calcification and increased resolution. Post therapy 2-3 weeks perilesional edema and cysts size and baseline cyst size are predictive of resolution and calcification.
KEYWORDS: Neuroinfectious Disease, Epilepsy

236. Role of Pulse Methyl Prednisolone in children with vasculitis due to Tubercular Meningitis

Saini L (Jodhpur, India), Manjunathan S, Laxmi V, Kumar A, Gunasekaran P K, Tiwari A K

OBJECTIVE: Vasculitis in Tubercular Meningitis (TBM) is a major determinant of mortality and long-term morbidity due to cerebral infarcts and stroke. In addition to anti-tubercular therapy, pulse methylprednisolone may result in a favorable outcome in vasculitis in Tubercular meningitis.
METHODS: An ambispective study was done for children aged one month to 18 years diagnosed with TBM who presented to our tertiary care center for a period of 4 years. The outcomes of children with TBM vasculitis who received pulse methylprednisolone and who did not receive pulse methylprednisolone were compared.
RESULTS: Over the study period, 33 children were diagnosed with TBM. 19 (57.6%) were females, and 14 (42.4%) were males. 3 (10%), 20(60%), and 10(30%) children had stages 1, 2, and 3 of TBM, respectively. Neuroimaging findings of basal exudates (24), arachnoiditis (8), vasculitic infarcts (22), hydrocephalus (24), and cranial nerve enhancements (12) were seen. Among the 22 children with TBM vasculitis, 13 received oral steroids, and nine received pulse methylprednisolone followed by oral steroids. The degree of disability assessed with the Modified Rankin Scale (mRS) among the 13 who did not receive pulse methylprednisolone was – 5(mRS – 0), 1(mRS – 2), and 7(mRS – 6), and those who received was 4(mRS – 0), 2(mRS – 3) and 3(mRS – 6).
CONCLUSIONS: In children with vasculitis in TBM, pulse methylprednisolone may confer a mortality benefit. Larger multicentric randomized controlled trials are warranted further to explore the role of pulse methylprednisolone in TBM vasculitis.
KEYWORDS: Neuroinfectious Disease

237. Mucormycosis due to Rhizomucor pusillus triggering a stroke alert; a case report

El Atrache R (Houston, TX), Levine J, Guzman M, Salazar K, Davila-Williams D, Sen S, Fisher K, Erklauer J

OBJECTIVE: Rhizomucor pusillus is an aggressive angio-invasive fungus causing severe rhino-orbito-cerebral and pulmonary infections in immunocompromised hosts. We present a case of intracranial mucormycosis in a pediatric patient with an atypical presentation.
METHODS: A case report.
RESULTS: A 16-year-old female with T-ALL in induction therapy developed abrupt focal neurologic deficits concerning for stroke. Exam showed left face and upper extremity weakness, reduced vibration sense in the left foot, and decreased strength at bilateral hip flexors.
Brain MRI was suggestive of acute ischemia in the right perirolandic region and centrum semiovale. Based on clinical history, exam, and imaging findings, her presentation was initially attributed to asparaginase-related infarction with vincristine-induced neuropathy.
Ten days later, she developed worsening weakness and speech difficulties. MRI showed hemorrhagic conversion with significant vasogenic edema, disproportionate to the degree of hemorrhage. As her symptoms continued to worsen, a repeat MRI showed a large ring-enhancing lesion with progressive surrounding edema. Other studies, including lumbar puncture, were non-diagnostic. Her lesion progressed, and she had a seizure.
Thus, she underwent an open biopsy, which revealed Rhizomucor pusillus on PCR eight weeks from presentation. She was subsequently treated with liposomal amphotericin B and Posaconazole. Post-treatment MRI showed collapsed abscess and edema with cystic changes consistent with

resolving fungal disease. Clinically, her headaches persisted, but her neurologic exam improved.
CONCLUSIONS: This case highlights a patient with an atypical presentation of intracranial Rhizomucor pusillus mucormycosis with stroke-like symptoms without signs of infection. It emphasizes the importance of comprehensive evaluation and vigilance for rare opportunistic infections in immunocompromised patients.
KEYWORDS: Neuroinfectious Disease, Neuroimaging

238. Clinical Features and Treatment Trajectory in Pediatric Bartonella Neuroretinitis: A Case Series

Tabatabai G (St. Louis, MO), Lee M

OBJECTIVE: To highlight the clinical features, imaging findings, and treatment trajectory of pediatric bartonella neuroretinitis.
METHODS: Medical records were reviewed and data summarized.
RESULTS: We present two patients (ages 14 and 17) diagnosed with bartonella neuroretinitis in 2023. Patient-1 presented with monocular vision changes with progression to central scotoma and painful upward gaze. Exam was notable for unilateral Grade 2-3 papilledema and an afferent pupillary defect. Brain MRI revealed fluid in the bilateral optic nerve sheaths with asymmetric fluid adjacent to the medial aspect of the inferior rectus. Patient-2 presented with bilateral blurry vision without painful eye movements. Brain MRI revealed bilateral optic nerve protrusion and corresponding FLAIR changes. Fundoscopic exam was notable for bilateral grade 4 papilledema. In both cases, reduced visual acuity was appreciated (20/07 OS for one and 20/30 bilaterally for the other.) CSF studies revealed lymphocytic predominant pleocytosis in each case. Batonella titers were sent given exposure history and returned positive for both (IgM>1:20) with concern for bartonella neuroretinitis. Repeat fundoscopic exam nine to thirteen days after symptom onset revealed a characteristic macular star in both cases. Both patients were treated with a steroids, doxycycline, and rifampin with notable improvement between one and three months later.
CONCLUSIONS: These cases highlight the importance of broad infectious testing, including bartonella henselae titers, when evaluating optic neuritis and optic neuropathy without clear optic nerve enhancement on neuroimaging. In these cases, notable clinical improvement was achieved with prompt diagnosis and initiation of appropriate therapy.
KEYWORDS: Neuroinfectious Disease

NEUROMETABOLIC

239. Exploring the genetic profile of mitochondrial disorders: A single centre-based study

Saini A (Chandigarh, India), Sharma Y, Attri S

OBJECTIVE: Background: Mitochondrial disorders are an inherited, heterogeneous group of disorders that arise due to dysfunction of the mitochondrial respiratory chain or oxidative phosphorylation. They are caused by mutations in either the nuclear DNA or mitochondrial DNA.
METHODS: Methodology: The children with a clinico-radiological suspicion of mitochondrial encephalopathy were enrolled and evaluated. A custom gene panel involving 57 genes responsible for mitochondrial encephalopathies was designed based and next generation sequencing was performed to identify the genetic variations.
RESULTS: Results: We had enrolled 32 children with suspected mitochondrial encephalopathy. Out of 32 children, 26 (81.25%) had mutation in the genes responsible for mitochondrial encephalopathy. The most common gene carrying mutation was NDUFV1 (30.76%). Other genes involved were SUCLG1, NARS2, MTO1, IBA57, FASTKD2, COQ9, NDUFS8, ACAD9, KCNQ2, LIPT2, PDHA, BTD, GLDC, DLAT, NDUFV1, GCH1, C19orf12, SLC22A5, HIBCH, HTT, NDUFS3, NDUFAF2 and POLG. Majority of cases were males 73.07% (n=19/26). Mean age of presentation was 3.5 years (1 month – 12 yrs). The most common symptoms were global developmental delay (84.6%), regression of milestones (46%), extrapyramidal symptoms (54%) and seizures (28%). MRS data was available for 14 children and 8 children (57.14%) had high lactate peak. Brain MRI showed T2 hyperintensity in mid brain and basal ganglia.
CONCLUSIONS: Conclusion: Mitochondrial disorders have variable neurological presentations across the childhood. Availability of genetic testing in developing countries has helped in confirming the diagnosis as well as understanding the complex phenotypes.
Keywords: next generation sequencing, genetic variations, children, respiratory chain disorders
KEYWORDS: Neurometabolic, Early Stage Investigator, Neurogenetics

240. N-of-1 Use of MOBERG CNS Monitor in an Inborn Error of Metabolism

Khaksari K (Washington, DC), Sen K, Chen W-L, Fraser J, Gropman A

OBJECTIVE: Hyperammonemic (HA) episodes in urea cycle disorders (UCD) are medical emergencies. Prompt interventions and neuromonitoring are crucial to prevent mortality and morbidity. Our previous work has demonstrated the ability of cEEG to detect specific background changes that correlate with ammonia levels, allowing timely intervention. The Moberg CNS Monitor is a state-of-the-art device that time-synchronizes EEG data with over 30 physiological parameters. This monitor has been used in adult ICU for traumatic brain injury, stroke, and other pathologies to provide precision care
METHODS: In this pilot study, we investigated the utility of CNS Monitor in a patient with N-acetylglutamate synthetase (NAGS) deficiency presenting with neonatal HA. Continuous measurements of heart rate (HR), perfusion (Perf), respiratory rate (RR), oxygen saturation (Spo2), arterial blood pressure (ABP), and EEG were collected over a course of 24 hours from the CNS Monitor and analyzed in MATLAB R2019b.
RESULTS: A pairwise correlation was run across all signals. Positive correlation was found between HR-RR, and between Spo2-ABP. Negative correlation was seen between HR-ABP,

and between RR-Spo2. During the HA episode, there was a significant increase of HR and RR compared with baseline. Continuous EEG revealed multiple electrographic seizures arising from occipital lobe as well as an increase in interburst interval that correlated with the high ammonia level.
CONCLUSIONS: We demonstrate the role of advanced neuromonitoring devices during acute neurometabolic decompensation in HA episodes. Time-synchronized data demonstrating changes in vitals, blood metabolites, and EEG can facilitate our understanding of biomarkers in UCD which can be used for treatment and outcome measurement.
KEYWORDS: Neurometabolic, Neuroimaging, Epilepsy

241. Unexpected diagnosis of MOCS2 metabolic encephalopathy: Case Report and Literature Review

Kinsinger M (Chicago, IL), Mithal D

OBJECTIVE: To place an atypically mild case of MOCS2 deficiency in the context of published literature on the topic. Molybdenum Cofactor deficiencies are a rare family of metabolic disorders with an increasingly broad phenotypic spectrum. MOCS2 is associated with a severe early life phenotype but the mild case described here prompted review of the published genotype-phenotype correlations and mapping of variants across the gene.
METHODS: Chart and literature review.
RESULTS: A 12 month old female of term gestation with normal development, presented with acute encephalopathy in the setting of an ear infection. Infectious, metabolic and toxic evaluations were unrevealing. CT scan identified hypodense lesions in the bilateral globus pallidus, which were confirmed as diffusion restricting lesions on MRI. At discharge motor and language regression were noted which persisted as an outpatient. WES identified a previously unreported homozygous variant of unknown significance in the MOCS2 gene. Confirmatory testing showed low uric acid and elevated urine sulfocysteine. Literature review revealed 52 published cases of MOCS2 with 8 (15%) categorized as mild. No reliable imaging pattern was identified. No genotype-phenotype correlation was identified for the 34 variants that were spread across the 7 exons of MOCS2. Approximately 30% were deletions, and no clustering of mild cases was noted. This patient represents the first mild case identified in exon 3.
CONCLUSIONS: MOCS2 is a rare disease frequently associated with a severe phenotype, but should remain on the differential for neurologic regression in the setting of illness. Further research is required to understand the genotype/phenotype correlations for MOCS2.
KEYWORDS: Neurometabolic, Neurogenetics, Neuroimaging

242. A mimicker of hypoxic-ischemic encephalopathy: a case of maple syrup urine disease with normal initial newborn screen

Tambunan D (Atlanta, GA), Russo R, Keller S, Gombolay G

OBJECTIVE: To discuss a patient with an initial concern for hypoxic ischemic encephalopathy (HIE) and "normal" newborn screen (NBS), found to have maple syrup urine disease (MSUD).
METHODS: Retrospective chart review, including clinical information and ancillary testing was collected.
RESULTS: A 15 day old boy full-term infant presented with progressive lethargy and poor feeding for 2 weeks, severe weight loss, and urine that smelled like maple syrup. Initial NBS on day-of-life (DOL) 1 was normal. Exam was notable for hypotonia. Pregnancy and delivery were normal, without known risk factors for HIE. Ammonia was normal. MRI brain revealed symmetrical pattern of restricted diffusion from the brainstem to the perirolandic areas, diffuse cerebral edema, and cerebellar herniation. EEG showed comb-like sharp theta-like frequency patterns. Repeat NBS sent on DOL 16 demonstrated elevated ratios of leucine:alanine and leucine:phenylalanine. Plasma amino acids showed elevated branched amino acids, consistent with MSUD. Genetic testing is pending.
CONCLUSIONS: MSUD is an autosomal recessive disorder due to decreased activity of the branched-chain alpha-ketoacid dehydrogenase complex, which can increase levels of branched amino acids. Acute metabolic crises (leucinosis) can cause worsening encephalopathy that may progress to coma and respiratory failure. While the initial NBS was normal, this was obtained in the setting of poor feeds on DOL 1 and without an adequate protein challenge to cause leucinosis. Markers for MSUD besides genetic testing and plasma amino acid levels include characteristic EEG rhythms and MRI findings. Thus, MSUD should be considered in infants with slowly progressive encephalopathy, even with an initial NBS.
KEYWORDS: Neurometabolic, Neonatal Neurology, Neurodevelopmental Disorders

NEUROMUSCULAR

243. A Unique Presentation of CMT1X: Factors in Diagnostic Delay and Opportunities for Improved Care

Wooten N (Chapel Hill, NC), Hung S-C, Malawsy D, Trau S, Shiloh-Malawsky Y

OBJECTIVE: We aim to investigate diagnostic delays in CMT1X patients with CNS phenotype and identify opportunities to shorten the process. CMT1X, a rare genetic condition caused by GJB1 gene mutations, can present with episodes of neurological dysfunction and reversible brain MRI abnormalities resembling other neurological disorders, such as stroke, demyelinating disease, or mitochondrial disorders, leading to delayed diagnosis.
METHODS: We examined two new, not previously reported, CMT1X cases with CNS presentation and conducted a targeted literature review of diagnostic time for similar cases. We analyzed the association between diagnostic delay and patient data, including demographics, history, exam, and testing information.
RESULTS: The two new cases had different diagnostic pathways: Case 1 had a 5-year delay, while Case 2 was diagnosed promptly. Among 47 previously reported cases, there was an average 5.3-year delay, ranging from 0 to 38 years. Factors associated with delayed diagnosis included younger age of

onset ($p<0.01$) and absence of limb weakness ($p=0.05$). In patients with an age of onset below 10 years, 90% had delayed diagnosis, compared to 38% of older patients. Two females had delay in diagnosis of 7 and 21 years.
CONCLUSIONS: Diagnosis of CMT1X's rare CNS phenotype is often delayed, but recognizing the unique clinical combination of symptoms, signs, and MRI findings can lead to earlier diagnosis and result in improved management and genetic counseling. The association of younger age of onset with delayed diagnosis underlines the need to raise awareness of this condition among pediatric neurologists.
KEYWORDS: Neuromuscular, Pediatric Demyelinating Disease, Neuroimaging

244. Impact of sedation on electrodiagnostic data quality in a large pediatric cohort

Mussorfiti S (Rochester, NY), Selouani Y, Ferguson M, Ackerman K, Mackenzie S

OBJECTIVE: Although electromyography and nerve conduction studies (EMG/NCS) are useful tools for diagnosing neuromuscular conditions in children, studies may be limited due to patient discomfort. While sedation may reduce discomfort, it also has the potential to confound results. We sought to determine the effect of sedation on electrodiagnostic data quality.
METHODS: We performed a retrospective institutional database and electronic medical record review of pediatric patients undergoing EMG/NCS over a 7-year period (May 2015 - August 2022). Statistical comparisons were made using one-way ANOVA.
RESULTS: We analyzed 165 unique EMG/NCS cases (74 female, 4.8 ± 3.3 years; 91 male, 3.7 ± 3.4 years) conducted on 113 patients. Sedation (6 general, 13 deep, 1 conscious) was used in 20 cases (12%) and was associated with greater number of nerves (4.80 ± 2.98) and muscles (2.30 ± 1.95) tested compared to cases with no sedation (2.77 ± 1.68, $F=20.54$, $p<.001$; 0.63 ± 1.25, $F=27.06$, $p<.001$). However, sedation use also showed a trend toward more limited studies (45%) compared with no sedation (25%; $F=3.642$, $p=.058$), most often due to an absence of volitional motor units on EMG. No major complications were associated with sedation use.
CONCLUSIONS: In this large, single-center retrospective review of pediatric patients undergoing EMG/NCS, we found that while sedation affords testing of more nerves and muscles, it was also associated with an almost two-fold increase of study limitations. Conscious sedation may mitigate patient stress while allowing for observation of volitional motor units. This will be a focus area for our team as we move toward a standardized institutional sedation protocol for pediatric EMG/NCS.
KEYWORDS: Neuromuscular, Early Stage Investigator

245. A case of SMA Type III with a novel SMN1 missense variant (p.Arg281Gly).

Stockman J (Los Angeles, CA), Ramos-Platt L, Deardorff M, Amin N

OBJECTIVE: Describe a case of SMA type III caused by a novel SMN1 (p.Arg281Gly) missense variant. This variant is described and the importance of investigating novel SMN1 variants is discussed. To our knowledge, this is the first reported case in which this novel variant is reported.
METHODS: Retrospective chart review was performed for one patient with SMA type III.
RESULTS: A four-year-old previously healthy girl presented with progressive weakness, hypotonia, and hyporeflexia. Diagnosis of SMA type III was suspected based upon EMG/NCV. A neuropathy gene panel demonstrated a heterozygous deletion of SMN1 and an in-trans variant of SMN1 (c.841A>G; p.Arg281Gly). Due to its location in the YG-box domain of SMN1, this variant was suspected to be pathogenic. Copy number testing noted a single copy of SMN2. She was started on the SMN2 upregulator oral risdiplam as she was out of the FDA indication for onasemnogene abeparvovec. On four-month follow-up, she had a 3-point improvement on her Hammersmith.
CONCLUSIONS: While the majority of patients with SMN1-related SMA have a homozygous deletion of SMN1, novel pathogenic SMN1 variants can also cause SMA clinical phenotypes. This patient's phenotype implies a dysfunctional protein product (p.Arg281Gly). Her response to risdiplam further supports the diagnosis of SMA type III. This case demonstrates the ongoing need to identify treatable variants in SMA and expand our clinical indications for treatment.
KEYWORDS: Neuromuscular, Neurogenetics

246. Diagnostic Challenges in Pediatric Multifocal Chronic Inflammatory Demyelinating Polyneuropathy with New-onset Type 1 Diabetes Mellitus

Vara A (Rochester, NY), Betha S, Hewitt A, Mackenzie S

OBJECTIVE: To describe diagnostic challenges in a pediatric case of multifocal chronic inflammatory demyelinating polyneuropathy (CIDP) variant that was confounded by diabetes, weight loss and pancreatic insufficiency following Whipple procedure.
METHODS: Case report: history provided by patient and parent as well as review of medical records.
RESULTS: 15-year-old girl presented with 6 months of progressive proximal left arm paresthesia, allodynia and weakness, left foot drop, and 30kg weight-loss. History was significant for pancreatic papillary neoplasm status post-Whipple procedure with resulting pancreatic insufficiency. Electrodiagnostic testing demonstrated slowed conduction in left-sided sensory and motor nerves, concerning for multifocal CIDP. Further workup revealed new-onset type 1 diabetes (DM1) complicated by bilateral diabetic cataracts. Brain, spine, and brachial plexus imaging, CSF studies and serum studies were otherwise normal. Treatment with IVIG and IV methylprednisolone with prednisone taper and physical therapy resulted in return to baseline function without pain at 6 months. She continues to be treated with insulin for DM1.
CONCLUSIONS: The atypical presentation of multifocal unilateral sensorimotor demyelinating polyneuropathy in the presence of confounding comorbidities requires a broad differential including CIDP, diabetic neuropathy, nutritional deficiencies, compressive neuropathy, Slimmer's paralysis,

paraneoplastic syndromes and genetic disorders. Variants of CIDP are uncommon in pediatrics. This case highlights how multiple comorbidities can complicate the already challenging diagnosis of CIDP variants. In particular, new onset diabetes can both confound the diagnosis and cause management challenges. Currently, limited pediatric literature is available for evaluation and treatment guidance.

KEYWORDS: Neuromuscular, Pediatric Demyelinating Disease

247. Diagnosis Delay in Duchenne Muscular Dystrophy Patients: A Systematic Review

Selouani Y (Rochester, NY), Mussorfiti S, Helmy S M, Mackenzie S J

OBJECTIVE: Duchenne Muscular Dystrophy (DMD) is a common X-linked condition associated with high morbidity and mortality, arising in the setting of out-of-frame mutations in the DMD gene. While sequencing of the DMD gene is the gold standard for diagnosis, lack of access to this testing has the potential to contribute to diagnostic delay. We aimed here to evaluate the quality of literature on age of symptom onset and diagnosis of DMD globally and explore the potential for meta-analysis.

METHODS: Following the PRISMA-P and the JBI critical appraisal tools, a systematic search was conducted in PubMed, Web of Science, and Scopus databases using a specific search string. Following screening by two independent authors, 14 papers were deemed eligible for qualitative synthesis. Authors noted cohort number, age at symptom onset, age at diagnosis, country, and period of time assessed in each study.

RESULTS: Of the 747 papers found, 14 were included in our initial review. Age at symptom onset was reported for 2888 patients, and age at diagnosis for 2947. Studies encompassed 10 countries, stratified by World Bank criteria as lower-middle-income (LMI; N=1), upper-middle-income (UMI; N=3), and high-income (HI; N=6). Mean age at symptom onset ranged from 1.75 to 4.6 years, while mean age at diagnosis ranged from 3.4 to 12.1 years, with the sole LMI study reporting the highest values.

CONCLUSIONS: This study supports further work evaluating diagnostic delay in DMD across the globe, particularly in middle-income and low-income countries. Greater attention and resources are likely needed to improve diagnosis and management of DMD worldwide.

KEYWORDS: Neuromuscular, Neurogenetics, Global Neurology

248. Study of compound muscle action potential (CMAP) amplitudes in infants with spinal muscular atrophy (SMA), pre- and post-gene therapy

Bery E (Atlanta, GA), Bheemisetty N, Schechner J, Xiang Y, He Z, Shah D, Carvell K, Ritchey M, Verma S

OBJECTIVE: Compound muscle action potential (CMAP) amplitudes are measured during electromyography and are reduced in neurogenic disorders affecting the motor neuron and/or its axon. Our objective was to determine the utility of CMAP measurements in patients with spinal muscular atrophy (SMA) pre- and post-gene therapy.

METHODS: We retrospectively reviewed 14 SMA newborns, pre- and post-gene therapy, for CHOP-INTEND scores and peak negative CMAP amplitudes of the right abductor pollicis brevis (APB), abductor digiti minimi (ADM), and tibialis anterior (TA). Median values and interquartile range were calculated.

RESULTS: Pre-treatment, at the median age of 15 days of life (DOL) [11-17.75], 2 SMN2 (n=6) copy number infants had lower median CMAP amplitudes in comparison to the 3 SMN2 (n=8) infants. This difference was statistically significant ($p < 0.05$) for the APB and ADM CMAP amplitudes. All infants received gene therapy (n=10, ZolgensmaTM, n=4, SpinrazaTM). Post-gene therapy, at the median age of 270 DOL [168-420], the median CMAP amplitudes increased for 2 SMN2 copy number infants and 3 SMN2 copy number infants. The difference was statistically significant ($p<0.05$) for the APB CMAP amplitudes only. CHOP-INTEND scores showed no statistically significant difference between 2 vs. 3 SMN2 copies number babies evaluated pre-and post-gene therapy.

CONCLUSIONS: Our study results indicate that right median APB CMAP amplitudes differ between 2 vs. 3 SMN2 copy number patients pre-and post-gene therapy, while the CHOP-INTEND scores showed no significant difference between the two groups.

KEYWORDS: Neuromuscular

249. Ultrasound Detects and Facilitates Prompt Reconstruction of a Nerve Transection Injury after Ballistic Trauma

Tabatabai G (St. Louis, MO), Zaidman C, Pet M

OBJECTIVE: We describe a case where nerve ultrasound successfully identified complete transection of an ulnar nerve after ballistic injury. This facilitated prompt ulnar exploration and successful reconstruction where prolonged waiting would have otherwise been indicated.

METHODS: Case report.

RESULTS: A 13 year-old male suffered a single gunshot wound to the distal right forearm. Initial physical examination revealed signs of median and ulnar nerve dysfunction. Nerve conduction studies showed absent median and ulnar CMAPS and SNAPS. Needle EMG showed fibrillations and positive sharp waves in the right first dorsal interosseous, abductor pollicis-brevis, and flexor digitorum profundus concerning for severe median and ulnar mononeuropathies. Neuromuscular ultrasound was elected rather than observation with serial eletrodiagnostic testing given suspicion for complete ulnar nerve transection. Ultrasound revealed complete transection of the right ulnar nerve and partial laceration of the right median nerve facilitating prompt exploration and reconstruction of the ulnar nerve with cabled sural nerve grafts and distal decompression of the median nerve. Ultrasound findings were confirmed intraoperatively. Intrinsic function was recovered 9 months later.

CONCLUSIONS: In cases of nerve dysfunction after ballistic injury, it is difficult to promptly distinguish low grade

(neurapraxic) from high grade (neurotmetic) injuries. Standard of care to date is observation and serial electrodiagnostic studies over several months. While this minimizes unnecessary exploration, it results in delayed treatment of severe injuries which are not destined to recover spontaneously. In this illustrative case, we demonstrate the capability of ultrasound to detect a transecting injury of the ulnar nerve, which resulted in early exploration and successful reconstruction.
KEYWORDS: Neuromuscular, Neuroimaging

250. Long-term follow-up study in patients with spinal muscular atrophy (SMA) receiving risdiplam treatment

Tanvir I (South San Francisco, CA), Tam S, O' Donnell D, Shapouri S, Lim E, Shah R, Sun C, Seth G

OBJECTIVE: SMA is a genetic, progressive neuromuscular disease characterized by motor neuron loss. Risdiplam (EVRYSDI®), an orally administered SMN2 pre-mRNA splicing modifier, is an FDA-approved treatment for pediatric and adult patients with SMA. This Phase 4, multicenter, prospective, long-term follow-up study (LTFU; NCT05232929) is designed to investigate the long-term safety and effectiveness of risdiplam in pediatric and adult patients with all SMA types.
METHODS: Patients with a genetically confirmed diagnosis of SMA who received risdiplam after FDA approval based on the prescriber's clinical judgment, per the risdiplam US prescribing information, are eligible for study entry. Exclusion criteria include risdiplam hypersensitivity or participation in a registrational trial of risdiplam (FIREFISH [NCT02913482], SUNFISH [NCT02908685], JEWELFISH [NCT03032172] or RAINBOWFISH [NCT03779334]).
RESULTS: Enrollment of ≈500 patients is planned. Patients will be followed for up to 5 years from enrollment or until withdrawal of consent, loss to follow-up or death. Primary outcomes are the rate of adverse events (AEs), AEs of special interest and serious AEs. Secondary outcomes include the percentage of participants considered improved on the CGI-C Scale. Exploratory outcomes include change in motor function measures, attainment of WHO gross motor milestones, changes in respiratory and bulbar function, hospitalizations, survival in infants aged <2 years with Type 1 SMA and patient- and caregiver-reported outcomes. Baseline characteristics of the enrolled cohort will be presented.
CONCLUSIONS: The LTFU study is actively recruiting participants at multiple sites across the US. The study is expected to provide data on the real-world use, safety and effectiveness of risdiplam in various SMA patient populations.
KEYWORDS: Neuromuscular

251. Dystrophinopathies in asymptomatic children with normal creatinine kinase levels: A case series

Angappan D (Beaverton, OR), Leach M, Finanger E

OBJECTIVE: The aim of this study was to clinically and genetically characterize male patients who have normal or mildly elevated creatinine kinase (CK) levels with a genetically confirmed dystrophinopathy, but no clinical symptoms of muscle weakness.
METHODS: This study was conducted as a retrospective chart review from a tertiary referral hospital's pediatric neuromuscular clinic. Male children presenting at less than 18 years of age, who had dystrophinopathy confirmed by genetic testing and had normal CK levels and no evidence of muscle weakness were enrolled. The clinical and genetic profile were analyzed.
RESULTS: A total of 6 cases were identified. Four had normal CK and 2 had mild CK elevation (<2x ULN). All had identified mutations in dystrophin gene. The patients age ranged from 20 months to 15 years at last follow up. All patients were ambulatory, 1/6 patients had mild global delay (walking after 15 months). No patients had evidence of muscle weakness[LM2] . 5/6 had positive family history.
CONCLUSIONS: Most commonly, mutations in DMD gene are associated with marked elevation in serum CK since birth (10–100 times). Serum CK levels are a valuable screening test for dystrophin related conditions in symptomatic patients. However, we show that a number of patients with DMD mutations can have a normal or near normal CK. While these patients do not have muscle symptoms presenting in childhood, they remain at risk for adult onset weakness, cardiomyopathy and exertional rhabdomyolysis. These findings are also relevant to proposed newborn screening for DMD which uses serum CK as the screening test.
KEYWORDS: Neuromuscular, Neurogenetics, Global Neurology

252. Single nucleus transcriptomic analyses of hippocampus in murine model of Duchenne Muscular Dystrophy

Nalamalapu R (Richmond, VA), Blinova L, Shallop S, Qu X, Liu J, Thangarajh M

OBJECTIVE: Dystrophin protein—highly expressed in the central nervous system—is critical for synaptogenesis and axonal guidance. The absence of brain dystrophin is considered the molecular correlate of the cognitive deficits seen in boys with Duchenne Muscular Dystrophy, an X-linked genetic disease caused by the lack of functional dystrophin. Single nucleus RNA-sequencing (snRNA-seq) permits unbiased transcriptomic investigation of cells of interest. We investigated the transcriptome of hippocampi of the mdx52 model of DMD to better understand how dystrophin deficiency affects brain development in the early postnatal period.
METHODS: Hippocampi were isolated from 4 male pups each from mdx52 and BL6 mice on postnatal day zero and single nuclei were partitioned using the Chromium system from 10x Genomics. Following library preparation, samples was sequenced on a NovaSeq6000. An average of 25,000 single nuclei with a read-depth of 100,000 transcripts were performed from each hippocampus. Raw sequencing reads were processed with Cell Ranger and cell type clustering was performed using Seurat v5. Cell clusters were labelled using cell-type specific gene expression markers.
RESULTS: A total of 19 cell clusters including neurons, GABAergic interneurons, choroid plexus, epithelial cells, astrocytes, oligodendrocytes, and microglia were identified.

There was no statistical difference in the cell-type composition between the two groups. Differential expression analysis demonstrated transcriptomic changes in a subset of GABAergic interneurons in the mdx52 hippocampi.
CONCLUSIONS: A compelling preliminary finding was the difference in a subset of inhibitory interneurons in the mdx52 model and we are conducting detailed follow-up experiments of these exciting findings.
KEYWORDS: Neuromuscular

253. An Unusual Presentation of an Adolescent with Lower Extremity Pain and Inability to Walk after a Single Dose of Sertraline

Abbasi Z (Woodbridge, VA), Zahir R, Lateef T

OBJECTIVE: Depression and anxiety among adolescents are common and frequently treated with selective serotonin uptake inhibitors (SSRIs). While highly effective, SSRIs can cause serous adverse effects such as Serotonin Syndrome, which typically occurs at high doses or with rapid upward titration of the SSRI.
We present a case of a 16-year-old female with acute onset lower extremity pain and inability to walk after a single dose of sertraline.
METHODS: Case Report
RESULTS: Patient was a 16 year old African American female who was at track practice the day prior to admission. She reported severe craps in her lower extremities during running. She also had a history of depression and received her first ever dose of Zoloft (25 mg) the day prior to symptom onset. Physical examination was notable for reduced functional mobility from lower extremity myalgias. Laboratory testing showed elevated creatine kinase levels which slowly declined (1443, 1400, 868, 649). Eventually she regained strength and had minimal pain upon discharge. Zoloft was discontinued.
There is only one other case reported in the literature on the occurrence of rhabdomyolysis after a single dose of sertraline (50 mg) given to a 9 year old child. A study by the US armed forces showed that African Americans do have a higher risk of rhabdomyolysis than whites possibly related to genetic risk and a higher pre-disease CK.
CONCLUSIONS: Although extremely uncommon, all potential adverse reactions of SSRIs should be considered, when selecting antidepressant therapy for children and adolescents, and appropriate counseling should be provided.
KEYWORDS: Neuromuscular

NEURO-ONCOLOGY

254. Maturation of Metastases in Peripheral Neuroblastic Tumours (Neuroblastoma) of Children

Sarnat H (Calgary, AB, Canada), Chan E, Ng D, Yu W

OBJECTIVE: This study compares primary peripheral neuroblastic tumours of childhood (neuroblastoma; ganglioneuroblastoma; ganglioneuroma) with metastases for maturation of neural cells and to discern whether target tissues of metastases or chemotherapy may influence differentiation of ganglion cells in the natural evolution of these neoplasms. This present study is a sequel to an earlier paper on maturation in primary neuroblastic tumours (Sarnat, Yu. Clin Neuropathol 2022;41:101-13).
METHODS: Four infants and toddlers with metastatic neuroblastoma were studied from surgical resection or at autopsy, comparing primary lesions of the adrenal medulla with visceral (pancreas, liver, spleen, lymph nodes) and cranial dura mater metastases. In addition to H&E, immunocytochemical reactivities were applied as neuronal, Schwann cell and primitive neuroblastoma markers: MAP2; synaptophysin; chromogranin-A; somatostatin; keratan sulfate; vimentin; S-100β protein; Phox2B.
RESULTS: Ganglion cell maturation was similar in metastases regardless of the target organ. Some large cells that histologically appear as ganglion cells showed no reactivity of neuronal lineage. Metastases were similar to primary tumours. Both neuronal and Schwannian lineages were represented in each tumour type but differed in proportions.
CONCLUSIONS: Neither the target organ nor chemotherapy appear to influence rates of neuroblastic or Schwann cell differentiation in metastases. Immunocytochemical markers of neuronal and of Schwann cell maturation provide greater diagnostic precision than histological criteria alone in these neural tumours with a unique natural course of cellular maturation despite their malignancy.
KEYWORDS: Neuro-oncology, Neonatal Neurology, Lifespan Manifestations of Childhood Onset Conditions

255. A single-center retrospective study of midbrain gliomas: clinically and radiographically heterogenous tumors

Garcia M (New York City, NY), Tsai C.-T., Raj Ghosh G, Movahed-Ezazi M, Jandhyala N, Feng Y, Rao H, Cohen B, Karajannis M, Snuderl M, Allen J, Segal D

OBJECTIVE: To identify radiographic or histological variables in midbrain gliomas that correlate with outcome.
METHODS: We reviewed 74 patients with midbrain gliomas followed at our center for over 30 years. Tumors were divided based on anatomical involvement: A) localized to the tectum with or without periaqueductal tegmentum involvement and B) diffuse, involving the midbrain, pons, cerebellum, and/or thalamus.
RESULTS: Out of the 74 tumors, 38 (55.9%) were classified as group A and 30 (44.1%) as group B. The average age of diagnosis was 10 years old. There was a male and female predominance in group A and B, respectively (<0.001). The most common clinical presentation was hydrocephalus (64.9%), and 13 (17.6%) of the tumors were found incidentally (<0.05). All patients with NF1 were classified as group A (<0.005). Twenty-two tumors had pathology available, and 20 (54%) were pilocytic astrocytoma. The majority of patients in group A required only endoscopic third ventriculostomy (p=0.007) while patients in group B often required multiple treatment modalities including surgery (p<0.005), chemotherapy (p=0.006), and/or radiation

(p<0.005). All of our patients were alive at last known follow-up.
CONCLUSIONS: Midbrain gliomas are a clinically heterogeneous group of tumors, a subset of which behave aggressively and require multiple treatment modalities. The vast majority of these tumors remain stable after diagnosis. Cerebrospinal fluid diversion via endoscopic third ventriculostomy or ventriculoperitoneal shunt alone may be sufficient treatment for a large subset of these tumors. Overall, all of our patients survived, reinforcing the notion that these are manageable tumors with generally excellent outcomes.
KEYWORDS: Neuro-oncology

PEDIATRIC DEMYELINATING DISEASE

256. Increased Anxiety, Depression and Suicidal Ideation in Children with Neuromyelitis Optica Spectrum Disorder (NMOSD), Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD), and Pediatric Onset Multiple Sclerosis (POMS).

Codispoti M (Shreveport, LA), Shukla N, Fisher K, Lotze T, Balasa A

OBJECTIVE: To examine the prevalence of anxiety, depression, and suicidal ideation among pediatric patients diagnosed with NMOSD, MOGAD, or POMS.
METHODS: An IRB-approved retrospective chart review for pediatric patients meeting international diagnostic criteria between 2006 and 2022 for one of the following, NMOSD, MOGAD, or POMS was completed by an independent examiner. The data was harvested with EPIC SlicerDicer software. The following was collected: demographics, age and year of diagnosis, serostatus, and indication of suicidality, anxiety and/or depression. The prevalence was compared to the general pediatric population.
RESULTS: A total of 161 patients with POMS were identified, 65.2% (105) female and 34.8% (56) male. The mean age of diagnosis was 14.6 years (SD±2.5). The following was indicated: 41.0% (66) anxiety (p<0.0001), 34.8% (56) depression (p<0.0001), and 8.7% (14) suicidal ideation (p=0.02). A total of 47 pediatric patients with MOGAD were identified, 59.6% (28) female, and 40.4% (19) male. Average age of diagnosis was 7.6 years (SD±4.6). The following was indicated: 23.4% (11) anxiety (p=0.005), 12.8% (6) depression (p=0.03), and 2.1% (1) suicidal ideation (p=0.90). A total of 33 pediatric patients with NMOSD were identified, 27.3 % (9) male and 72.7% (24) female. The mean age of diagnosis was 10.8 years (SD±4.8). 43.4% (14) of patients were seropositive, and 57.6% (19) were seronegative. The following was indicated: 33.3% (11) anxiety (p=0.0002), 36.4% (12) depression (p<0.0001), and 6.1% (2) suicidal ideation (p=0.21).
CONCLUSIONS: Children with demyelinating disorders have a higher risk for anxiety and depression. Moreover, children with POMS have a significantly increased risk for suicidality.
KEYWORDS: Pediatric Demyelinating Disease

257. Presenting Characteristics of Pediatric Acute Transverse Myelitis

Grezzo L (Pittsburgh, PA), Walker E, Thakkar K

OBJECTIVE: Our study aims to examine the clinical, laboratory and imaging characteristics of pediatric presentations of Transverse myelitis(TM).
METHODS: Retrospective chart review was performed on patients with TM presenting to our tertiary center between 2012 to 2022. Inclusion criteria was based on Transverse Myelitis Consortium Working Group criteria. Metabolic, genetic, neoplastic, and vascular disorders were excluded.
RESULTS: 351 patients were identified. 57 met inclusion criteria. Etiologies included NMOSD(4) (3 MOG, 1 AQP4 antibody mediated), Multiple sclerosis(7), Acute flaccid myelitis(10) and Idiopathic(36). Median age was 10.4years (Range 1.7 to 20.1 with bimodal distribution at 4 and 17). The median age was 4.2years in AFM, 9.9years in NMOSD, 16.5years in MS and 11.5years in idiopathic TM. Amongst idiopathic TM patients, MOG antibody was negative in 13/13(100%), AQP4 antibody was negative in 36/36(100%) and CSF oligoclonal bands were negative in 25/27(93%). Antecedent illness was noted in 39/57(68%). CSF pleocytosis was seen in 31/57(54%). CSF elevated protein was seen in 16/57(28%). Imaging showed cervical involvement in 72% patients. Long segment myelitis was noted in 27(75%) of idiopathic TM, 6(60%) of AFM, 3(75%) with NMOSD and 3 (43%) with MS. Peripheral T2 lesions were seen in 5(71%) of MS, central mixed grey and white matter involvement in 3 (75%) of NMOSD, central grey matter involvement 10(100%) of AFM. Idiopathic patients had mixed pattern in 22(61%).
CONCLUSIONS: Pediatric transverse myelitis has bimodal peak of presentation. Majority of the patients are idiopathic. Age of presentation and patterns on imaging helped with differentiation amongst diagnoses.
KEYWORDS: Pediatric Demyelinating Disease, Neuroimmunology

258. NMOSD and MOGAD dually positive in a Pediatric Patient

Dinov D (Richmond, VA), Khan Z, Morton L

OBJECTIVE: The pathogenesis and presentation of neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein associated diseases (MOGAD) is not completely clear. Despite similar presentations, response to therapies and relapse course differentiate them. We present a 9-year-old female who is antibody dually positive.
METHODS: Patient presented with encephalopathy, fatigue, and febrile episodes. This sub-acutely progressed to ataxia, loss of bowel and bladder function, and then flaccid paralysis. Patient was started on a 3-day course of IVIG and a 5-day course of high dose IV methylprednisolone. By discharge patient improved mentation, bladder control, and

ambulation. However, at 3 months patient had a left optic neuritis relapse requiring maintenance IVIG therapy.
RESULTS: Initial laboratory evaluations were negative for an infectious workup; however, significant for leukocytosis and CSF pleocytosis. MRI imaging showed cerebral hyperintensities and diffuse central cord involvement in an "H" sign. Serum studies after this showed elevated AQP4 antibodies, 4.6, and positive MOG antibody titers, 1:10,000.
CONCLUSIONS: This case presents the youngest dually positive patient in the literature to our knowledge. Although, the patient presents with more MOGAD features on imaging, with the "H" or central cord sign, and rapid improvement, the relapse that occurred is unusual for MOGAD. The pathogenic effect of MOG is unclear with literature indicating it varies on T cell response, while NMO pathogenesis does not depend on immune response. Understanding the pathogenic effect of each antibody and impact of age on pathogenesis may help delineate natural history including why MOGAD generally remains a monophasic illness.
KEYWORDS: Pediatric Demyelinating Disease, Neuroimmunology

259. MRI Brain and Spine Characteristics of a Pediatric Cohort with MOGAD

Doerfler M (Chicago, IL), Zhang J, Rubin J, Jaju A, Aw-Zoretic J

OBJECTIVE: Myelin-oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a recently-defined demyelinating disorder with an age-related phenotypic spectrum. At disease onset, there is considerable clinical and radiographic overlap between MOGAD and other demyelinating conditions. This study aims to enhance our understanding of defining radiographic features of MOGAD in children.
METHODS: We performed a retrospective cohort study including all children presenting to our center with acute demyelination between 2010 and 2020 with positive anti-MOG antibodies and negative aquaporin-4 antibodies. Sixteen patients met inclusion criteria. Each patient had MRI imaging of the neuroaxis on presentation and imaging of at least the brain on all relapses. These images were independently reviewed by two fellowship-trained pediatric neuroradiologists blinded to patient history. Involvement of disease by location was measured, and clinical features such as number of relapses and presenting syndromes were analyzed in relation to the imaging.
RESULTS: Nine of sixteen patients (56%) developed recurrent disease. The brain was involved in all patients, and eleven out of sixteen (69%) had spinal cord lesions. The brachium pontis was involved in nine patients (56%), consistent with its known association. The area postrema was never affected. There was no clear association with length of spinal segment involvement and presenting syndrome. The average annualized relapse rate (AARR) was highest for patients with involvement of the optic pathway, at 1.68.
CONCLUSIONS: This study contributes longitudinal data to our understanding of neuroimaging in children with MOGAD, with the goal of enhancing diagnosis and prognostication.
KEYWORDS: Pediatric Demyelinating Disease, Neuroimaging

260. Acute CNS demyelination in children: A single centre experience.

Vamshi V (Nagpur, India), Jain S, Choudhary A, Chauhan U, Bang A, Girish M

OBJECTIVE: To study the clinical profiles of children with first attack of acute CNS demyelination who were on follow up.
METHODS: It is a retrospective study of children admitted in tertiary care hospital in India over a period of 18 months (October 2021 to March 2023).
RESULTS: A total of 10 children were included with the mean age of presentation being 15 years. Male to female ratio was 1:1.2. Motor deficits followed by visual symptoms were most common presenting features. MOGAD was diagnosed in 3 children and were treated with pulse steroids. Aquaporin 4 antibody was positive in 3 children and received both steroids and IVIG, one of them presented with bulbar paralysis (invasively ventilated) required Rituximab. Two children fulfilled the criteria of NMO-SD without Aquaporin. Based on clinical and radiologic features, 2 children were labelled with ADEM. During follow-up, children with ADEM were treated with tapering oral steroids for 6 weeks; MOGAD were treated with tapering oral steroids for 3 months and NMOSD with long term immunomodulation with either Rituximab or Mycophenolate mofetil. In the mean follow up period of 5 months, no relapse seen in any of the children.
CONCLUSIONS: With newer diagnostic criteria, children with acute CNS demyelination can be better classified even in the first attack, thereby treating them appropriately for prevention of relapse. As relapse leads to long term sequelae in children, prompt diagnosis and adequate treatment helps to increase the quality of life of children, however long term follow up is required.
KEYWORDS: Pediatric Demyelinating Disease

261. Management and follow-up strategy of Pediatric acquired demyelination syndrome in a developing-world setting: an ambispective observational study

Chakrabarty B (New Delhi, India), Gulati S, Kumar A, Choudhary P, Upadhyay A, Meena A

OBJECTIVE: To describe management and follow-up strategy of Pediatric ADS in a developing-world setting
METHODS: New and follow-up ADS cases classified according to McDonald 2017 criteria presenting to a tertiary-care-teaching-hospital in north-India between January 2020-March 2023 with follow-up of minimum 6 months were enrolled. Acute episodes were treated with pulse followed by tapering oral steroids. Azathioprine was the long term immunomodulator of choice for recurrent/progressive entities. Rituximab was used for steroid-refractory acute episodes and relapses on azathioprine.
RESULTS: Seventy-eight cases were enrolled (44 males, median age:120 months, IQR:72-144) with MOGAD (29/78-37.2%) being commonest final diagnosis followed by monophasic CIS (19/78-24.4%) and MS (16/78-20.5%). A current PCPCS score of 1-2 was seen in 85.9%.

Majority were monophasic (62.8%-49/78; 34.5% MOGAD, 81.3% MS and 60% NMOSD were recurrent/progressive). Monophasic variants had significantly less CSF OCB positivity, requirement for rituximab and MS diagnosis compared to recurrent/progressive entities; they didn't differ significantly on current PCPCS score, age, and MOGAD diagnosis. Current PCPCS score was significantly low and high in MOGAD and MS respectively compared to rest of the cohort; only 2 MS cases relapsed on azathioprine.

The predominant presentation in first episode was polyfocal CIS (32/78-41%) followed by ADEM (15/78-19.2%). Amongst all presentations, only presence of non-ON-non-TM CIS in the first episode was significantly associated with occurrence of recurrent/progressive entities and MS.

CONCLUSIONS: Azathioprine is an effective long-term immunomodulator in developing-world settings. Non-ON-non-TM CIS in first episode is predictive of progressive/recurrent entities. MOGAD shows better outcome but can have both monophasic and recurrent/progressive presentations.

KEYWORDS: Pediatric Demyelinating Disease

262. The Effect of Social Determinants of Health and Adverse Childhood Experiences on Disease Outcomes in Pediatric Onset Multiple Sclerosis

Miller A (Phoenix, AZ), Held H, Mubarak H, Vaidyanathan V, Bassal F

OBJECTIVE: Although the causes of multiple sclerosis (MS) are not yet fully understood, there is likely a complex interaction between genetic, environmental, and social factors, such as social determinants of health (SDOH) and adverse childhood experiences (ACEs). However, there is very little data that has looked at the effect of SDOH and ACES on the disease burden and outcomes of POMS.

METHODS: The participants in this study included consenting parents and assenting adolescent POMS patients. Two surveys will be distributed to the POMS patients and their parents. The data collected includes information on socioeconomic status, healthcare access, and social support, as well as an ACE score on the patient survey and the validated parent version called PEARLS (in case the child is unable to fill out the survey).

RESULTS: We propose that ACEs should be considered as an additional social determinant of health for POMS patients. Furthermore, we hypothesize that patients of lower socioeconomic status and higher ACE scores have poorer disease outcomes.

CONCLUSIONS: SDOH and ACEs may play a significant role in the development, progression, and management of POMS. Pediatric patients face unique challenges, such as school, bullying, and childhood trauma that could directly affect the patient's disease course. The goal of this study is to identify current barriers in POMS medical care, so future interventions may be done to improve patient outcomes.

KEYWORDS: Pediatric Demyelinating Disease, Diversity, Equity, Inclusion

263. Effects of Obesity on Prevalence and Disease Burden in Pediatric Onset Multiple Sclerosis (POMS)

DeCesare T (Phoenix, AZ), Held H, Miller A, Vaidyanathan V

OBJECTIVE: We aim to investigate the association between childhood obesity and increased prevalence and disease burden in children diagnosed with MS.

METHODS: 52 patients, aged 0-18 years, were identified within Barrow Neurological Institute at PCH with a diagnosis of MS, seen at the institution from 1/1/2012 to 1/1/2023. Patients were grouped by presence or absence of obesity. Information on patients' age at presentation, racial identity, disease modifying therapies, and symptoms at onset was collected and analyzed between the two groups.

RESULTS: 22 of the 52 patients diagnosed with POMS were obese, making up 42.3% of our sample, compared to the national prevalence of 19.3%. The mean age at presentation did not differ significantly between the two groups. Patients with obesity were more likely to return to the hospital after diagnosis with an average of 0.72 visits for obese patients, and 0.43 visits for non-obese patients. Additionally, individuals who identified as Hispanic/Latino comprised 59.1% of the obese group, while making up 50% of the non-obese group.

CONCLUSIONS: Similar to the adult population, obesity likely plays a significant role in the prevalence and disease burden in POMS. Further analysis should investigate frequency and severity of relapses in POMS patients with obesity compared to those without.

KEYWORDS: Pediatric Demyelinating Disease

264. A novel drug Sapropterin (Kuvan) ameliorates the disease phenotype in a mouse model of multisystem smooth muscle dysfunction syndrome.

Musolino P (Boston, MA), Krishnan V, Das S, Orrego J, Shamber C

OBJECTIVE: Pathogenic missense mutation at the arginine 179 position in the gene ACTA2, encoding for alpha smooth muscle actin (α-SMA), develop a profound systemic smooth muscle cell dystrophy named multisystem smooth muscle dysfunction syndrome (MSMDS). There is a paucity in characterization of this phenotype, and an unmet need for effective and accessible treatments for this debilitating disease. Recent molecular interaction studies predict that the drug Kuvan (Sapropterin) binds to the mutant ACTA protein monomers and restores protein integrity. In this study we explore the effects of Kuvan, on improving phenotypic function in a murine model of MSMDS.

METHODS: A cre-inducible knock in, mutation murine model of MSMDS was generated in whole body smooth muscle, with Myh11-cre (Myh11-Cre:Acta2R179fl/+). Ad-libitum access to water containing Sapropterin (10mg/kg) was provided to pregnant moms to ensure maternal fetal drug access. Eight weeks post treatment, animals were subject to a battery of physiology, behavior, and immunohistochemistry modalities, to assess systemic improvements in disease.

RESULTS: We report that the treated Myh11-Cre:Acta2R179fl/+ mice had significantly higher survival rates vs. untreated Myh11-Cre:Acta2R179fl/+. Systemic blood pressure measurements show a significant improvement in

baseline mean arterial pressure in treated Myh11-Cre:Acta2R179fl/+ vs untreated mutant mice. Significant sensorimotor recovery (p=0.02) was observed in open field test in Kuvan treated Myh11-Cre:Acta2R179fl/+ mice (total distance travelled 905.5 ± 236.6cm vs. untreated Myh11-Cre:Acta2R179fl/+ cohort 269.3 ± 106.9cm.

CONCLUSIONS: These findings show Kuvan shows promise as an effective pharmacotherapeutic in restoration of phenotypic characteristics in a mouse model of MSMDS.

KEYWORDS: Pediatric Demyelinating Disease, Experimental Therapeutics, Autonomic Disorders

265. Racial and Ethnic Disparities in Pediatric Onset Multiple Sclerosis (POMS)

Held H (Phoenix, AZ), Miller A, DeCesare T, Mubarak H, Vaidyanathan V, Bassal F

OBJECTIVE: Multiple sclerosis (MS) is an autoimmune disease of the CNS, and the risk of developing MS differs based on race and ethnicity. Research suggests that the social determinants of health (SDOH) influence outcomes in MS. Previous literature has reported that Hispanic patients present younger and more often with optic neuritis compared to Caucasian patients. There is limited data that has looked at SDOH in POMS. Our objective is to evaluate differences in clinical MS presentation and treatment in POMS patients.

METHODS: Patients identified within the Barrow Neurological Institute at Phoenix Children's Hospital were ages 0-18 with a diagnosis of MS, seen at the institution from 1/1/2012 to 1/1/2023. Data was obtained for 52 POMS patients. We analyzed metrics from each group: mean age of presentation, disease modifying therapies (DMTs) prescribed, and clinical symptoms at presentation (e.g. BMI, optic neuritis, cerebellar symptoms, headache, and dysarthria).

RESULTS: The mean age of presentation was similar across all racial and ethnic groups. Among the Hispanic patients with MS, Fingolimod was the most commonly prescribed DMT (28.57%). 43% of Hispanic patients were obese at the time of diagnosis. Compared to other groups, there was increased prevalence of optic neuritis and cerebellar symptoms in Hispanic patients (57.14% and 50%, respectively).

CONCLUSIONS: Consistent with previously published literature, our data demonstrates that optic neuritis is highly prevalent among our Hispanic MS patients. Additionally, obesity was highly prevalent at time of presentation in Hispanic patients, and we plan to focus on this in further data analysis and potential interventions.

KEYWORDS: Pediatric Demyelinating Disease

SLEEP

266. Changes in Sleep Patterns in Korean Early Adolescents during Sexual Maturation

Han TH (Seoul, South Korea)

OBJECTIVE: The sleep patterns of teenagers have been reported show physiological delays influenced by sexual maturation and other external factors related to time. However,Korean adolescents have shorter sleep durations compared to their peers worldwide and have differences in the onset of pubertal development. Therefore, we evaluated the relationship between sleep patterns and sexual maturation in Korean adolescents with chronic sleep restriction.

METHODS: From March to August 2017, we surveyed children aged 10 to 12 years in Seongnam-si (SAP). We evaluated items related to sleep and sexual maturation, assessed sleep duration and sleepiness scale scores, and analyzed the changes in sleep parameters in relation to sex, height, weight, and sexual maturation rating (SMR).

RESULTS: The study included 620 children, and the sleep duration was found to be 8.63 ± 0.81 hours in boys and 8.40 ± 0.98 hours in girls. Sleep onset time was delayed with an increase in sexual maturation rating (SMR), while wake-up time was not affected. Sleep duration decreased as SMR increased, and sleepiness scale scores remained unchanged. The delay in sleep onset time was 0.251 ($P = 0.001$; 95% CI, 0.105-0.397) for each increase in SMR, while the decrease in sleep duration was 0.258 ($P = 0.001$; 95% CI, -0.403 to -0.114) for each increase in SMR, after adjusting for sex and standardized body mass index (BMI).

CONCLUSIONS: Sleep patterns in teenagers show changes with sexual maturation and sleep duration and sleep onset times are especially influenced in children with chronic sleep restriction.

KEYWORDS: Sleep

267. Severe mixed sleep apnea in a patient with epilepsy and gene mutation EEFIA2.

Gupta D (Orange, CA), Galion A

OBJECTIVE: EEFIA2 gene mutation has been linked to epilepsy and intellectual disability. The gene mutation has been linked with with epilepsy and possible phenotypes of broad nasal bridge and tented upper lip however there has been no description of sleep disordered breathing. Here, we present a case of sleep apnea in a patient with intractable epilepsy with a specific gene mutation.

METHODS: Patient is a toddler-aged female with epilepsy. She was diagnosed with infantile epileptic encephalopathy with a pathogenic mutation in EEF1A2 gene with intractable generalized myoclonic epilepsy, hypotonia, and developmental delay. With epilepsy medications she had side effects of swallowing difficulties and increased sedation. She was noted to have frequent night time awakenings. She was scheduled to have a combined polysomnography and 24 hour electroencephalogram.

RESULTS: Polysomnography showed evidence of severe mixed central and obstructive sleep apnea-hypopnea syndrome with AHI of 100/h, CAI 42/H, OAHI - 57/h, and REM AHI of 106/h. EEG performed at the same time and showed multiple atonic and myoclonic seizures with multifocal discharges. She was titrated on bilevel positive airway pressure during a split-titration sleep study.

CONCLUSIONS: In this case we present a rare genetic mutation EEFIA2 which has presented as intellectual disability, hypotonia, and intractable epilepsy in this patient. Given

some daytime somnolence and night time awakenings, a polysomnography was pursued and showed severe obstructive sleep apnea. In cases where phenotypes are not widely known, it is important to screen for sleep disorders.
KEYWORDS: Sleep, Epilepsy, Neurogenetics

268. Sleep and behavioural comorbidities in primary monosymptomatic nocturnal enuresis: a polysomnography-based observational study with controls

Chakrabarty B (New Delhi, India), Thosare P, Gulati S, Jaryal A, Jauhari P, Pandey R M, Upadhyay A, Kabra S, Hari P, Sikka K

OBJECTIVE: To evaluate sleep and behavioural comorbidities in 5-18year-olds with primary monosymptomatic nocturnal enuresis (PMNE) and understand its therapeutic implications
METHODS: Cases with PMNE, aged 5-18 years, presenting to a tertiary-care-teaching-hospital in north-India, during March 2021-November 2022 were enrolled. Those with chronic systemic illness, IQ (Intelligence quotient)>70, daytime symptoms and receival of any therapy for PMNE in last 6 months were excluded.
The cases underwent evaluation on Childhood and Adolescent Sleep Evaluation Questionnaire (CASEQ), overnight PSG, CBCL (Childhood Behaviour Checklist) and HTP (House-Tree- Person) test. Subsequently, they received standard behavioural therapy for 12 weeks.
RESULTS: Twenty-one subjects were enrolled (26 screened, 10.6+/-3.2 years, 16 boys). Impaired CBCL was seen in 47.6% (10/21, hyperactivity in 9-42.9%). Academics-related stressor was seen in 9/21 (42.9%) on HTP test.
On CASEQ and overnight PSG evaluation, sleep related breathing disorder and sleep related movement disorder (SRMD) were seen in 71.4% (15/21) and 61.9% (13/21) respectively.
Compared to age-matched normal controls (n=20) significant findings ($p<0.05$) on PSG were
- lower sleep efficiency (72.3+/10.9% versus 80.6+/-9.1%),
- higher proportion of N2 (76.4+/2% versus 63.1+/-2.8%),
- lower proportion of N3 (16.3+/1.7% versus 28.2+/-1.5%) and
- subjects with arousal index >14 (19% versus 0%).

One-third responded well to standard behavioural therapy. Presence of other primary sleep disorders, particularly SRMD was significantly associated with poor response.
CONCLUSIONS: Cases with PMNE have lighter, fragmented sleep with reduced efficiency with majority having other primary sleep disorders for which they should be routinely screened. Behavioural and psychological evaluation help in holistic management of cases.
KEYWORDS: Sleep

269. Pediatric Insomnia: the need for an interdisciplinary approach

Polat P (Aurora, CO), Wesley K

OBJECTIVE: Insomnia is a common sleep complaint among children and adolescents. Insomnia is especially common complaint in children with comorbid neurologic conditions such as epilepsy and migraine. Behavioral strategies and cognitive behavioral therapy for insomnia are often the first line treatment and recommendation. The primary purpose of this study was to 1) describe treatment recommendations for patients presenting to sleep clinic for a primary concern of insomnia, 2) examine time to starting treatment based on recommendation, and 3) discuss alternative models, including an interdisciplinary approach, of service delivery to improve access to treatment.
METHODS: A retrospective chart review was completed for patients seen in a pediatric sleep clinic. Patient referral concern, visit diagnosis, and treatment recommendation were extracted from the electronic medical record and analyzed.
RESULTS: In a 3-month period, 37 new patients presented with a primary complaint of insomnia. Of these, 82% were referred to a sleep psychologist for behavioral therapies as part of the treatment plan; 52% were referred to a sleep psychologist as the main treatment modality; 18% were treated with pharmacological agents only; and 26% were recommended both pharmacological therapies and a referral to a sleep psychologist. For patients referred to a sleep psychologist, the average time to start behavioral therapy was 6 weeks from their initial visit in the sleep clinic.
CONCLUSIONS: The results of this study demonstrate the importance of and need for integrating a sleep behavioral specialist into an interdisciplinary clinic model to manage pediatric insomnia and increase access to recommended treatments.
KEYWORDS: Sleep

270. Sleep Characteristics May Differ in Toddlers with Epilepsy Compared with Children without Epilepsy – A Pilot Study

Saylam E (Columbus, OH), Gupta G, Patel A, Dang L T, O'Brien L M, Ibadat S, Sturza J M, Neff K E, Shellhaas R A

OBJECTIVE: The interaction between sleep and epilepsy is not completely understood. Sleep is a prominent concern of many caregivers of children with epilepsy; however, this issue has not been examined systematically.
METHODS: Toddlers (ages 12-36 months) with epilepsy were recruited from Pediatric Neurology clinics. Children without epilepsy were recruited from Pediatric clinics and social media. Caregivers responded to a novel sleep questionnaire being developed for infants and toddlers. Two domains were analyzed (Caregiver/Child Behavior and Comfort Object/Bedtime Routine). The domain score equaled the sum of the scores for each item divided by the number of items answered.
The nine items in the Caregiver/Child Behavior domain related to parental worry and frustration, insomnia, restless sleep, behavioral sleep patterns, excessive daytime sleepiness, and nocturnal leg movements.
The two items in the Comfort Object/Bedtime Routine domain related to parental presence during sleep initiation, and the use of comfort objects during sleep.
RESULTS: Responses of the caregivers of 11 toddlers with epilepsy were compared with responses for 343 control toddlers. The Caregiver/Child Behavior score was higher (worse)

in toddlers with epilepsy (mean 3.4±SD 0.72) compared with controls (1.94±0.93) p< 0.0001. Yet, toddlers with epilepsy had lower (better) scores in the Comfort Object/Bedtime Routine domain (2.23±1.25) compared with controls (3.20±1.25) p=0.01.
CONCLUSIONS: Sleep behavior is complex in toddlers with epilepsy and may lead to more parental frustration and worry compared to toddlers without epilepsy. Further investigation into this relationship could provide opportunities to improve sleep and quality of life for children with epilepsy.
KEYWORDS: Sleep, Epilepsy

STROKE

271. Isolated Cervical Cord Infarct in a Neonate

Yang K (New York City, NY), Garcia M, Segal D

OBJECTIVE: To analyze a rare case of an isolated cervical spinal infarct in a neonate and evaluate the different suspected etiologies.
METHODS: Case report.
RESULTS: An 18-day-old ex-full-term boy presents to neurology clinic for evaluation of a cervical spine lesion. Prenatal history is significant for decreased fetal movements at 38 weeks. A week later, patient was born via emergency C-section for meconium-stained amniotic fluid and failure to progress. Patient was born floppy with respiratory distress needing brief intubation, APGAR scores 2, 7, and 8 at 1, 5, and 10 minutes of life. He was noted to have diminished spontaneous movement of his extremities prompting neuroimaging. A brain and cervical spine magnetic resonance imaging (MRI) with and without contrast showed an intramedullary region of increased T2 signal abnormality from C2-T1 with edema consistent with cervical cord infarct. Three lumbar punctures were negative for infection and malignancy. Hypercoagulable workup was also unremarkable. At age 2 he was noted to have significant language delay and failure to thrive. His exam demonstrated profound flaccid paraplegia, sensory loss on the left arm, areflexia on the right, and global delay.
CONCLUSIONS: Cervical cord ischemic strokes are rare among neonates and when they occur are always accompanied by cerebral ischemia. We present a perinatal case of an isolated cervical ischemic stroke, demonstrating that this may not always be the case. An isolated cervical ischemic stroke can profoundly impact an individual's long-term neurological sequalae.
KEYWORDS: Stroke, Neonatal Neurology

272. Use of Atorvastatin Reduces Stroke Lesion Volume in a Juvenile Photothrombotic Rat Stroke Model

Sare D (Toronto, ON, Canada), Li D, Waspe A, Domi T, Dlamini N, Kassner A

OBJECTIVE: This study aims to longitudinally assess acute ischemic stroke (AIS) and blood-brain barrier (BBB) integrity following the use of atorvastatin in a juvenile photothrombotic rat stroke model using quantitative MRI.
METHODS: Photothrombotic stroke was induced in 10 five-week-old male Sprague Dawley rats. Stroke was confirmed using DWI/T2W MRI. Five rats were treated with 20 ml/kg of atorvastatin via peritoneal injection after baseline MRI, while the remaining five rats acted as a control group. Quantitative MRI was performed on a 3.0T MRI system (Philips Healthcare) at the hyperacute (Day 0), sub-acute (Day 2), and chronic stages (Day 7) following photothrombosis. The MRI protocol included T2-weighted FLAIR, diffusion (DWI), and dynamic contrast-enhanced MRI (DCE). Image analysis was performed on specific regions of interests (ROIs) using 3D slicer and MATLAB. Student's t-test was used to compare the results of both 2 groups.
RESULTS: T2W lesion volumes were 82, 88, and 44 mm3 for the statin group, and 99, 115, and 70 mm3 for the control group for days 0, 2 and 7, respectively. Lesion volume was significantly reduced in the statin group compared to controls, on day 2 ($p = 0.042$) and 7 ($p=0.012$) following AIS. Diffusion and DCE values showed no significant changes between groups over time.
CONCLUSIONS: Findings of this study potentially support the effectiveness of atorvastatin in reducing lesion volume a juvenile rat stroke model. More research is needed to validate and translate findings to children with stroke.
KEYWORDS: Stroke, Neuroimaging

273. Time to treatment in Pediatric AIS: Riley Hospital for Children initial experience after initiation of our pediatric stroke protocol

Sun F (Indianapolis, IN), Martinez M, Golomb M, Tejada J, Friedman M

OBJECTIVE: Delay to imaging and diagnosis of stroke in the pediatric population has remained a significant problem (1,2). Successful implementation of pediatric stroke protocols has decreased time to imaging and diagnosis and allowed offering of hyperacute therapies (3). We share our experience of implementing a pediatric stroke protocol and compare the amount of time it took for our patients to receive hyperacute therapies in comparison to the goals established for adults who present to comprehensive stroke centers.
METHODS: We performed a retrospective analysis of our institutional pediatric stroke alert activations from April 2021 to October 2022. Clinical characteristics and timing parameters were collected and compared to stroke standards for a comprehensive stroke center.
RESULTS: Preliminary Data-There were 36 activations, consisting of 33 patients. Of these patients, there were 13 confirmed strokes by imaging, but only 4 patients were eligible for either tPA or thrombectomy. A total of 1/13 patients received tPA and 3/13 patients underwent thrombectomy. Time from stroke activation to tPA administration was 172 minutes (goal 45 mins). Average time from stroke activation to thrombectomy was 145 minutes (goal 90 min).
CONCLUSIONS: Initiating a stroke protocol allows increased offering of hyperacute therapies to children,

decreased delay in diagnosis and treatment, and commencement of quality improvement initiatives that will only continue to improve outcomes for children suffering from acute ischemic stroke.

KEYWORDS: Stroke

274. Prolonged Post-Stroke Hyperperfusion in Children with Congenital Heart Disease

Parulekar M (Pittsburgh, PA), Paldino M, Cummings D

OBJECTIVE: Children with congenital heart disease (CHD) are at a greater risk of developing arterial ischemic stroke (AIS) and require multiple corrective surgeries, making them a high-risk population. Post-stroke perfusion profiles represent important biomarkers for understanding pathophysiology, clinical outcome, and risk of hemorrhagic transformation. This study aimed to determine if prolonged post-stroke hyperperfusion was common in CHD patients.

METHODS: This study involved a single-center retrospective analysis of patients aged 1 month to 18 years with MRI confirmed arterial ischemic stroke from January 2010 to December 2021. Patients with CHD and moderate-to-large middle cerebral artery (MCA) infarcts were analyzed. Cerebral perfusion was quantified using arterial spine labeling (ASL). ADC and ASL images were analyzed by a pediatric stroke neurologist and pediatric neurology fellow. Regions of Interest (ROI) were collected from 15 brain regions based on modified ASPECTS. ROI were compared to similar regions of the unaffected hemisphere.

RESULTS: Out of 75 patients with AIS, 27 (36%) had CHD. Five CHD patients with MCA infarcts were included in analysis, with a mean age of 5.4 years (IQR 0.9). Cardiac pathology included TGA in one, VSD in one, and HLHS in three patients. ADC ratios were lower near stroke onset and eventually normalized to 1. Elevated ASL ratios (hyperperfusion) were observed in affected regions up to 10 days after stroke.

CONCLUSIONS: The study demonstrated that hyperperfusion can persist more than 10 days post-stroke in CHD patients despite normalization of ADC. This highlights the need for further research to understand the mechanisms of prolonged hyperperfusion.

KEYWORDS: Stroke, Neuroimaging, Neurocritical Care

275. A Case Study of Motor Outcomes in Twins with Perinatal Stroke: Insights from MRI and MEG

Hsu P (Toronto, ON, Canada), Cheyne D, Dlamini N

OBJECTIVE: Perinatal arterial ischemic stroke (AIS) affects ~13 in 100,000 children, with cases of affected twins being exceedingly rare. Dystonia affects 20% of pediatric AIS survivors, but the reasons for its emergence are unclear. This study describes MRI and MEG findings in twins with similar perinatal strokes but different motor outcomes.

METHODS: 11-year-old monozygotic twin brothers, one with perinatal AIS and the other with a previously undiagnosed perinatal stroke, were studied. One child developed dystonia in the contralesional hand while his twin was asymptomatic, although he showed hand preference contralateral to the unaffected hemisphere (left hand). To investigate changes in motor control, MEG functional imaging was performed during a response inhibition task.

RESULTS: 3D T1 and 2D FLAIR imaging revealed that the twin with dystonia had a right MCA infarct involving the right frontal lobe, basal ganglia, with ex vacuo enlargement of the right lateral ventricle, and Wallerian degeneration in the cerebral peduncle. In contrast, his asymptomatic twin had a left MCA infarct, similar lesion patterns but without basal ganglia involvement. Both performed well on the cognitive motor task with few errors. Notably, MEG showed robust movement-locked gamma (60-90 Hz) oscillatory power in both twins when using their contralesional hand, and lower gamma power when using their ipsilesional hand suggesting sensorimotor feedback was upregulated in the contralesional hand to maintain sensorimotor control.

CONCLUSIONS: This interesting case suggests that basal ganglia involvement may be a key factor in post-stroke dystonia development, and gamma activity reveals compensatory changes in motor control, with or without dystonic symptoms.

KEYWORDS: Stroke, Movement Disorders, Neuroimaging

276. A case of tenecteplase for pediatric acute ischemic stroke

Lee M (St. Louis, MO), Tabatabai G, DeKorver N, Mills K, King T, Timm T, Bray-Aschenbrenner A, Galardi M, Guilliams K

OBJECTIVE: We report the use of tenecteplase in a case of pediatric acute ischemic stroke (AIS), as prior reports have been limited to adult stroke.

METHODS: A 13-year-old female with depression presented with acute onset left-sided weakness. Her initial NIHSS was 13 – scored for drowsiness requiring stimulation to maintain wakefulness, right gaze preference, left facial droop, dysarthria, left upper and lower extremity weakness, and left-sided neglect. Presentation was concerning for right middle cerebral artery (MCA) territory stroke. Hyperacute MRI demonstrated diffusion restriction with ADC correlate and lack of FLAIR hyperintensity within right MCA territory involving lentiform nucleus and frontal and insular cortices (core volume estimated 9 mL). Non-contrast MRA identified a large vessel occlusion within the proximal M1 segment of the right MCA. She received tenecteplase (0.25 mg/kg) three hours from symptom onset prior to undergoing successful endovascular mechanical thrombectomy . Post-intervention head CT at 12 and 36 hours did not have any intracranial hemorrhage. Patient participated in inpatient neuro-rehabilitation with improvement in functional outcomes. Her NIHSS at time of discharge was 6 with a modified Ranken score of 3.

RESULTS: Intravenous thrombolysis with tenecteplase was safely provided as a rapid single bolus to a pediatric patient with AIS prior to thrombectomy. She had no evidence of hemorrhagic conversion on follow-up imaging and improvement in function.

CONCLUSIONS: This case demonstrates the safe use of tenecteplase prior to thrombectomy in the treatment of pediatric AIS with good functional outcome. Prospective studies

are needed to determine the safety and efficacy of tenecteplase in pediatric stroke.
KEYWORDS: Stroke, Neurocritical Care, Neuroimaging

277. Atypical Posterior Circulation Focal Cerebral Arteriopathy in a 15 year-old Male

Kung M (Orange, CA), Pearson R

OBJECTIVE: Focal cerebral arteriopathy (FCA) is a common etiology for pediatric stroke. While FCA typically presents with unilateral, anterior circulation stenosis, posterior circulation FCA has also been described. We report an atypical case of posterior circulation FCA.
METHODS: Case Report.
RESULTS: 15-year-old male presented with left-sided numbness. CT head showed hypo-attenuation in the left parietal lobe. MRI/MRA head and neck showed bilateral posterior circulation infarcts with right posterior cerebral artery (PCA) stenosis and distal occlusion. Aside from recent respiratory symptoms, history was unremarkable. PCR was positive for Coronavirus-229E. Additional labs showed: CRP 20.5 mg/L, ESR 17mm/hr, ANA+. Other diagnostics including echocardiogram and CSF studies were unrevealing. He improved and was discharged on aspirin.
A week later, he returned for new right upper quadrantanopia. Repeat imaging showed new bilateral PCA-territory infarcts. Cerebral angiography showed bilateral PCA occlusions, concerning for possible vasculitis. Despite initiation of high-dose steroids, his symptoms worsened, correlating with new infarcts on MRI. Given pure posterior circulation involvement, rotational vertebral arteriopathy was considered and c-collar was placed. Rotational angiography, however, failed to demonstrate dynamic stenosis or occlusion. Cervical X-rays were normal. He was escalated to dual antiplatelet therapy (DAPT). A week later he was clinically improving with stable imaging and discharged on DAPT and a steroid taper
CONCLUSIONS: This was an atypical presentation of FCA involving bilateral posterior circulation, possibly mediated by preceding viral illness. It is important to consider FCA on the differential for pediatric stroke as it is associated with high risk of stroke recurrence, and steroids may improve outcomes.
KEYWORDS: Stroke

278. SARS-CoV-2 Infection and Increased Risk for Pediatric Stroke

Vielleux M (Salt Lake City, UT), Swartwood S, Nguyen D, James K, Barbeau B, Bonkowsky J

OBJECTIVE: There is an increased risk of stroke in adults with SARS-CoV-2 (COVID-19) infection, but whether there is a similar association with stroke in children is unclear. Our objective was to determine whether there is a correlation between COVID-19 infection, multisystem inflammatory syndrome in children (MIS-C), and pediatric ischemic stroke.
METHODS: This was a retrospective, population-based cohort analysis between 3/1/2020 and 6/30/2021, conducted at a children's hospital. Pediatric patients with a diagnosis of ischemic stroke were identified using ICD-10 diagnoses of ischemic stroke, cerebrovascular accident, or cerebral infarction.
RESULTS: We identified 16 patients, 7 male and 9 female, with ischemic stroke. Ages were 8 months to 17 years (median 11.5 years). More Asian (6%) and Black (13%) patients had strokes compared to population prevalence (2% each, respectively). No patients had active COVID-19 infection. COVID-19 antibodies were identified in 5 of 11 patients tested (45%), of whom 3 were diagnosed with MIS-C. 82% of the strokes occurred between February and May 2021. The peak incidence was in February 2021, which was 2 months after peak incidence of pediatric cases of COVID-19 and 1 month after the peak of MIS-C cases.
CONCLUSIONS: Our study suggests that prior COVID-19 infection, but not acute infection, is correlated with a risk for stroke in the pediatric population. The risk for stroke appears to be distinct from the risk for MIS-C.
KEYWORDS: Stroke

279. Neuroimaging Correlates of Dystonia and Intellectual Abilities after Pediatric Arterial Ischemic Stroke of the Basal Ganglia and/or Thalamus

Ledochowski J (Toronto, ON, Canada), Rajani N, Feldman S, Ertl-Wagner B, Robertson A, Westmacott R, Desrocher M, Dlamini N

OBJECTIVE: To examine lesion characteristics on acute neuroimaging in children with basal ganglia/thalamus arterial ischemic stroke (AIS) with and without dystonia as well as associations with intellectual ability.
METHODS: A retrospective study of 41 children with neonatal or childhood AIS (mean age at stroke= 5.89[4.58] years; 22 no dystonia). Volumetric analysis, detailed lesion classification, and markers of remote injury (Wallerian degeneration [WD], diaschisis) were obtained from diffusion weighted magnetic resonance imaging scans performed during initial presentation. Intellectual ability (IQ) was assessed with the age-appropriate Wechsler Scales of Intelligence (mean age at testing= 11.71[4.01] years).
RESULTS: Dystonia was associated with involvement of the putamen ($\chi2$= .839, p= .004), caudate nucleus ($\chi2$= 4.14, p= .042), and anterior limb of the internal capsule (ALIC; $\chi2$= 7.16, p= .007), and larger lesion size (U= 302, p=.015). No children with dystonia had infarcts involving only the thalamus. There were no significant group differences by presence of WD or diaschisis. Nested logistic regression and hierarchal linear regression analyses were used to examine the putamen, ALIC, caudate nucleus, and lesion volume as predictors of dystonia and IQ, respectively. Only the putamen was a significant predictor of dystonia ($\chi2$ [1]= 9.56, p= .002, Nagelkerke R2= .28) and IQ (F[1, 39]= 9.34, p= .004, adj. R2= .17).
CONCLUSIONS: Infarct characteristics implicate the cortico-striatal-thalamo-cortical loop which is consistent with the conceptualization of dystonia as a network disorder. Results suggest that the putamen may be a structure that mediates an underlying neurobiological substrate of both motor and cognitive outcome.
KEYWORDS: Stroke, Movement Disorders, Neuroimaging

280. Stimulation for Perinatal Stroke: Optimizing Recovery Trajectories (the SPORT trial)

Hilderley A (Calgary, AB, Canada), Dunbar M*, Andersen J, Fehlings D, Metzler M, Carlson H, Zewdie E, Hodge J, O'Grady K, Carsolio L, Dlamini N, Hill M D, Kirton A, SPORT Investigators*

OBJECTIVE: To determine if transcranial direct current stimulation (tDCS) can enhance intensive motor learning in children with perinatal stroke and hemiparesis.

METHODS: A multicentre, randomized, sham-controlled, double-blind, phase III trial enrolled children aged 6–18 years with perinatal stroke and hemiparetic cerebral palsy. Participants completed a customized 10-day intensive motor learning camp, randomized 1:1 to daily contralesional, cathodal tDCS or sham stimulation. Primary objective and subjective outcomes were the Assisting Hand Assessment (AHA) and Canadian Occupational Performance Measure (COPM), assessed at baseline and 1-week/2-months/6-months post-treatment. Intention to treat analysis explored tDCS versus sham groups for change in scores from baseline to 6-months (student's t-test), proportions with significant improvement at 6-months (≥5 AHA; ≥2 COPM, Fisher's), and changes over time (repeated measures mixed model). Safety outcomes included decline in function of either hand.

RESULTS: Of 89 children enrolled, 81 (44 sham, 45 tDCS) completed all measures (56% male). High proportions of both groups achieved clinically significant increases in AHA (49% and 50%, p=0.9), and COPM (71% and 76%, p=0.6) with large effect sizes (d=0.9 AHA, 1.53 COPM) that were sustained at 6 months (p<0.001). There were no differences between sham and tDCS groups for mean change from baseline for AHA (5.2, SD=5.3 vs 4.6, SD=5.7, p=0.63) or COPM (3.0, SD=2.0 vs 3.6, SD=2.3, p=0.25). Procedures were safe and well-tolerated with no serious adverse events.

CONCLUSIONS: Patient-centred intensive motor learning programs can produce marked and sustained improvements in upper extremity function in children with perinatal stroke and hemiparesis. Gains are not enhanced by contralesional cathodal tDCS.

KEYWORDS: Stroke, Cerebral Palsy

281. Watershed White Matter Involvement in Children with Moyamoya is Not Significantly Different Between Symptomatic and Asymptomatic Hemispheres

Lehman L (Boston, MA), Ahtam B, Berto L, Lildharrie C, Solti M, Justin J, Feldman H, Vyas R, Zhang F, O'Donnell L, Rathi Y, Smith E, Orbach D, See A, Grant P

OBJECTIVE: We previously demonstrated that children with moyamoya without stroke or silent infarct have alterations in white matter watershed tracts. With controversy regarding when or if to revascularize children with asymptomatic moyamoya, we investigated if altered white matter in children with moyamoya was significantly different, depending on whether the moyamoya-affected hemisphere in question correlated with symptom localization or not.

METHODS: We recruited children with moyamoya without stroke or silent infarct who had diffusion magnetic resonance imaging (dMRI) prior to revascularization surgery. We obtained mean diffusivity (MD) in white matter watershed tracts using unscented Kalman filter tractography and white matter analysis pipeline. Hemispheres affected by moyamoya were labeled "symptomatic" if transient ischemic attack (TIA), seizure or movement disorder were localizable to that hemisphere. Any affected hemisphere was labeled "symptomatic" if child had headaches. Hemispheres with moyamoya were "asymptomatic" if the child did not have symptoms attributable to that hemisphere. Asymptomatic and symptomatic hemispheres were compared to control children using factorial ANOVA.

RESULTS: We enrolled 21 children with moyamoya in 32 affected hemispheres (22 symptomatic, 10 asymptomatic), and 25 control children. Watershed white matter tracts had similar MD in symptomatic and asymptomatic hemispheres (p =0.85) but higher MD than controls (p= 0.02 and p=0.02).

CONCLUSIONS: Children with moyamoya without stroke or silent infarct had similar white matter alterations in symptomatic and asymptomatic moyamoya affected hemispheres, suggesting that symptoms do not accurately detect severity. Children with moyamoya who are asymptomatic but have altered watershed white matter tracts may benefit from early revascularization surgery to prevent cognitive deficits.

KEYWORDS: Stroke, Neuroimaging

282. Neurological Patient-reported Outcomes and Quality-of-Life Survey Patients with Multisystemic Smooth Muscle Disorder Syndrome (MSMDS) Caused by Arginine 179 Pathogenic Variants

Lynch A (Boston, MA), Gandhi A, Kelly D, Shamber C, Orrego J, Seyedasadjadi R, Hausman Kedem M, Musolino P, Tambala D

OBJECTIVE: To assess self-reported outcomes and the impact in quality-of-life of neurological symptoms in patients with MSMDS caused by ACTA2 R179 pathogenic variants.

METHODS: Working together with the patient community, caregivers, medical providers and advocacy groups we surveyed 35 patients (0-44 years old, median 8) using disease-specific and NIH tool kit NeuroQL questionnaires. The survey was distributed to eligible individuals in the MGH Pediatric Stroke Clinic and by the Young Genetic Stroke Alliance MSMDS Working Group. De-identified data was analyzed with conventional statistical comparison and regression methods.

RESULTS: Stroke was reported by 51.4% with a median age of 3 years for first event and a cumulative risk of 85% by 10 years. Of these patients 55% suffered one or more recurrent strokes. Within the cohort, 37.1% participants reported having at least one seizure (n=13). More than a third of patients reported seizures requiring hospitalization. All patients (35) reported having had developmental delays in the motor, cognitive, and/or language spheres. Motor delays were most reported with walking delay or regression most severely affecting their quality of life in 20% of patients.

CONCLUSIONS: Our survey for the first time reports functional outcomes, disease burden, and its impact in patients

with ACTA2 R179 quality-of-life. We found higher rates of stroke and seizure when compared to retrospective cross sectional published studies. Developmental delays appear to be ubiquitous and cause severe burden in patient quality-of-life. Further longitudinal patient-centered studies are needed to determine the full impact of this systemic disease.
KEYWORDS: Stroke, Neurogenetics

283. The Comparative Advantage of Granularity in Language Scores in Relating Lesion Location to Language in Perinatal Stroke

Miller G (Boston, MA), Basu M, Chui C, Musolino P, Cohen A

OBJECTIVE: The Pediatric Stroke Outcome Measure (PSOM) is a 20-minute assessment of neurological deficits across five domains, including language. Here, we assess the utility of PSOM language scores in relating language functioning to lesion location in perinatal stroke patients.
METHODS: MRI data from 22 perinatal stroke patients was segmented and registered to MNI space. Voxel-wise lesion symptom mapping (VLSM) analyses were performed to relate PSOM language scores and binary language delay diagnostic group classification from two time points to lesion locations. Results were then compared to the Language association map from the Neurosynth Meta-analysis Repository.
RESULTS: Using the more recent data (n=22; mean age 7.41 years), VLSM found 10 clusters >10 voxels (FWE-corrected) related to language that overlapped with an a priori language map using PSOM, while no clusters were found using diagnostic group. For the earlier time point (n=21; mean age 2.41 years), only 2 clusters >10 voxels (uncorrected) overlapped the language network using PSOM scores while diagnostic group identified 3.
CONCLUSIONS: Although the PSOM is often considered a rough measure of language functioning, our findings suggest that the granularity offered by PSOM language scores is still more effective than using the presence/absence of a clinical diagnosis to relate lesion location to function in children with perinatal stroke, particularly as children develop. Future studies should consider using metrics, even if brief (PSOM), instead of the presence or absence of clinical diagnosis alone to inform predictive network models for outcomes in this population.
KEYWORDS: Stroke, Neuroimaging

284. Outcome trajectories after arteriovenous malformation rupture in pediatric patients

Keenan J (Washington, DC), Yan F, Peter P, Fleming M, Sepeta L, Sansevere A, Harrar D

OBJECTIVE: To describe outcome trajectories of pediatric patients with intracranial hemorrhage (ICH) due to arteriovenous malformation (AVM) rupture.
METHODS: Retrospective study of pediatric patients <18 years with ICH secondary to AVM rupture admitted to the intensive care unit at a single center from 2011–2023. Outcomes were evaluated using the Pediatric Stroke Outcome Measure (PSOM) at discharge and at follow-up at 0-3, 3-6, 6-12, and 12-24 months, and >2 years. The PSOM is a validated measure of outcome after pediatric stroke, with zero indicating no deficits and 10 indicating maximal deficits. A negative difference between PSOM score at discharge and follow-up indicates improvement.
RESULTS: Forty-seven patients were included, 87% (n=41) of whom had follow-up data. Median PSOM at discharge was 1 (IQR .25-3), with 62% (29/47) having a poor discharge outcome (PSOM ≥1). Median PSOM difference scores were -0.25 (IQR -1-0) at 0–3-months, -0.5 (IQR -1.5-0) at 3-6 and 6-12 months, and -1 (IQR -2.125-0) at 12-24 months and >2 years. At last follow-up, 56% (23/41) of patients had improved (median PSOM difference: –1.5 [IQR –2.75 to –1]), 7% (3/41) had worsened (median difference: 1 [IQR 1-1]), and 37% (15/41) remained stable. At last follow-up, 46% (19/41) had motor deficits, 32% (13/41) had cognitive deficits, and 10% (4/41) had epilepsy.
CONCLUSIONS: While many pediatric patients with ruptured AVMs demonstrate improvement over time, several stabilize or worsen. A better understanding of outcome trajectories may improve rehabilitation strategies, especially for those who do not improve over time.
KEYWORDS: Stroke, Neurocritical Care

285. Incidence and Predictors of Epilepsy After Pediatric Arteriovenous Malformation Rupture

Keenan J (Washington, DC), Staso K, Conley C, Harrar D, Sansevere A

OBJECTIVE: To assess electrographic seizures (ES), EEG findings, and epilepsy in pediatric arteriovenous malformations (AVM).
METHODS: Retrospective review of pediatric patients admitted to the pediatric intensive care unit at a single center with intracranial hemorrhage from AVM from January 2011- April 2022. EEG background, within the first 24 hours, was categorized as slow/disorganized, discontinuous, burst suppressed, and attenuated. Other EEG features included background asymmetry, ES, and epileptiform discharges. Seizures were defined as acute (within 7 days since presentation) and remote (>30 days since AVM detection). Fisher's exact test was used to assess associations between seizure type and epilepsy.
RESULTS: Forty-two patients met criteria (mean age: 11.1 years; standard deviation (SD): 4.09) and 48% (20/42) were female. Fifteen percent (6/42) presented with a clinical seizure. Mean initial Glasgow Coma Score (GCS) was 9.13 (SD 4.8). EEG was performed in 62% (26/42) of patients. The most common background was slow/disorganized (81%, 21/26), 50% (13/26) had asymmetry and one patient had ES (both generalized and focal. Seventeen percent (7/42) had acute seizures, 14% (6/42) had remote seizures, and 10% (4/42) had epilepsy. Patients with epilepsy were diagnosed 1.5 years (SD 0.74) after presentation. Acute seizures were not associated with epilepsy (14% vs. 10 %, p=0.5) while remote seizures were (67% vs. 10%, p< 0.0001).
CONCLUSIONS: Electrographic seizures are uncommon in the acute AVM setting while patients with remote seizures are at risk to develop epilepsy.
KEYWORDS: Stroke, Epilepsy, Neurocritical Care

TELEMEDICINE

286. Effects of COVID-19 Pandemic on Change Adaptive Behaviors in a Clinical Cohort of Children with Autism

Aitken A (Brooklyn, NY), Marco E, Hattangadi N, Shapiro K

OBJECTIVE: The COVID-19 pandemic resulted in unprecedented disruptions in the availability of therapy services for autistic children. To maintain continuity of care, many providers of Applied Behavioral Analysis (ABA) and other therapies shifted to telehealth settings. In the current study, we retrospectively analyzed measures of adaptive function in autistic children between 2019 and 2022 to understand the effects of pandemic-related shifts in therapy modality on functional outcomes.

METHODS: Our study compared cohorts of children (matched on age and sex) who received ABA therapy at our clinical centers and completed initial Vineland-3 assessments before the pandemic (N=275) and after pandemic shutdowns ended (N=275). Growth curve multilevel linear models assessed the interactive effects of age, era (Pre-COVID or Peri-COVID), and assessment-wave on adaptive behaviors.

RESULTS: We found that baseline adaptive behaviors varied as a function of age in the pre- and peri-COVID groups. Older children in the pre-COVID group had lower communication, socialization, and composite ABC scores than older children in the peri-COVID group. Younger children in the pre-COVID group did not differ from their post-COVID counterparts. However, longitudinal models revealed similar rates of improvement in both groups.

CONCLUSIONS: Our results suggest that children who were able to participate in ABA therapy during the period of COVID-related lockdowns had similar improvement in adaptive behavior outcomes compared to a matched cohort who received therapy before the pandemic. Baseline characteristics of older children in these groups differed somewhat, suggesting that older children with more severe impairments may have had less access to therapy during the pandemic period.

KEYWORDS: Telemedicine

TRAUMATIC BRAIN INJURY

287. Early Brain Magnetic Resonance Imaging Features Predict Time to Command Following after Pediatric Severe Traumatic Brain Injury

Janas A (Aurora, CO), Miller K, Ruzas C, Messer R, Stence N, Samples D, Wyrwa J, Fink E, Maddux A

OBJECTIVE: Early brain MRI features may provide prognostic data for children with TBI.

METHODS: Children (3-18 years) admitted (2010-2021) for severe TBI (GCS < 9) were identified using our site's National Trauma Data Bank. We used multivariable Cox proportional hazard modeling to determine if diffuse axonal injury (DAI) grade and number of regions with restricted diffusion (subcortical white matter, corpus callosum, deep grey matter, and brainstem) were independently associated with time to command following. We controlled for age, pre-admission cardiac arrest, pupil reactivity, motor GCS, and fever in first 12 hours.

RESULTS: Of 260 patients, 161 (61.9%) underwent MRI at median 3 days (interquartile range [IQR] 2, 6). Patients were median 11 years (IQR 7, 14), 10 (6%) had a pre-admission cardiac arrest, 24 (15%) had bilateral unreactive pupils, median motor GCS was 1 (IQR 1, 4), and 98 (61%) had fever. Grade 3 DAI was present in 50 (31%) patients, and restricted diffusion was noted in white matter, corpus callosum, deep grey matter, or brainstem in 29 (18%), 88 (55%), 35 (22%), and 25 (16%) patients. After controlling for core variables, higher DAI grade (Hazard Ratio [HR] 1.24, 95% confidence interval [CI] 1.00, 1.53) and more regions with restricted diffusion (HR 1.43, 95% CI 1.18, 1.75) were independently associated with longer time to command following. Addition of MRI features to core variables improved ability to discriminate command following at 14 days (c-statistic 0.75 vs 0.82).

CONCLUSIONS: Early MRI features of restricted diffusion and DAI grade improve prognostication in children with severe TBI.

KEYWORDS: Traumatic Brain Injury, Neurocritical Care, Neuroimaging

288. The CARE4Kids Research Study Rationale and Protocol

Otallah S (Winston Salem, NC), Choe M, Cook L, Asarnow R, Snyder A, Babikian T, Thompson P, Bazarian J, Miles C, Kamins J, Rosenbaum P, Chrisman S, Gioia G, Rivara F, Giza C

OBJECTIVE: A substantial proportion (~20%) of adolescents exhibit persistent post concussive symptoms (PPPCS) beyond the typical recovery period. As part of an NIH/NINDS funded study, the CARE4Kids (C4K) consortium (https://www.care4kidsstudy.com/) are currently recruiting the first of two cohorts of adolescents (ages 11-17) with concussion that will be utilized to define a clinically useful algorithm that will predict which adolescents will have prolonged recovery after acute concussion.

METHODS: A collection of autonomic, neurocognitive, biofluid, and imaging biomarkers will be utilized to develop the predictive algorithm. The recruitment goal is 740 adolescents across 6 sites. Unique methods from this ongoing study relevant to child neurologists include: 1) The focus on better defining endophenotypes leading to post-traumatic headache. Extensive headache clinical data will be correlated with neuro-imaging features pertinent to migraine. 2) The array of fluid biomarkers being assessed. 3) The autonomic factors being assessed and the protocol we have developed. 4) The correlation of imaging with the other biomarkers. 5) The combination of multiple biomarkers in a large prospective PPCS cohort.

RESULTS: After completion of the development cohort, a second validation phase including a further 360 adolescents

will confirm the clinical utility and applicability of the identified clinical algorithm.

CONCLUSIONS: Upon study completion, we will have generated a battery of measures predictive of high risk for PPCS which will allow for testing of interventions to prevent PPCS in the most high-risk youth. The final clinically useful algorithm will be disseminated and the data will be made available for use in further research.

KEYWORDS: Traumatic Brain Injury, Headache, Autonomic Disorders

289. Evaluating utilization trends in concussion: A retrospective cohort analysis of a large database

Johnson-Kerner B (San Francisco, CA), Ma G, Senter C

OBJECTIVE: Describe provider referral and treatment trends in treating pediatric and adult patients with concussion including diagnostic modalities, subspecialist referrals, medications prescribed.

METHODS: Data was analyzed from the Mariner database, M91 Ortho subset (151 million patients seen by an Orthopedist). The analysis focused on the timeframe of 2010-2019 (pre-COVID19 pandemic) and concussion without a loss of consciousness (ICD-9 and ICD-10 codes). Diagnostic and therapeutic modalities linked to the concussion were identified using Current Procedural Terminology codes or name.

RESULTS: 889,900 patients met inclusion criteria. 55% were female. 51% of the cohort was under 19 years old. Of the full cohort, 79% had commercial insurance and 91% had public insurance (dual insurance was present). PT and OT were the most referred to therapies (12%) followed by psychology and psychiatry referrals (5%), with both referral categories becoming increasingly common over time. Imaging trends were stable during the time period, with MRI at 6% and HCT at 0.2%. NSAIDs were the most prescribed medication class (39%), followed by opiates (30%). Over 2010-2019, opiate prescribing declined, with an increase in the prescription of NSAIDs, SSRIs, SNRIs and acetaminophen. NSAIDs were most prescribed in the 10-18yo bracket (37%), followed by opiates (34%). In the under 10 population, ondansetron was most likely to be prescribed (25%) followed by NSAIDS (21%).

CONCLUSIONS: Provider referral and prescribing trends are suggestive of increasing recognition of the link between mental health and concussion recovery. There is decreasing but still widespread use of opiates, including in the pediatric population.

KEYWORDS: Traumatic Brain Injury, Practice Parameters

290. Streamlining pediatric neurology care for children with abusive head trauma through a clinical pathway and multidisciplinary clinic

Messer R (Aurora, CO), Madison C, Graber S, Connery A

OBJECTIVE: Children with abusive head trauma (AHT) benefit from pediatric neurology care due to a high risk of early post-traumatic seizures (EPTS) and later post-traumatic epilepsy (PTE). In 2015, neurology providers began participating in the multidisciplinary Nonaccidental Brain Injury Care Clinic (NABICC), which provides longitudinal follow-up with rehabilitation medicine, neuropsychology, neurosurgery, child protection, therapies, and social work. In addition, the traumatic brain injury clinical pathway was updated to include neurology consultation during hospital admission.

METHODS: We utilized a retrospective database of 382 patients admitted with AHT in 2012-2020, with follow-up data through March 2023 for 266 patients seen in NABICC. Patients were divided into an early cohort admitted 2012-2015 (n=150) and a later cohort admitted 2016-2020 (n=232), based on neurology inclusion in NABICC.

RESULTS: For the entire cohort, the median age at admission was 5.1 months. EEG was obtained for 70%(268/382), with EPTS in 44%(117/268). Between the two cohorts, neurology consultation during the admission increased from 49%(73/150) to 66%(153/232). Of the early cohort patients, 27%(26/87) were eventually seen by neurology within NABICC, which increased to 72%(129/179) in the later cohort. Post-traumatic epilepsy developed in 12% of all NABICC patients (31/266), including infantile spasms, myoclonic seizures, and tonic seizures. In the early cohort, only 54%(7/13) received their epilepsy care through NABICC, compared to 100%(18/18) of the later cohort.

CONCLUSIONS: Our efforts brought pediatric neurology expertise to more inpatients and consolidated outpatient neurology care into a longitudinal, multidisciplinary clinic. Next, we will evaluate whether streamlining neurology involvement improves time to epilepsy diagnosis and neurodevelopmental outcomes.

KEYWORDS: Traumatic Brain Injury, Neurocritical Care, Epilepsy

291. Opportunities for CAARE to Optimize Pediatric Concussion Management in Primary Care Settings

Baham M (Irvine, CA), Rhivera R, Aijaz A, Harris M, Kim G, Pearson R, Taylor Lucas C

OBJECTIVE: Primary care providers (PCPs) are often the first medical professionals to assess pediatric concussion patients. However, gaps in concussion knowledge and referral practices exist amongst front-line providers. We aimed to characterize the attitudes and practices of PCPs to inform the development of a quality improvement (QI) project designed to improve pediatric concussion care.

METHODS: Cross-sectional analysis of PCPs in Orange County, CA. Responses were obtained using an electronically distributed 22-item UC Irvine Concussion Clinical Awareness, Assessment, and Referral Equity (CAARE) QI Questionnaire developed by an interdisciplinary team including a pediatrician and pediatric neurology concussion specialist.

RESULTS: 36 PCPs completed the survey. 16 (44.4%) providers indicated they had previously referred to a subspecialty concussion clinic. Of the 20 (55.6%) who had not referred, 14 (73.7%) indicated they did not know such clinics existed. Most respondents indicated they were somewhat (14, 38.9%) or quite (13, 36.1%) confident in diagnosing concussion. However, in determining when to clear a patient for return to play (RTP), many providers indicated they were not at all confident (10, 27.8%) or only slightly (11, 30.6%) to somewhat (11, 30.6%) confident.

CONCLUSIONS: Our findings suggest that there are gaps in concussion knowledge. Inadequate knowledge of proper RTP guidelines may contribute to prolonged concussion recovery. Moreover, some patients who may benefit from care in a Concussion Clinic may not be receiving this care due to lack of knowledge of such resources. These findings indicate that PCPs in Orange County may benefit from further evidence-based concussion education.

KEYWORDS: Traumatic Brain Injury, Diversity, Equity, Inclusion, Education

292. Return to School Following Severe Traumatic Brain Injury

Dahlson N (Cincinnati, OH), Broomall E

OBJECTIVE: Recent studies show the difficulties children face in returning to school following a mild traumatic brain Injury. However, no similar data exists for children with severe traumatic brain injury (sTBI), despite their more extensive rehabilitation needs and comparatively prolonged recovery course. Returning to school full time is identified by families as an important outcome for a satisfactory recovery. This case series highlights barriers to return to school following sTBI and suggests a framework for studying and overcoming them.

METHODS: A retrospective chart review was conducted, focusing on patients with sTBI seen in follow up. Charts were reviewed for potential predictors of the time to return to school including hospital course, neuropsychological evaluations, prior school evaluations, and demographics.

RESULTS: A series of cases outlining 3 teenagers timeline for returning to school following sTBI are presented. Preliminary data from these cases identify possible factors including socioeconomic stressors, prior school performance and physical needs as barriers to returning to school fulltime. Results show that multidisciplinary evaluations are helpful to assess for potential barriers and offer therapeutic interventions; however, there is no standardized method of predicting time to return to school.

CONCLUSIONS: These cases highlight obstacles including socioeconomic stressors, prior school performance and physical needs faced by patients returning to school fulltime after sTBI. Further studies of a larger population in multidisciplinary follow up clinic are underway to help identify important risk factors during hospitalization for difficulties returning to school. The overall aim is to have a proactive approach to accelerated school re-entry.

KEYWORDS: Traumatic Brain Injury, Education, Neurocritical Care

293. Use of Acute Clinical Indicators as Determinants of Neurodevelopmental Outcome in Infants with Head Trauma: A Retrospective Chart Analysis

Morgan V (Houston, TX), Sarpong K, Oikeh M, Record S, Risen S

OBJECTIVE: While developmental outcomes are reported to be worse in infants with abusive head trauma (AHT) compared to accidental (ACC) etiologies, inpatient providers have insufficient information to predict long-term developmental outcomes. The primary aim is to describe acute clinical conditions in children with AHT and ACC; secondarily, this study explores the relationships between these clinical variables and developmental outcome.

METHODS: This is a retrospective chart review of 60 children (birth-5 years) with AHT (25) or ACC (35) admitted to a large tertiary children's hospital, seen acutely by the child protection team, and subsequently evaluated in the child head injury clinic with validated developmental testing. Spearman's rho and point-biserial correlation coefficient analyses evaluate the associations between acute clinical variables and developmental outcomes.

RESULTS: Of infants admitted with head trauma, ACC is associated with specific acute clinical signs (lack of retinal hemorrhages, negative skeletal survey, no cutaneous injuries, absence of subdural hematoma) and less severe brain injury (shorter length of stay, shorter intubation time, higher Glasgow Coma Score, normal EEG, fewer seizures, and shorter duration of seizures). In addition to more severe acute injury, AHT resulted in significantly lower developmental quotients across all domains.

CONCLUSIONS: This study highlights that children with AHT have longer hospitalizations, more severe brain injury, and worse overall developmental outcomes than children with ACC. Given the potential for neuroplasticity following pediatric brain injury and the high risk for developmental delays, children with AHT require consistent neurodevelopmental monitoring and should receive intensive, comprehensive, and prompt therapy services following injury.

KEYWORDS: Traumatic Brain Injury, Neurodevelopmental Disorders

294. Soccer-related concussion in children and adults over the past 10 years: a systematic review

Castillo P (Boston, MA), Beletanga M, Restrepo-Rodas G, Benitez D, Perez A, Torres A

OBJECTIVE: It is understood that soccer is the most popular sport worldwide. With its increasing popularity, concussions have increased dramatically as they decrease broadly across other sports. Our goal is to analyze existing data and consolidate knowledge of soccer related concussions over the past 10 years.

METHODS: A systematic review of available literature including studies with children and adults diagnosed with soccer-related concussions published between 2013-2023 was conducted. From 1,210 published studies, 45 met our inclusion criteria.

RESULTS: The USA has the largest number of published studies followed by the United Kingdom, Canada and Australia. Soccer-related concussions were more frequent in females (58%). A higher number of concussions have been reported in midfielders, and the most common mechanism is player-to-player. Certified athletic trainers were the first to diagnose within the first 24 hours. About 42% of the studies included a neurological evaluation, 16% SCAT (post-concussive symptom questionnaire) and 11% ImPACT evaluation. Approximately 9% required hospitalization and only one player required surgical intervention. At the time

concussion was reported, confusion, dizziness, and amnesia were also reported. However, after the concussion, headaches and dizziness were prevalent. Follow-up data was included on 36% of the studies. On average, children missed 15 practice days, and returned to school in 8 days.

CONCLUSIONS: We concluded that midfielders are more commonly affected and the most common mechanism of injury is player to player. There is clear evidence of the absence of proper neurological evaluation post-concussion on the field including follow-up. Future research is suggested to focus on LMICs countries.

KEYWORDS: Traumatic Brain Injury, Global Neurology, Headache

LATE BREAKING

295. Long-term efficacy and safety of elivaldogene autotemcel (eli-cel) gene therapy: an integrated analysis of 67 patients with cerebral adrenoleukodystrophy (CALD)

Eichler F (Boston, MA), Duncan C, Kühl J-S, De Oliveira S, Thrasher A, Dalle J-H, Sevin C, Shah A, Locatelli F, Amartino H, Engelen M, Downey G, Dietz A, Orchard P, Williams D, Himal Thakar, Bluebird Bio, Inc.

OBJECTIVE: To describe recent long-term pooled efficacy and safety data from patients with CALD treated with eli-cel in ALD-102 (NCT01896102) and ALD-104 (NCT03852498).

METHODS: Boys age ≤17 with active CALD received eli-cel (autologous CD34+ cells transduced with ABCD1 cDNA-encoding Lenti-D lentiviral vector) after myeloablation. After 2 years in ALD-102/ALD-104, monitoring continued in LTF-304 (up to 13 years; NCT02698579).

RESULTS: As of February 1, 2023, median (min, max) follow-up among 67 enrolled patients was 39.8 (13.4, 106.9) months. The probability of survival free of major functional disability (MFD) at 36 months was 85%. At last assessment, 63/67 (94%) patients had a stable neurological function score (NFS; maintaining NFS ≤4 with ≤3-point increase from baseline), with 51/63 (81%) maintaining NFS <1. Loes score remained stable (score ≤9 or <6-point increase from baseline) in 60/67 (90%) patients. Gadolinium enhancement was resolved at last visit in 62/67 (93%) patients. Fourteen investigator-assessed eli-cel–related AEs occurred in 10/67 (15%) patients. Investigator-assessed eli-cel–related serious AEs were reported in 6 patients: myelodysplastic syndrome (MDS; n=3; plus 2 additional cases occurred after data cutoff), pancytopenia (n=2), disease progression (n=1; plus 4 additional patients had allogeneic hematopoietic stem cell transplant for reasons related to efficacy), and viral cystitis (n=1).

CONCLUSIONS: In ALD-102 and ALD-104, most patients achieved stable neurologic function without developing MFD. Safety was consistent with known effects of mobilization/apheresis and myeloablation. MDS associated with lentiviral vector–related insertional oncogenesis deserves particular attention. These data extend previous findings of eli-cel efficacy and safety.

KEYWORDS: Pediatric Demyelinating Disease, Neurometabolic, Experimental Therapeutics

296. Exploring the real-world performance of an artificial intelligence-based diagnostic device for autism: an aggregate analysis of early Canvas Dx prescription and output data

Shannon J (Seattle, WA), Taraman S, Liu-Mayo S, Salomon M, Seal M, Kraft C, Wall D

OBJECTIVE: Canvas Dx is the first FDA-authorized autism diagnostic device which utilizes a machine learning algorithm to aid healthcare providers in diagnosing or ruling out autism for children 18-72 months of age with concern for developmental delay.

The study goal was to measure performance of Canvas Dx in real-world settings through analysis of early post-market authorization prescription and output data.

METHODS: A de-identified aggregate data analysis of the initial 124 Canvas Dx prescriptions post-market authorization was conducted to determine: proportion of determinate device output (positive or negative for autism), key prescriber and patient characteristics. Cognoa performs algorithmic performance checks using two independent specialists who evaluate the Canvas Dx inputs and determine if autism is present based on DSM-5 criteria. When two specialists disagree, a third specialist is consulted, majority decision determines the clinical reference standard.

RESULTS: Children had a median age of 39.6 months and a 51.6% autism prevalence rate. Compared to the clinical reference standard, Canvas Dx had a NPV of 95.2% (20/21, 95% CI [76.2%, 99.9%]) and PPV of 94.4% (51/54, 95% CI [84.6%, 98.8%]) with 60.5% (75/124, 95% CI [51.3%, 69.1%]) receiving a determinate result.

CONCLUSIONS: In this analysis, the device provided highly accurate positive and negative outputs for autism that aligned with the specialist reference standard. Children were provided a positive output over 1 year earlier than the current median age of autism diagnosis in the United States. This finding highlights the potential of the device to support HCPs to act rapidly and allow for earlier autism diagnosis

KEYWORDS: Neurodevelopmental Disorders

297. Zatolmilast Ph2/3 program for Fragile X Syndrome - Study Design and Results of Part 1 in Adolescents

Berry-Kravis E (Chicago, IL), Skljarevski V, Kivel F, Pedapati E, Erickson C

OBJECTIVE: Zatolmilast (BPN14770) is a selective phosphodiesterase-4D allosteric inhibitor in development for fragile X syndrome (FXS). In a small Phase 2a study, zatolmilast improved cognition, daily function, and EEG biomarkers in adults with FXS. The objectives of the current study are to assess the efficacy and safety of zatolmilast in adolescents, and to establish the optimal clinical dose.

METHODS: This is a two-part study. Part 1 is an open-label safety and pharmacokinetics (PK) study of a single oral dose of zatolmilast 25 mg. Part 2 is a double-blind, placebo-controlled, efficacy study of 25 mg BID, for 13 weeks in 150 patients. Key entry criteria: male with full FXS mutation, age 12-18, <3 psychoactive medications, no major medical/psychiatric illnesses, stable pharmacological/behavioral treatment. Multiple novel efficacy measures are included, with cognition crystallized composite from the National Institutes of Health Toolbox Cognitive Battery as primary outcome.

RESULTS: In Part 1, 8 patients enrolled at 2 sites. All subjects completed the study with no adverse events. Average age was 13.9 years (12-16), average weight 57.4 kg (39.9-88.5). Mean Cmax was 362 ng/mL, mean time to maximum

concentration 2.1 hours, and mean AUC0-tlast 2101 h*ng/mL. Review of subject profiles determined the 2 lowest-weight subjects had Cmax 3x higher and AUC 25-50% higher than the 6 heavier subjects, indicating a need for weight-based dosing.
CONCLUSIONS: In Part 1 of this study, zatolmilast was safe and well-tolerated. The PK profile in adolescents was found to be weight-dependent, requiring weight-based dosing. Part 2 of the study is ongoing.
KEYWORDS: Neurodevelopmental Disorders

298. Adverse Childhood Experiences Are Associated with Seizures in Children: A Cross-Sectional Analysis

Shipley S (Philadelphia, PA), Anto M, Massey S, Szperka C

OBJECTIVE: We aim to (1) assess the relationship between adverse childhood experiences (ACE/ACEs) and epilepsy and (2) determine if specific ACEs are more strongly associated with an epilepsy or seizure disorder diagnosis.
METHODS: We performed a cross-sectional retrospective cohort analysis using population-based data from the 2018 and 2019 National Survey of Children's Health to examine ACE and their relationship to epilepsy in children. ACEs elicited in the survey included questions about experience of violence, household dysfunction, and food and housing insecurity. Adjusting for age, race, and income level, we utilized logistic regression to test the relationships between cumulative ACE score and current seizure disorder or epilepsy diagnosis, and to examine which specific ACEs were individually associated with current seizure disorder diagnosis.
RESULTS: The study population consisted of 59,963 participants; 52.2% female and 47.8% male. Participant ages ranged from 0 to 17 years, and 69.2% identified as White. A current diagnosis of epilepsy or seizure disorder was reported in 377 participants (0.63%), and 22,749 participants (37.9%) had one or more ACE. As the number of ACEs increased, odds of current epilepsy or seizure disorder diagnosis increased by 1.14 (95% confidence interval 1.07–1.22). Five ACE exposures demonstrated a high association with a current diagnosis of epilepsy or seizure disorder: food/housing insecurity, witnessing domestic violence, household mental illness, neighborhood violence, and parent/guardian incarceration.
CONCLUSIONS: Multiple ACE exposures were individually associated with reporting a diagnosis of epilepsy or seizure disorder. An increase in cumulative ACE exposures increased odds of having current diagnosis of epilepsy or seizure disorder.
KEYWORDS: Epilepsy, Lifespan Manifestations of Childhood Onset Conditions, Diversity, Equity, Inclusion

299. A Functionally Uncharacterized, Novel GRIA2 Variant: Advances in Targeted Epilepsy Management

Philliben R (Salt Lake City, UT)

OBJECTIVE: To present an infant with a novel GRIA2 variant resulting in intractable epilepsy treated with perampanel who saw markedly decreased seizures.
METHODS: A rare genetic epilepsy treated with a targeted therapeutic approach is presented.
RESULTS: A 3-week-old term male presenting for fussiness was found to have focal seizures arising from >2 regions on EEG during initial hospitalization. Workup including brain MRI and Invitae Epilepsy Panel were unremarkable. The following month he trialed multiple ASMs without improvement requiring lengthy hospitalizations for increasing seizure frequency. Trio Genome Sequencing at 2 months of age identified a novel de novo heterozygous likely pathogenic variant in GRIA2. He was then clinically seizing 30-50 times daily with concordant developmental delays and perampanel was added to his ASMs. As a novel variant, it could not be confirmed quickly whether this caused a gain or loss-of-function variant in the GLUA2 channel. The dosage was titrated slowly to monitor for further increasing seizure frequency. Following titration he saw markedly decreased seizure burden with multiple seizure-free weeks and developmental progress.
CONCLUSIONS: This supports that perampanel provides therapeutic benefit to a subset of patients with GRIA2 variant epilepsy. It is also significant that the function of this variant was unknown at the time of medication initiation. In rare, progressive diseases awaiting analyses of variant modeling to determine function may not be practical. This case demonstrates an alternative by administering low medication doses with close observation and increasing therapeutically in patients with novel variants. Molecular modeling is currently in progress to investigate this variant further.
KEYWORDS: Epilepsy, Neurogenetics, Experimental Therapeutics

300. Glymphatic dysfunction coincides with lower GABA levels and sleep disturbances in succinic semialdehyde dehydrogenase deficiency

Tokatly Latzer I (Boston, MA), Yang E, Afacan O, Arning E, Rotenberg A, Lee H, Roullet J-B, Pearl P

OBJECTIVE: Succinic semialdehyde dehydrogenase deficiency (SSADHD) is an inherited metabolic disorder of γ-aminobutyrate (GABA) catabolism. Cerebral waste clearance along glymphatic perivascular spaces depends on aquaporin 4 (AQP4) water channels, the function of which was shown to be influenced by GABA. Sleep disturbances are associated independently with SSADHD and glymphatic dysfunction. This study aimed to determine whether indices of the hyperGABAergic state characteristic of SSADHD coincide with glymphatic dysfunction and sleep disturbances and to explicate the modulatory effect GABA may have on the glymphatic system.
METHODS: The study included 42 individuals (21 with SSADHD; 21 healthy controls) who underwent brain MRIs and magnetic resonance spectroscopy (MRS) for assessment of glymphatic dysfunction and cortical GABA, plasma GABA measurements, and circadian clock gene expression. SSADHD subjects responded to an additional Children's Sleep Habits Questionnaire (CSHQ).
RESULTS: Compared to the control group, SSADHD subjects did not differ in sex and age but had higher severity of enlarged perivascular spaces in the centrum semiovale ($p<0.001$), basal ganglia ($p=0.01$), and midbrain ($p=0.001$),

as well as higher MRS-derived GABA/NAA peak (p<0.001). Within the SSADHD group, the severity of glymphatic dysfunction was specific for a lower MRS-derived GABA/NAA (p=0.04) and lower plasma GABA (p=0.004). Additionally, the degree of their glymphatic dysfunction correlated with the CSHQ-estimated sleep disturbances scores (R=5.18, p=0.03). In the control group, EPVS burden did not correlate with age or cerebral and plasma GABA values.

CONCLUSIONS: The modulatory effect that GABA may exert on the glymphatic system has therapeutic implications for sleep-related disorders and neurodegenerative conditions associated with glymphatic dysfunction.

KEYWORDS: Neurometabolic, Neuroimaging, Sleep

301. Acute Treatment of Migraine in Pre-Adolescents: Real-World Analysis of Remote Electrical Neuromodulation (REN)

Stark-Inbar A (Netanya, Israel), Werner K, Gerson T, Shmuely S, Ironi A, Rao R

OBJECTIVE: Migraine is a prevalent neurological disorder that severely impacts both children and adolescents, causing significant disability. However, only a single pharmacological treatment is approved for ages 6-12 years, and thus other treatments are often prescribed off-label, despite limited efficacy and low tolerability they may have, beyond parental concern regarding prescription medications. Remote Electrical Neuromodulation (REN) is a nonpharmacological, prescribed, wearable device, FDA-cleared for acute and/or preventive treatment of migraine with or without aura in patients 12 years or older. Multiple studies have shown that REN has high safety, tolerability, and efficacy in adults and adolescents. This study aims to evaluate REN's real-world safety and efficacy in pre-adolescents, 9-11 years old.

METHODS: Prospective data on pre-adolescent users who used REN at least once was collected through the REN device (Nerivio®) smartphone application. Device safety was measured using an adverse event tracking system. Efficacy was measured in patients who voluntarily reported prospective migraine symptoms at treatment onset and at 2-hours later.

RESULTS: The study included 26 pre-adolescents (69.2% female) with a mean (± SD) age of 11.04 ± 0.55. No adverse events were reported by these patients. Post 2-hour pain relief and pain freedom in the first REN treatment were achieved by 50% (6/12) and 40% (6/15) of patients, respectively. Consistent pain relief and pain freedom in at least 50% of the treatments were achieved by 75% (6/8) and 50% (4/8) of patients, respectively.

CONCLUSIONS: Providers seeking a safe and effective treatment option for pre-adolescents suffering from migraine may consider REN.

KEYWORDS: Headache

302. Eladocagene exuparvovec gene therapy improves motor development in patients with aromatic L-amino acid decarboxylase deficiency

Hwu P (Taipei, Taiwan), Sierra J, Chien Y-H, Lee N-C, Wang A, Turna J, Penematsa V, Golden L, Tai C-H

OBJECTIVE: Aromatic L-amino acid decarboxylase deficiency (AADCd) is caused by pathogenic variants in the DOPA decarboxylase gene and is characterized by delayed or failed motor development. We report long-term efficacy and safety of eladocagene exuparvovec gene therapy in three open-label, single-arm trials (AADC-CU/1601 [n=8], AADC-010 [n=10], and AADC-011 [n=12]; data cut-off: June 16, 2023).

METHODS: Thirty children with AADCd aged 19–102 months received eladocagene exuparvovec via bilateral intraputaminal infusion. The primary efficacy analysis assessed motor milestones using the Peabody Developmental Motor Scale 2nd edition, and included head control (partial/full), sitting (assisted/unassisted), standing (with/without support) and walking (with assistance, to toy and up stairs). Motor milestones were measured every 3 months for 1 year following gene therapy and every 6–12 months thereafter. Safety was also assessed.

RESULTS: Patients were followed up for up to 127 months. At baseline, no patients had mastered head control or more advanced milestones. At Year 1, patients were developing the following skills (n): partial head control (26), full head control (15), sitting unassisted (7) and standing with support (2). By Year 5, patients were developing more advanced milestones (n): full head control (24), sitting unassisted (21), walking with assistance (8), walking to toy (7) and walking up stairs with support (4). The most common treatment-emergent adverse events (>50% patients) were pyrexia (100%), dyskinesia (86.7%), upper respiratory tract infection (70.0%), pneumonia (63.3%), gastroenteritis (60.0%) and upper gastrointestinal hemorrhage (53.3%).

CONCLUSIONS: Eladocagene exuparvovec had a durable, positive impact on motor development in patients with AADCd, with an acceptable safety profile.

KEYWORDS: Neurodevelopmental Disorders, Neurometabolic

303. Efficacy of Outpatient Infusion Therapy for Abortive Treatment of Status Migrainosus Using Normal Saline, Prochlorperazine, Ketorolac and As Needed Valproic Acid.

Kaufman J (Washington, DC), McCracken E, Dickey C, Langdon R, DiSabella M, Strelzik J

OBJECTIVE: An estimated 587,000 US children suffer status migrainosus annually. While infused saline, prochlorperazine, ketorolac, and valproic acid are effective status migrainosus treatment in adults, limited data exists in pediatrics. This study aims to evaluate pediatric status migrainosus response to outpatient infusion therapy.

METHODS: Patients requiring outpatient infusion completed surveys immediately pre-infusion and post-infusion. Infusion protocol Phase-1 included intravenous normal saline (20ml/kg, maximum=1L), ketorolac (0.5mg/kg, maximum=30mg), and prochlorperazine (0.15mg/kg, maximum=10mg). Persistently symptomatic patients received Phase-2: intravenous valproic acid (20mg/kg, maximum=1000mg). Pre-infusion surveys queried headache characteristics, pain score, therapies failed, past head injury, school missed in past week, and patient-defined post-infusion pain goal. Post-infusion surveys queried current pain level and migraine symptoms.

RESULTS: Patients included 14 females and 3 males, ages 6-19 (median=15.9YO), with median migraine duration 11 days and median home medications failed 3. Median pain was 7 (SD=1.93) pre-infusion and 2 (SD=2.31) post-infusion out of 10. All patients met patient-defined post-infusion pain goals from pre-infusion surveys. Median pain reduction in recipients of only Phase-1 was 4.75 (SD=1.22, n=8) and in those requiring Phase-2 was 6 (SD=2.60, n=11). Photophobia resolved in 60% (N=15), phonophobia resolved in 70% (n=10), and nausea resolved in 83% (n=6) of patients with those symptoms. An inverse relationship exists between pain relief and age (P=0.038) and home medication trials (P=0.017). No correlation was found between pain reduction and migraine duration, home abortive medication trials, or pain location.

CONCLUSIONS: Outpatient pediatric infusion with normal saline, ketorolac, prochlorperazine and as needed valproic acid reduces pain, photophobia, phonophobia, and nausea in status migrainosus.

KEYWORDS: Headache, Experimental Therapeutics, Practice Parameters

304. Clinical Phenotypes and Biomarkers of ASH1L-related Autism and Epilepsy

Papendorp C (Providence, RI), Kavanaugh B, Nie D, Best C, Liu JS

OBJECTIVE: ASH1L is a highly penetrant gene associated with neurodevelopmental disease (NDD), epilepsy, autism, and intellectual disability. Despite the clear link between ASH1L mutations and NDD, ASH1L-related NDD is poorly understood because longitudinal clinical characterization of humans with ASH1L-related NDD has never been done.

METHODS: The design of this study is a prospective observational natural history study. Participants receive neuropsychological testing to measure autism, adaptive functioning, and intelligence. We perform a full neurological examination. Participants also undergo electroencephalography to detect seizures and measure resting-state brain rhythms. Along with the measures performed during study visits, we review past medical records.

RESULTS: While ASH1L has been described as an autism-associated gene, not all children in our study meet diagnostic criteria for autism. About 50% of children (8/17) had seizures. EEGs show ~3Hz generalized activity characteristic of absence epilepsy. Possible sex differences exist in the prevalence of autism and epilepsy between boys and girls with ASH1L mutations, with girls more likely to have epilepsy without autism and boys more likely to have autism without epilepsy.

CONCLUSIONS: This study is the first ever to define the clinical phenotype of children with ASH1L mutations. This study will help families know what to expect when their child is diagnosed with a mutation in ASH1L. Baseline natural history data will pave the way for investigational drug trials to improve the lives of these children. Finally, understanding which symptoms families find most difficult will allow researchers to prioritize research into those symptoms and select the best outcome measures for future clinical trials.

KEYWORDS: Neurodevelopmental Disorders, Neurogenetics, Epilepsy

305. Structural brain abnormalities detected by Magnetic Resonance Imaging in Spinal Muscular Atrophy

Groulx-Boivin E (Montreal, QC, Canada), Oliveira-Carneiro A, Carlson H, Floer A, Kirton A, Mah J, Saint-Martin C, Oskoui M

OBJECTIVE: Brain involvement in spinal muscular atrophy (SMA) is severely understudied. We aimed to characterize structural brain abnormalities detected by magnetic resonance imaging (MRI) in individuals with SMA.

METHODS: We conducted a cross sectional case-control study of children and young adults with a confirmed genetic diagnosis of 5q SMA, and peer controls matched by age and sex. Brain MRIs acquired through a standardized protocol were reviewed to identify structural changes. Demographic and clinical variables, including SMN2 copy number and motor function (Hammersmith Functional Motor Scale Expanded and Revised Upper Limb Module scores), were then assessed for correlation with neuroimaging findings.

RESULTS: A total of 41 participants completed the study procedures (mean age 17.4, range 7-40; 66% male). Of 21 individuals with 5q SMA, 8 (38%) had structural brain abnormalities identified on MRI compared to 1/20 (5%) of peer controls (odds ratio 11.7, 95% confidence interval 1.6-79.6). The most common structural changes were widening of the arachnoid spaces and ventriculomegaly. Among individuals with SMA, structural brain abnormalities were more frequent in those with 2 SMN2 copies (3/5, 60%) compared to 3 or 4 SMN2 copies (3/10, 30% and 2/6, 33% respectively). We found no association between the frequency of structural changes and motor function.

CONCLUSIONS: Individuals with SMA have higher rates of structural brain abnormalities than their typically developing peers, suggesting central nervous system involvement in SMA. Understanding changes in the brain architecture of the SMA population can inform the development of adjunct therapies targeting the central nervous system.

KEYWORDS: Neuromuscular, Neuroimaging

306. Epitope-level profiling in children with mitochondrial disease reveals limitations in the antibacterial antibody repertoire

Gordon-Lipkin E (Bethesda,MD), Banerjee P, Thompson E, Kruk S, Marin Franco J, McGuire P

OBJECTIVE: Mitochondrial diseases (MtD) are genetic disorders defined by deficits in the structure and function of mitochondria, resulting in ineffective oxidative phosphorylation (OXPHOS) and translating to multisystemic disease, frequently affecting the nervous system. Children with MtD may experience neurologic decline with infection, and the role that the immune system plays in this phenomenon is incompletely understood. In this study, we aimed to define the humoral immunophenotype in MtD.

METHODS: We performed extracellular flux analysis on lymphoblastoid B cell lines from children with MtD and

controls (N = 4/group). We conducted a cross-sectional multiplex serology study of the antibacterial antibody repertoire in children with MtD (N = 16) and controls (N = 16) using phage display and immunoprecipitation sequencing (PhIPseq). The PhIPseq library contained >3000 peptides covering > 150 species of bacteria that infect humans.
RESULTS: B cell lymphoblastoid cell lines from MtD displayed depressed baseline oxygen consumption, ATP production and reserve capacity. Characterization of the bacterial exposome revealed comparable bacterial species between groups, mostly Streptococcus and Staphylococcus. By interrogating the antibacterial antibody repertoire, we found that MtD had less robust antibody fold changes to common epitopes. We also found MtD failed to show a direct relationship between the number of bacterial epitopes recognized and age, unlike controls.
CONCLUSIONS: OXPHOS deficiency extends to B cells in children with MtD, leading to limitations in the antibacterial antibody repertoire. The timing of bacterial exposures was asynchronous, suggesting different periods of increased exposure or susceptibility. Overall, the antibacterial humoral response is distinctive in children with MtD.
KEYWORDS: Neuroimmunology, Neurometabolic, Neurogenetics

307. Remote Electrical Neuromodulation (REN) for acute treatment of migraine in adolescents suggests preventive benefits

Monteith T (Miami, FL), Stark-Inbar A, Shmuely S, Harris D, Ironi A, Kalika P, Irwin S

OBJECTIVE: Migraine is the most common disabling headache in adolescents. However, only a very limited number of pharmacological treatments are available for migraine prevention in adolescents. Remote Electrical Neuromodulation (REN) Nerivio device is a non-pharmacological acute and/or preventive treatment of migraine with or without aura for patients ≥ 12 years. This real-world study aimed to assess preventive benefits measured by change in monthly treatment days following frequent use of REN for acute treatment of migraine in adolescents.
METHODS: Prospective data was collected through the Nerivio smartphone application from adolescent patients who acutely treated their migraine attacks with REN on at least 10 days in their first month of Nerivio usage, and at least 3 days in each of the subsequent 2 months. The change in number of treatment days per month was used as a proxy measure for the number of monthly migraine days.
RESULTS: Eighty-three patients were included in the analysis (average ± SD age 15.9 ± 1.3 years). Results demonstrate a significant reduction in mean REN treatment days from 12.6 (±3.2) treatment days in the 1st month, to 9.0 (±4.8) treatment days in the 2nd month of consecutive use ($p<0.001$), and down to 7.4 (±4.2) treatment days in the 3rd month of consecutive use ($p<0.001$).
CONCLUSIONS: Frequent use of REN for the acute treatment of migraine was shown to reduce the number of monthly treatment days in adolescents, suggesting potential preventive benefit in this age group, similar to what was seen in a pivotal prevention trial with adults.
KEYWORDS: Headache

308. Diagnosis and Information Management of Dravet Syndrome in Recently Diagnosed Pediatric Patients: Results From a Dravet Syndrome Foundation Caregiver Insight Survey

Wilkinson A (Emeryville, CA), Kaye D, Hood V, Meskis M, Bailey L, Burns R, Lothe A

OBJECTIVE: Dravet syndrome (DS) is a rare, lifelong, developmental and epileptic encephalopathy characterized by high seizure burden, multiple comorbidities, and reduced quality of life. To gain additional insight into unique challenges with early diagnosis of DS, caregivers were surveyed.
METHODS: The Caregiver Insight Survey was distributed via DS Foundation (DSF) Family Network e-blast and social media to caregivers of children ≤4 years of age diagnosed with DS. The survey included 27 multiple choice questions and 9 open-text response questions. Topics included demographics, age at symptom onset/diagnosis, health care provider (HCP) information, sources of DS information, and communication preferences. Descriptive analysis was used.
RESULTS: The survey was distributed to 352 caregivers; 73 (20.7%) responded. Most caregivers (89%) were millennials (25-44 years); 65 (89%) were mothers. Mean age at symptom onset was 5 months (range, 1-11); mean age at DS diagnosis was 12 months (range, 2-32). Change (≥1 occurrence) in pediatricians (36%) and neurologists/epileptologists (71%) was most commonly due to clinical expertise (51%) and trust (30%). Caregivers sought out information using Google/search engines (82%), the DSF website (81%) or Facebook DSF caregiver support groups (68%), from HCPs (64%), and via DSF social media updates (51%).
CONCLUSIONS: Results from this survey indicate these patients were diagnosed with DS an average of 7 months after symptom onset. Despite early connections and resources, caregivers feel overwhelmed when receiving a DS diagnosis. They often seek out information online and from trusted patient advocacy groups and support groups as they may not receive information from their HCPs.
KEYWORDS: Epilepsy

309. PREVeNT trial results: Epilepsy and neurocognitive outcomes in infants with tuberous sclerosis complex

Porter B (Palo Alto, CA), Study Group PREVeNT

OBJECTIVE: Does treatment with vigabatrin in infants with tuberous sclerosis complex (TSC) prior to epilepsy onset improve neurocognition and prevent the development of epilepsy.
METHODS: Infants with TSC less than 6 months of age were enrolled and followed with serial EEGs to 24 months of age. Vigabatrin or placebo was initiated at the time of first epileptiform EEG. The primary outcome was the Bayley-III cognitive assessment score at 24 months. Secondary outcomes: prevalence of drug resistant epilepsy, and vigabatrin safety.

RESULTS: Eighty-four infants were enrolled, 12 were screen failures, four went straight to open label vigabatrin, and 12 were not randomized (normal EEG throughout). 56 were randomized to early vigabatrin (n=29) or placebo (n=27). 19 of 27 in the placebo arm transitioned to open label vigabatrin with a median delay of 44 days after randomization. Bayley-III cognitive scaled scores at 24 months were similar for participants randomized to vigabatrin or placebo. No significant differences were found between groups in the overall incidence of epilepsy or drug resistant epilepsy at 24 months. However the overall incidence of infantile spasms and time to onset after randomization of spasms was later in the vigabatrin treatment group. Adverse events were similar across groups.
CONCLUSIONS: Preventative treatment with vigabatrin based on EEG epileptiform activity prior to seizure onset does not improve neurocognitive outcome at 24 months in TSC; nor delay onset or lower the incidence of focal seizures and drug resistant epilepsy at 24 months. Preventative vigabatrin was associated with later onset and lower incidence of infantile spasms.
KEYWORDS: Epilepsy, Neuro-Cutaneous Disorders, Experimental Therapeutics

310. NGN-401: A Novel Regulated Gene Therapy for Rett Syndrome

Jaggumantri S (New York, NY), Burstein S, Ross P, Gadalla K, Selfridge J, Hector R, Thomson S, Biezonski D, Benito J, Albanis E, Patroneva A, Cobb S

OBJECTIVE: Rett syndrome (RTT) is an X-linked disorder caused by mutations in the MECP2 gene that lead to deficiency of the methyl cytosine binding protein 2 (MeCP2). Conventional gene therapy for RTT is faced with the challenge that MECP2 is a dosage sensitive gene, with both animal studies and the human duplication disorder suggesting that MeCP2 levels need to be kept within a narrow range to avoid toxicity associated with overexpression.
METHODS: Neurogene developed NGN-401 which uses EXACT transgene regulation technology designed to deliver targeted levels of MeCP2 and avoid toxicity from overexpression. NGN-401,containing the full-length MECP2 transgene in an AAV9 vector, is administered intracerebroventricularly (ICV) to maximize vector distribution to key brain areas.
RESULTS: Preclinical animal studies show NGN-401 delivers safe and efficacious levels of MeCP2, rescuing functional phenotypes without toxicity. In nonhuman primates, NGN-401 was well-tolerated at >4x the clinical dose and showed broad biodistribution. In contrast,an unregulated vector resulted in higher and more variable mRNA levels and in 2 animals,an adverse effect on sural nerve conduction was reported.
CONCLUSIONS: The safety data from preclinical models supported an FDA IND clearance to initiate a Phase1/2 study of NGN-401. RTT-200 is a phase 1/2, open-label study designed to assess the safety, tolerability, and efficacy of a single dose of NGN-401 administered via ICV delivery,in female pediatric subjects with typical RTT. Safety will be assessed by monitoring adverse events and changes in physical, neurological,and laboratory values. Exploratory efficacy will be evaluated using clinician and caregiver administered assessments,as well as objective assessments of key symptoms.
KEYWORDS: Experimental Therapeutics, Neurodevelopmental Disorders

311. Mitochondrial dysfunction due to mRNA transport defects as a mechanism of pediatric neurodegeneration? Unraveling the role of TBCK in a human neuronal model

Ortiz-Gonzalez X (Philadelphia, PA), Flores-Mendez M, Tintos-Hernandez J, Ramos-Rodriguez L

OBJECTIVE: Biallelic variants in the TBCK gene cause a pediatric-onset, severe neurodegenerative disorder. The underlying mechanisms for selective neuronal vulnerability remain unclear as the physiologic function of the TBCK protein is poorly understood.
METHODS: We generated iPSC-derived neurons from patients homozygous for the Boricua (p.R126*) variant as a novel disease model. We examined the effects of TBCK-deficiency in induced cortical forebrain neurons (iNeu) relative to healthy controls; in assays including neuronal survival, morphology, mitochondrial respiration and ATP production. Unbiased comparative proteomics and protein-protein interaction analysis were performed in human iNeu. Microfluidic chambers were used to examine compartment-specific phenotypes(soma vs axonal) in human neurons.
RESULTS: We found TBCK-deficient neurons exhibit limited survival and aberrant morphology at DIV14. We also found significantly reduced levels of mitochondrial DNA, reduced maximal respiratory capacity and mitochondrial ATP production. Protein interactome analysis revealed TBCK binds to 3 proteins (PPP1R21, C12orf4, Cryzl1), which form a novel mRNA transport complex. Our data suggest a novel subcelluar localization for TBCK protein, along endolysosomal vesicles. Furthermore, we find TBCK can co-localize with mRNA, consistent with a role in neuronal mRNA transport. We found that axonal mRNA levels are reduced relative to the soma in TBCK-deficient iNeu.
CONCLUSIONS: Our data supports TBCK protein functions in neuronal endolysosomal-mediated mRNA trafficking. We propose that TBCK-deficiency may lead to impaired transport of mRNA transcripts, including nuclear-encoded mitochondrial transcripts, which may preferentially impact polarized cells such as neurons. Therefore, our data support an expanding role of mRNA transport defects as contributors to neurodegeneration across the age spectrum.
KEYWORDS: Neurogenetics, Neurodevelopmental Disorders, Early Stage Investigator

312. Electroconvulsive Therapy in New Onset Refractory Status Epilepticus (NORSE) in a Pediatric Patient

Eberhard S (Whitestown, IN), Sun F, Hanson A, Walsh L, Jackman C, Maue D, Pablo X, Kyrychenko L, Conroy S

OBJECTIVE: NORSE refers to new onset refractory status epilepticus in patients without known epilepsy or seizure etiology. Electroconvulsive therapy (ECT) has been occasionally

used, but rarely in children. We report a previously healthy 8-year-old female with NORSE whose epileptic burden improved with aggressive therapies including ECT.

METHODS: Our patient presented with a week of headaches and fever before developing multiple focal seizures that rapidly evolved into RSE. Extensive infectious, autoimmune, metabolic, neoplastic, and genetic workup was unrevealing. Sequential brain MRIs remained normal. Aggressive antiseizure medications (ASMs), pentobarbital coma, high-dose propofol and ketamine infusions, pulse-dose steroids, IVIg, ketogenic diet, cannabidiol, and rituximab were initiated during her first 12 hospital days. Despite these measures, EEG remained highly epileptic prior to ECT initiation on day 12. ECT was performed daily for 7 days with two stimulations per session using a Thymatron device with bitemporal electrode placement.

RESULTS: ECT achieved seizures lasting between 7-19 seconds in all treatments with median post-ictal suppression of 70.5%, indicating good seizure quality. All ASM infusions were weaned one day post-ECT completion with EEG showing decreased epileptic burden. A vagal nerve stimulator was placed on day 29 and soon after became completely seizure free.

CONCLUSIONS: Our 8-year-old with NORSE responded well to a 7-day course of ECT. Multiple ASMs and infusions failed to improve overall epileptic burden. The therapeutic effect of ECT is supported by robust seizure quality and timing of response, but limited by close succession of other treatments including rituximab, cannabidiol, phenobarbital, and ketosis.

KEYWORDS: Epilepsy, Neuroimmunology, Experimental Therapeutics

313. Cerliponase alfa for the treatment of CLN2 disease in a patient cohort including children <3 years old

de los Reyes E (Columbus, OH), Schulz A, Specchio N, Gissen P, Aylward S, Slasor P, Bondade S, Cohen-Pfeffer J

OBJECTIVE: Open-label studies demonstrated that biweekly intracerebroventricular (ICV) infusion of 300 mg cerliponase alfa slowed deterioration in motor and language function in children with CLN2 disease. Here, we report findings from a study to assess safety and efficacy of cerliponase alfa in an expanded cohort including children <3 years.

METHODS: Cerliponase alfa dosage was based on age. Safety was assessed by adverse event (AE) frequency. The primary efficacy endpoint was rate of decline in score on the motor and language (ML) domains of the CLN2 Clinical Rating Scale, comparing treated subjects with matched historical controls.

RESULTS: A total of 14 subjects were enrolled (8 female, 6 male). Mean (SD) baseline ML score was 4.6 (1.7); mean (SD) age at baseline was 3.1 (1.5) years (range: 1.1-6.0). Twelve subjects were matched to historical controls: mean (SD) rate of decline in ML score was 0.15 (0.24) points/48 weeks for treated subjects and 1.30 (0.86) points/48 weeks for controls (difference: 1.15; 95% CI: 0.80, 1.50). Among subjects <3 years at baseline (n=8), 7 had an ML score of 6 at baseline and at end of study. All subjects experienced ≥1 AE; the most common drug-related AEs were pyrexia and hypersensitivity.

CONCLUSIONS: Cerliponase alfa slowed decline in motor and language function in children with CLN2 disease, including those <3 years of age, with a safety profile consistent with prior studies. Additionally, results may suggest that early initiation of treatment can delay symptom onset.

KEYWORDS: Neurodevelopmental Disorders, Epilepsy, Movement Disorders

314. Outcomes Among Individuals With Dravet Syndrome Using Fenfluramine: A Retrospective Analysis Using US Claims Data

Jaganathan S (Smyrna, GA), Ems D, Sederman R, Chen C, Wu S

OBJECTIVE: Dravet syndrome (DS) is a rare and lifelong developmental epileptic encephalopathy marked by treatment-resistant seizures, significant developmental, motor, and behavioral impairments, and increased risk of mortality and sudden unexpected death in epilepsy. The objective of this analysis was to quantify the relationship between fenfluramine and seizure-related healthcare events using claims data following fenfluramine approval in June 2020 for the treatment of seizures associated with DS in the US.

METHODS: Komodo, a US healthcare claims database, was used to measure healthcare utilization, including rescue antiseizure medication (ASM) use and healthcare visits (ER, outpatient, neurology, and inpatient). Individuals with DS were identified by ICD-10 codes. Individuals with prior/concomitant use of cannabidiol or stiripentol were excluded. Claims for each metric were counted only with a seizure-related ICD-10 (G40.x). Primary outcomes were measured as percentage change 6 months prior to the first fenfluramine prescription claim ("Pre") to the first 6 months of continuous fenfluramine use.

RESULTS: The analysis included 108 individuals with DS with Pre data, of which 91 (84%) used fenfluramine continuously for ≥6 months. Of the 91 individuals, there was a 77% reduction in rescue ASM use ($p<0.001$). For healthcare visits, there was a 50% reduction in ER visits ($p=0.013$), 27% in outpatient visits ($p=0.009$), 24% in neurology visits ($p=0.07$) and 24% in inpatient hospitalizations ($p=0.39$).

CONCLUSIONS: Meaningful reductions in healthcare utilization were seen among individuals with DS treated with fenfluramine for ≥6 months. The 6-month persistency in fenfluramine use is high, suggesting efficacy and/or tolerability are also high.

KEYWORDS: Epilepsy

315. The development of the eIF2B activator ABBV-CLS-7262 as a potential treatment for Vanishing White Matter disease

Jeong A (North Chicago, IL), Malik P, Rosebraugh M, Han Y, Bellemin E, Serone A, Asundi J, Baruch A, Castro A, Cao C, Mohler E, Sidrauski C, Cho W

OBJECTIVE: Vanishing White Matter (VWM) disease is a rare leukodystrophy caused by recessive partial loss-of-

function mutations in any of the five genes encoding the subunits of eIF2B, a translation initiation factor that is essential for protein synthesis and is an effector of the integrated stress response (ISR). ABBV-CLS-7262 is a small molecule activator of eIF2B that stabilizes the complex and boosts its guanine nucleotide (GEF) activity including that of complexes carrying pathogenic VWM mutations. We describe preclinical and Phase 1 healthy volunteer results and describe a Phase 1b study of ABBV-CLS-7262 in VWM.

METHODS: A mouse model of VWM was generated to evaluate preclinical efficacy of ABBV-CLS-7262. Initial safety/tolerability, pharmacokinetics, and pharmacodynamics were explored in healthy volunteers.

RESULTS: ABBV-CLS-7262 rescues white matter loss and neuroinflammation, as well as motor deficits, in the mouse model of VWM. In healthy volunteers, ABBV-CLS-7262 was well-tolerated following dosing for up to 14 days. All adverse events were mild to moderate in severity. Cerebrospinal fluid drug concentrations were measured at levels predicted to activate eIF2B. After a single dose, ABBV-CLS-7262 increased eIF2B enzyme activity and suppressed the ISR in blood cells. A Phase 1b study, designed in consultation with the VWM Consortium, is currently assessing safety/tolerability, pharmacokinetics, and exploratory efficacy of ABBV-CLS-7262 in people with VWM (NCT05757141).

CONCLUSIONS: ABBV-CLS-7262 is being developed as a potential first-in-class treatment for VWM, supported by preclinical studies and Phase 1 healthy volunteer data. A Phase 1b study in people with VWM has been initiated which may enable future studies.

KEYWORDS: Experimental Therapeutics

316. Infantile epileptic spasms syndrome – A predictive model for 3-month electroclinical remission

Mytinger J (Columbus, OH), Ahrens S, Albert D, Beatty C, Haffner D, Herbst J, Ostendorf A, Ream M, Slaughter L, Twanow J, Vidaurre J, Rust S

OBJECTIVE: Early remission rates with hormone therapy are superior to vigabatrin in non-tuberous sclerosis complex-associated infantile spasms. We developed a predictive model for 3-month remission that included hormone as first treatment.

METHODS: This was a quality improvement project that combined a prospective intervention cohort (5/2019–2/2023, N=81) and a retrospective cohort (11/2015-4/2019, N=67). Employing logistic regression, we modeled 3-month remission vs. hormone first and child characteristics, with propensity weights determined from a model of hormone first vs. child characteristics (gender, unknown etiology+normal development, all other etiology, abnormal development, no prior seizures, onset < 3 months corrected age, onset ≤ 12 months corrected age, and treatment lag > 30 days). We removed statistically insignificant predictors from the model one at a time until remaining predictors had two-sided p-values <5%.

RESULTS: Onset age ≤ 12 months was the strongest predictor of successful remission (OR 3.98, p=0.045), followed by no prior seizures (OR=3.34, p=0.007) and then hormone first (OR=2.38, p=0.035). For onset age < 12 months, no prior seizures was predictive of successful remission, as was hormone first. The benefit of hormone first may be greater for children with prior seizures. For onset age > 12 months and prior seizures, hormone first had borderline statistical significance as a predictor of successful remission (p=0.057).

CONCLUSIONS: Significant predictors of successful 3-month remission include onset age ≤ 12 months, no prior seizures, and hormone first. Of these, only hormone first can be modified. Hormone therapy should be prioritized over other therapies as the first treatment for infantile spasms.

KEYWORDS: Epilepsy

317. Circulating Organ-enriched microRNAs as Peripheral Epigenetic Biomarkers of Rett Syndrome

Ablordeppey K (New Haven, CT), Kunwar A, Jacobs A, Sheinerman K, Kiefer M, Mireskandari A, Kumar G, Umansky S

OBJECTIVE: Minimally invasive diagnostic tools are needed to better characterize and monitor disease progression and treatment response in Rett syndrome (RTT) patients. At DiamiR, we developed an approach based on targeted selection and quantitative analysis of microRNAs enriched in specific brain regions and other organs/tissues known to be affected by RTT, and detectable in blood plasma. microRNAs are regulatory molecules whose levels change in disease. The main objective of this study was to evaluate pre-selected microRNAs as peripheral biomarkers of RTT in plasma samples from RTT patients and age-matched healthy participants.

METHODS: Concentrations of 45 pre-selected microRNAs were analyzed in EDTA plasma samples of 163 study participants, including 81 RTT patients and 82 age-matched controls. RNA from plasma samples was isolated using the MagMAX mirVana kit (ThermoFisher). microRNA concentrations were measured by qPCR using custom plates (Qiagen) pre-plated with lyophilized miRCURY LNA-based primers for a 45-microRNA panel. Differentiation of RTT, RTT sub-groups, and control by microRNA pairs and their combinations (classifiers) was evaluated using a proprietary software program developed at DiamiR.

RESULTS: microRNA pairs/classifiers were shown to effectively differentiate between RTT patients and control of three age groups (best classifier AUC=0.94 for <5-yr-olds, AUC=0.91 for 6-15-yr-olds, AUC=0.77 for >16-yr-olds). Several microRNAs were also shown to present efficient biomarkers of secondary pathology: walking ability (AUC=0.81), hyperventilation/breathing problems (AUC=0.75), and epilepsy (AUC=0.89).

CONCLUSIONS: These data support the development of assays based on the analysis of circulating brain/organ-enriched microRNAs to facilitate better understanding of RTT-associated pathophysiological processes and development of therapeutics for RTT.

KEYWORDS: Neurodevelopmental Disorders

318. Resolving the genomic architecture of MECP2 Duplication Syndrome unravels genotype-phenotype correlations and paves the way for personalized medicine

Pehlivan D (Houston, TX), Bengtsson J, Bajikar S, Grochowski CM, Suter B, Gandhi M, Du H, Fatih JM, Lun MY, Sedlazeck FJ, Jhangiani SN, Jolly A, Lupski JR, Zoghbi HY, Carvalho CM

OBJECTIVE: Objective: MECP2 Duplication Syndrome (MDS) is an X-linked neurodevelopmental disorder with variable clinical features and severity caused by copy-number gains encompassing MECP2. The duplication size and genome content differ between individuals, with no clear association between duplication size and disease severity. We hypothesized that the genomic structure architecture of the duplication plays a role in phenotypic variability.
METHODS: Methods: To test this hypothesis, we applied a comprehensive genomic approach including custom-designed high-resolution aCGH, droplet digital PCR, whole-genome sequencing, and optical genome mapping techniques to resolve the genomic structure in 126 MDS probands. Furthermore, we conducted RNA-sequencing and Western blot of patient lymphoblastoid cell lines to assess the impact of distinct genomic structures on the gene expression profile and clinical presentation.
RESULTS: Results: The duplication size within the cohort ranged from 64 kb to 16.5 Mb, with 47% tandem duplications, 23% terminal duplications/translocation, 23% duplication-triplication-duplication structure and 7% other complex genomic rearrangements (CGRs). RNAseq and Western blot studies showed that MECP2 expression is statistically different from healthy controls but not between specific classes of genomic structures. Genotype-phenotype analyses indicate the phenotype gradually worsens for overall survival, developmental skills, microcephaly, epilepsy, genitourinary/eye abnormalities in the following order: tandem duplication, other CGRs, terminal duplications/translocation and finally triplications encompassing MECP2.
CONCLUSIONS: Conclusion: This work provides significant insight into the genomic structures underlying MDS and supports the contention that structural complexity contributes to the phenotypic variability/severity in MDS patients. Given that triplications have higher MeCP2 levels than duplications, the dosage of genetic-based therapies needs to be adjusted accordingly.
KEYWORDS: Neurogenetics, Neurodevelopmental Disorders

319. Acute Features and Neurodevelopmental Sequelae of Parechovirus Meningitis and Encephalitis in Young Infants

Jewell J (Denver, CO), Neuberger I, Mirsky D, Rosenthal S, Lesser M, Guistolisi S, Messacar K, Dominguez S, Dingman A

OBJECTIVE: Parechovirus central nervous system (CNS) infection is common in infants, but there is limited data about neurologic sequelae. The objective of this study is to describe the clinical, electroencephalographic, and imaging features of parechovirus CNS infection in infants and neurodevelopmental outcomes.
METHODS: This is a single-center descriptive retrospective cohort study of patients admitted from 2021 to 2022 with parechovirus detected in CSF by PCR testing. Clinical, continuous electroencephalogram (cEEG), and imaging data were evaluated.
RESULTS: Fifty-three patients met inclusion criteria (53% male). Median age was 22 days (IQR 11-40 days). Only 5 (9.4 %) patients underwent cEEG, of which 4 were abnormal, and 3 had seizures. Nine patients (17%) had MRI brain performed, five of which were abnormal, ranging from punctate white matter lesions to diffuse leukoencephalopathy. Twenty-five patients (47%) had follow-up encounters at our institution, of which 2 (8%) had documented developmental delays, and 1 (4%) developed infantile spasms.
CONCLUSIONS: In our cohort, most patients had uncomplicated courses with few negative neurodevelopmental outcomes documented. However, this study is limited by low rates of cEEG, imaging and formal developmental follow-up. All patients who had clinical seizures also had electrographic seizures without clinical correlate, indicating the need for cEEG monitoring in infants with parechovirus CNS infection and clinical seizures. There was a high rate of electrographic seizures among infants with EEG. Likewise, 56% of MRIs obtained had abnormal findings. Therefore, future prospective studies are needed to better assess rates of electrographic seizures and MRI abnormalities in this population.
KEYWORDS: Neuroinfectious Disease, Neonatal Neurology

320. Two novel homozygous variants in DNAJB4 cause a chaperonopathy presenting with axial-predominant myopathy and respiratory failure, with possible cardiac involvement.

Jayaraman D (Boston, MA), Inoue M, Ibaceta R, Genetti C, Aldeeri A, Al-Husayni S, Schmitz-Abe K, Rodan L, Agrawal P, Weihl C, Beggs A

OBJECTIVE: DNAJB4 myopathy is a recently discovered chaperonopathy that presents with myopathy and respiratory failure. Only three homozygous variants in DNAJB4 (including one stopgain and two missense variants) and one dominantly inherited missense variant have been reported. As such, the full phenotypic spectrum and possible genotype-phenotype correlations are yet to be fully described.
METHODS: We enrolled two consanguineous but unrelated Saudi Arabian families with a clinical syndrome of axial-predominant myopathy and respiratory failure, with possible cardiac involvement. We carried out whole exome sequencing of affected individuals and their parents, followed by functional validation in cell culture and yeast.
RESULTS: Here, we report two novel homozygous pathogenic variants in DNAJB4: a stop gain variant (c.547C>T, p.Arg183Ter) and a nonsynonymous missense variant (c.105G>C, p.Lys35Asn). All affected individuals presented with severe torticollis in infancy; had a "rigid spine syndrome" phenotype with axial weakness out of proportion to appendicular weakness; and developed acute respiratory failure with life-threatening hypercapnia necessitating prolonged ventilatory support. Functional studies revealed that the

p.Lys35Asn missense variant disrupted the protein's function as it failed to disaggregate TDP-43 aggregates post-heat shock or complement DNAJB4 function.
CONCLUSIONS: In summary, DNAJB4 is an emerging cause of myopathy with rigid spine syndrome of variable age of onset and severity and should be suspected in individuals with suggestive symptoms, especially if presenting with torticollis during infancy. It is prudent to screen patients with DNAJB4 myopathy regularly for early cardiac and respiratory manifestations and proactively institute life-saving supportive measures.
KEYWORDS: Neuromuscular, Neurogenetics, Early Stage Investigator

321. Following Pediatric Hemispherectomy, the Composition of the Patient's Healthcare Team Expands: An Analysis of the Global Pediatric Epilepsy Surgery Registry

Granovetter M (Pittsburgh, PA), Robert S, Patterson C, Behrmann M

OBJECTIVE: Hemispherectomy--the resection or disconnection of a single hemisphere--is an effective and sometimes necessary intervention for reducing seizure burden in pediatric drug-resistant epilepsy patients. While seizure reduction burden following hemispherectomy is well-established, the procedure is associated with comorbidities, presumably necessitating an interdisciplinary healthcare team to guide postoperative care. Here, we examine changes in the composition of hemispherectomy patients' healthcare team pre- to post-surgery.
METHODS: Hemispherectomy patient data (n=142) were obtained from the Pediatric Epilepsy Surgery Alliance's Global Pediatric Epilepsy Surgery Registry. Parents indicated patients' providers, pre- and post-surgery, as well as patients' postoperative comorbid neuropsychological disorders. McNemar tests compared pre- and postoperative proportions of patients who followed with each provider. A Pearson coefficient was calculated to correlate number of postoperative providers and number of comorbid neuropsychological conditions.
RESULTS: A significantly greater proportion of patients were followed by these providers post-surgery relative to pre-surgery ($p<0.05$, corrected): audiologists, behavioral therapists, developmental pediatricians, endocrinologists, neuro-ophthalmologists, neuropsychologists, occupational therapists, ophthalmologists, optometrists, orthopedic surgeons, orthotists, physiatrists, physical therapists, psychologists, rehabilitation doctors, social workers, and speech therapists. Following surgery, 86% of patients had at least one neuropsychological comorbidity. Notably, number of postoperative providers was moderately correlated with number of postoperative neuropsychological comorbidities ($r=0.31$, $p<0.01$).
CONCLUSIONS: Hemispherectomy is associated with neuropsychological comorbidities (here, in 86% of cases), necessitating interdisciplinary care that a patient may not have required pre-surgery. We identified the expansion of involved providers pre- to post-surgery. The number of involved providers directly correlates with the number of neuropsychological comorbidities, further demonstrating their critical role in postoperative care.
KEYWORDS: Epilepsy

322. The Critical Role of Patient Education in Pediatric Headache Management: A Preliminary Analysis

Touma E (Lexington, KY), Jones K, Hall M, Qaiser S

OBJECTIVE: Headache is one of the leading causes of morbidity and missed school days in children aged 6-17 years, with 80% of school-aged children reporting some form of headache. In the era of personalized medicine, it is critical to assess headache knowledge and awareness for patients seen by headache specialists to improve patient education and supplemental educational tools.
METHODS: A questionnaire-based study was conducted to identify patient and guardian understanding of diagnoses, awareness, education, and barriers to treatment. Patients completed an IRB-approved, in-person, paper questionnaire prior to initial headache clinic visit and on subsequent follow-up visits. Following completion of the initial questionnaire, a significant portion of patient's first appointment was dedicated to education. Visual aids were also given to patients to reinforce understanding of diagnosis and plan. Data from 89 patients was collected at multiple time points between August 2020 to February 2022.
RESULTS: Strikingly, only 18.2% (16 of 88) of patients and/or guardians knew their diagnosis at the initial visit. Additionally, 66.3% (59 of 89) reported they did not know how often they could take their acute medications. Following educational interventions, patients were reassessed at up to two subsequent follow-up appointments– 89.4% of responses (93 of 104) indicated understanding of diagnosis, 85.8% (91 of 106) knew how to treat their headaches, and 92.2% (94 of 102) reported knowing how often they could take acute medication.
CONCLUSIONS: Overall, the study suggests that simple educational tools, in conjunction with active education during appointments, can help dramatically improve patient understanding and ability to manage headaches.
KEYWORDS: Education, Headache

323. Delayed Initiation of Disease Modifying Therapy Increased Relapse Frequency and Motor Disability in Pediatric Onset Multiple Sclerosis

Jafarpour S (Los Angeles, CA), Pinto S, Khoshnood M, Ahsan N, Mitchell W, Vu M, Saucier L, Santoro J

OBJECTIVE: This study assessed pre-morbid demographics in the ultimate severity of pediatric-onset Multiple Sclerosis (POMS).
METHODS: A retrospective analysis of children with POMS from three tertiary referral pediatric Neuroimmunology clinics. Outcome measures comprised annualized relapse rate (ARR), MRI lesion burden (T1, T2-FLAIR, and post-GAD contrast sequences), EDSS, and 25-ft walk duration at the latest follow-up visit. Associations between patient characteristics and outcomes were assessed via correlations, Wilcoxon/

Kruskal-Wallis rank sum tests, and multivariate linear/logistic regressions as appropriate.
RESULTS: In total, 68 patients were reviewed. More than half of patients were female (62%) and Hispanic/LatinX (51%). Median age at diagnosis was 14.2 years (IQR: 11-16.5), and median duration from diagnosis to the latest follow-up was 2.4 years (IQR: 1.4-4.8). Sensory (29.4%), brainstem (23.5%), and pyramidal (19.1%) symptoms were most common. Interferon beta (32.4%), dimethyl fumarate (27.9%) and rituximab (26.5%) were the most frequently used first-line disease modifying treatment (DMT). Patients had a median ARR of 0.5 (IQR: 0.28-0.84), and EDSS score of 1.0 (IQR: 0.0-2.0) at the most recent follow up. Delayed DMT initiation correlated with higher ARR (R=0.38, p=0.0016) and longer 25-ft walk duration (R=0.34, p=0.0077). In multivariate analysis, delayed DMT remained a significant predictor of higher ARR (p=0.002) and longer 25-ft walk duration (p=0.047). Delayed DMT initiation and use of low/moderate efficacy DMT predicted GAD enhancing lesions at the latest follow-up (p=0.004 and 0.019 respectively).
CONCLUSIONS: Delayed DMT initiation in POMS is linked to unfavorable outcomes, including higher ARR and longer 25-ft walk duration.
KEYWORDS: Neuroimmunology, Pediatric Demyelinating Disease, Practice Parameters

324. Effects of Explainable Artificial Intelligence in Neurology

Gombolay G (Atlanta, GA), Silva A, Schrum M, Dutt M, Hallman-Cooper J, Gombolay M

OBJECTIVE: Artificial Intelligence (AI)-based decision support systems are increasingly utilized in medicine but underlying decision-making processes are usually unknown. Explainable AI (xAI) provides insight into such processes, but little is known on how to design xAI for clinicians. Here we assess various xAI techniques optimal for clinicians.
METHODS: A randomized, blinded study in neurologists from all genders from the Child Neurology Society and the American Academy of Neurology was compared to a general population and analyzed using ANOVA and Tukey's test post-hoc models.Each participant was randomly assigned to 1/8 explainability conditions: Decision Tree, Crowd Sourced agreement, Case-based Reasoning, Probability Scores, Counterfactual, Natural Language, Feature Importance Templated language, and No Explanations.Primary outcomes included objective measures: accuracy, reliance, and compliance with the explanation. Secondary outcomes included subjective metrics: perceived explainability, trust of the digital agent, understandability, and agreement.
RESULTS: We recruited 81 medical and 284 lay participants. Three explanation modalities were more usable in clinicians and differed from the general population: Decision Tree explanations (Absolute Difference-AD=24.2, p=0.0005 [95% CI: 7.7-40.6]), Crowd-Sourced explanations (AD=16.3, p=0.044 [95%CI 0.26-32.43]), and Case-Based explanations (AD=19.1429, p=0.046 [95% CI 0.22-38.1]). Explainability exhibited a moderate-weak correlation to anthropomorphism (R=0.35, p=0.0012).
CONCLUSIONS: xAI methods have different impacts on a medical vs. general population, calling into question commonly-held beliefs about the right way to approach XAI. Our results encourage further user-centered xAI research targeted at medical populations to identify optimal xAI methods as xAI methods that work for the general population may be less applicable to clinicians.
KEYWORDS: Practice Parameters

325. Bypassing the metabolic block in an inborn error of vitamin metabolism: a phase 2 clinical trial of 4'-phosphopantetheine in PKAN

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OBJECTIVE: Pantothenate kinase-associated neurodegeneration (PKAN) is an inborn error of vitamin metabolism that affords opportunities for rational nutritional approaches to treatment utilizing accelerated FDA pathways. We sought to establish the safety, tolerability and biomarker response of a compound that bypasses the metabolic block in PKAN.
METHODS: We conducted a phase 2 clinical trial of 4'-phosphopantetheine, a downstream product of vitamin B5 metabolism, in people with PKAN in the US and Canada, employing a novel approach with all activities done remotely in the participant's local community. The 2-year trial consisted of a 6-month randomized, double-blind, placebo-controlled, dose-ranging phase followed by an 18-month open-label, single-dose phase. We assessed adverse events and laboratory abnormalities as measures of safety, and participant retention and product compliance as measures of tolerability. To assess target engagement, we measured expression of a gene encoding an enzyme downstream of the metabolic block that is down-regulated in PKAN.
RESULTS: Sixty-five unique participants aged 5 months to 58 years were randomized; 64 completed the double-blind phase (16 each in placebo and 3 dose-groups). There were no serious adverse events or clinically-significant laboratory abnormalities attributed to the study product. The biomarker demonstrated dose-responsive up-regulation to substrate replenishment by 4'-phosphopantetheine.
CONCLUSIONS: 4'-phosphopantetheine is safe and well-tolerated in pediatric and adult patients with PKAN, with its use as a rational agent supported by a pharmacodynamic molecular measure of target engagement in the disease pathway. The remote trial conduct reduced barriers to participation, lessened burden on families, reduced risks to participants, lowered study costs, and minimized pandemic-related trial disruptions.
KEYWORDS: Experimental Therapeutics, Movement Disorders, Neurometabolic

328. A Randomized Double-Blind Placebo-Controlled Phase 2 Clinical Trial of Fasoracetam for Neuropsychiatric Symptoms in Children with 22q11.2 Deletion Syndrome

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OBJECTIVE: This phase-2 trial, sponsored by Nobias Therapeutics, examined fasoracetam, a non-stimulant mGluR activator, as a novel treatment for non-psychotic psychiatric symptoms of 22q11.2-deletion syndrome (22q11DS).

METHODS: Children and adolescents with 22q11DS, ages 6-17, were eligible for this randomized double-blind placebo-controlled cross-over trial based on moderate or greater anxiety, attention, and/or social communication symptoms. Endpoints were safety/tolerability (primary), and target symptom improvement on the Clinical Global Impression-Improvement Scale (CGI-I) (secondary). Mixed-effect models were used to examine CGI-I in treatment versus placebo at 6 weeks.

RESULTS: 37 participants were randomized; 32 completed the study (mean age=11.8 years (SD 3.08), 66.7% male). Fasoracetam was well tolerated; all adverse events were mild to moderate (54.5% during treatment vs 70.6% during placebo), with no severe/serious events due to treatment. The least squares mean CGI-I for the treatment period was 3.31 (standard error: 0.16) versus 3.68 (0.16) for placebo (delta=−0.37 (0.20), p=0.07). Improvement was observed in CGI-I for patients entering the trial with subclinical/clinical ADHD (p=0.03), anxiety (p=0.07) and autistic traits (p=0.09). Importantly, 66% of patients scored "Minimally Improved" or better on CGI-I during treatment vs. only 45% with placebo (p=0.10).

CONCLUSIONS: Our findings demonstrate the safety, tolerability, and potential efficacy of fasoracetam for the treatment of non-psychotic psychiatric symptoms associated with 22q11DS. Innovative elements include target population selection based on genetic etiology and transdiagnostic definition of target symptoms. These promising results support further evaluation in a more robustly powered Phase 3 setting.

KEYWORDS: Neurogenetics, Behavioral Neurology, Neurodevelopmental Disorders

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