FORTIETH NATIONAL MEETING
OF THE CHILD NEUROLOGY SOCIETY

PLANNING COMMITTEE

Child Neurology Society Executive Board
Donna Ferriero, President San Francisco, CA
E. Steve Roach, President-elect Columbus, OH
Harvey Singer, Secretary-treasurer Baltimore, MD
Sidney Gospe, Councillor Seattle, WA
Gary Clark, Councillor Houston, TX
Sakkubai Naidu, Councillor Baltimore, MD
Warren Lo, Councillor Columbus, OH

CNS Scientific Selection and Program Planning Committee

Steven Miller, Chair Vancouver, BC
Maria Acosta Washington, DC
Denis Altman St. Louis, MO
Donna Antonucci Yardley, PA
Miya Asato Pittsburgh, PA
Nigel Bamford Seattle, WA
William Dobyns Seattle, WA
S. Ali Fatemi Bethesda, MD
Heather Fullerton San Francisco, CA
William Gaillard Chevy Chase, MD
Howard Goodkin Charlottesville, VA
Andrea Gropman Washington, DC
Imad Jarjour Houston, TX

Stephen Maricich Cleveland, OH
Jayne Ness Birmingham, AL
Jeffrey Neul Houston, TX
James Owens Houston, TX
Sumit Parikh Cleveland, OH
Vinay Puri Louisville, KY
Robert Rust Charlottesville, VA
Mustafa Sahin Boston, MA
Bradley Schlaggar St. Louis, MO
Renee Shellhaas Ann Arbor, MI
Michael Shevell Montreal, QC
Janet Soul Boston, MA
William Weiss San Francisco, CA

National Office
Mary B. Currey, Executive Director St. Paul, MN
Roger B. Larson, Associate Director St. Paul, MN

Presented at Savannah International Trade & Convention Center, Savannah, GA
October 26-29, 2011

ACCREDITATION

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

The Minnesota Medical Association designates this live learning activity for a maximum of 27.25 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

To receive CME credits, physicians must complete the on-line CME survey posted on the CNS website (www.childneurologysociety.org) on or before November 19, 2011.
PAST OFFICERS

President
Kenneth Swaiman 1972–73
Gerald Fenichel 1973–74
Manuel Gomez 1974–75
James Schwartz 1975–76
Richard Allen 1976–77
Bruce Berg 1977–78
N. Paul Rosman 1978–79
Arthur Prensksy 1979–80
Paul Dyken 1980–81
Mary Anne Guggenheim 1981–82
Raymond Chun 1982–83
Robert Eiben 1983–85
David Stumpf 1985–87
Marvin Fishman 1987–89
Darryl C. De Vivo 1989–91
Peter H. Berman 1991–93
Joseph J. Volpe 1993–95
Michael E. Cohen 1995–97
Alan K. Percy 1997–99
Michael J. Painter 1999–2001
James Bale 2003–2005
John Bodensteiner 2007–2009

Secretary-Treasurer
Richard Allen 1972–75
Raymond Chun 1975–78
Robert Eiben 1978–81
Lawrence Lockman 1981–84
Marvin Fishman 1984–86
Ira Lott 1986–89
Peggy Copple 1989–93
Stephen Ashwal 1993–97
Patricia Crumrine 1997–2002
Ann Tilton 2003–2004
Nina Schor 2004–2010

Councillor
Isabelle Rapin 1972–73
Manuel Gomez 1972–74
John Menkes 1972–74
James Schwartz 1973–75
Karin Nelson 1973–74
Raymond Chun 1973–75
Bruce Berg 1974–76
Paul Dyken 1974–76
Arthur Prensksy 1975–77
N. Paul Rosman 1975–77
Jack Madsen 1976–78
Peggy Ferry 1976–78
Joseph French 1977–79
Francis Wright 1977–79
Mary Anne Guggenheim 1978–80
Gerald Golden 1978–80
Gerald Erenberg 1979–81
John Freeman 1979–81

Marvin Weil 1980–82
Marvin Fishman 1980–82
Peter Huttenlocher 1981–83
Michael Bresnan 1981–83
David Stumpf 1982–84
Gwendolyn Hogan 1982–84
Joseph Volpe 1983–85
Barry Russman 1983–85
Russell Snyder 1984–86
Ian Butler 1984–86
W. Edwin Dodson 1985–87
Michael Painter 1985–87
Robert Zeller 1986–88
Doris Trauner 1986–88
Darrel De Vivo 1987–88
Gary Goldstein 1987–89
Robert Vannucci 1988–89
Stephen Ashwal 1988–90
Jack Pellock 1988–90
Joseph Pasternak 1989–91
Patricia Duffner 1989–91
O. Carter Snead 1990–92
Edwin Meyer 1990–92
Israel Abroms 1991–93
William Logan 1991–93
Mary Johnson 1992–94
Alan Percy 1992–94
Phyllis Sher 1993–95
Gregory Holmes 1993–95
W. Donald Shields 1994–96
John Bodensteiner 1994–96
Patricia Crumrine 1995–97
James Bale 1995–97
Alan Hill 1996–98
Ann Tilton 1996–98
Edward Kovnar 1997–99
Richard Nordgren 1997–99
Michael Goldstein 1998–2000
Faye Silverstein 1999–2001
Michael Johnston 1999–2001
Carmela Tardo 2000–2001
Pauline Filipek 2000–2001
Carl Crosley 2001–2006
Julie Parke 2002–2006
Roy Eltman 2002–2006
Marc Patterson 2003–2006
Douglas Nordli 2003–2006
Donna Ferriero 2004–2006
Leon Dure 2004–2006
Laura Ment 2005–2006
Leslie Morrison 2006–2006
Anne Anderson 2006–2006
Steven Leber 2007–2006
Jonathan Mink 2007–2006
Robert Rust 2008–2006
<table>
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<td>Washington, DC</td>
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<td>Ottawa, Ontario, Canada</td>
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<td>Los Angeles, CA</td>
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<td>Pittsburgh, PA</td>
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<td>2007</td>
<td>Quebec City, PQ, Canada</td>
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<td>2008</td>
<td>Santa Clara, CA</td>
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<td>2009</td>
<td>Louisville, KY</td>
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<td>Providence, RI</td>
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| 2011 | Savannah, GA                     | October 26–29, 2011
| 2012 | Huntington Beach, CA             | October 31–November 3, 2012
HOWER AWARD RECIPIENTS

1974 Douglas Buchanan
Chicago

1975 Randolph K. Byers
Boston

1976 Sidney Carter
New York

1977 David B. Clark
Lexington

1978 Philip R. Dodge
St. Louis

1979 Paul I. Yakovlev
Boston

1980 John H. Menkes
Beverly Hills

1981 Kenneth F. Swaiman
Minneapolis

1982 Patrick F. Bray
Salt Lake City

1983 Betty Q. Banker
Cleveland

1984 Peter R. Huttenlocher
Chicago

1985 Raymond D. Adams
Boston

1986 Jean Aicardi
Paris

1987 Isabelle Rapin
Bronx

1988 Bruce Berg
San Francisco

1989 Manuel Gomez
Rochester

1990 Joseph J. Volpe
Boston

1991 Karin B. Nelson
Bethesda

1992 Darryl C. De Vivo
New York

1993 Bengt D. Hagberg
Goteborg

1994 Hugo Moser
Baltimore

1995 Salvatore DiMauro
New York

1996 William Bell
Iowa City

1997 Gerald Fenichel
Nashville

1998 N. Paul Rosman
Boston

1999 Marvin Fishman
Houston

2000 Arthur Prensky
St. Louis

2001 Charles Barlow
Boston

2002 Peter H. Berman
Philadelphia

2003 Michael E. Cohen
Buffalo

2004 John Freeman
Baltimore

2005 Alan Percy
Birmingham

2006 Michael Painter
Pittsburgh

2007 Robert S. Rust
Charlottesville

2008 Stephen Ashwal
Loma Linda

2009 Peter Camfield
Halifax

2010 Sakkubai Naidu
Baltimore

2011 Deborah Hirtz
Bethesda
INVITED SPEAKERS AND BERNARD SACHS LECTURERS

1977  George Cahill  
      Boston

1978  W. Maxwell Cowan  
      St. Louis

1979  Fred Plum  
      New York

1980  Dominick Purpura  
      New York

1981  Pasko Rakic  
      New Haven

1982  John O’Brien  
      La Jolla

1983  Roger N. Rosenberg  
      Dallas

1984  William L. Nyhan  
      La Jolla

1985  Patricia Goldman-Rakic  
      New Haven

1986  Louis Sokoloff  
      Bethesda

1987  Hugo Moser  
      Baltimore

1988  Victor Dubowitz  
      London

1989  Salvatore DiMauro  
      New York

1990  Roscoe O. Brady  
      Bethesda

1991  Marcus E. Raichle  
      St. Louis

1992  Louis M. Kunkel  
      Boston

1993  C. Thomas Caskey  
      Houston

1994  David Prince  
      Stanford

1995  Gerald D. Fischbach  
      Boston

1996  Verne S. Caviness  
      Boston

1997  Martha Bridge Denckla  
      Baltimore

1998  Andrew Engel  
      Rochester

1999  Carla Shatz  
      Berkeley

2000  Joseph Volpe  
      Boston

2001  Huda Zoghbi  
      Houston

2002  Francis Collins  
      Bethesda

2003  Darryl C. De Vivo  
      New York

2004  Karin Nelson  
      Bethesda

2005  O. Carter Snead, III  
      Toronto

2006  Donna Ferriero  
      San Francisco

2007  Frederick Andermann  
      Montreal

2008  Michael Johnston  
      Baltimore

2009  Gregory Holmes  
      Lebanon, NH

2010  Thomas Jessell  
      New York

2011  Laura Ment  
      New Haven
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<th>Year</th>
<th>Name</th>
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<tr>
<td>1983</td>
<td>Michael Pranzatelli</td>
<td>Washington</td>
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<td>Richard J. Konkol</td>
<td>Milwaukee</td>
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<td>1986</td>
<td>Faye S. Silverstein</td>
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<td>Vinodh Narayanan</td>
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<td>1988</td>
<td>Huda Zoghbi</td>
<td>Houston</td>
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<td>1989</td>
<td>Scott L. Pomeroy</td>
<td>St. Louis</td>
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<td>1990</td>
<td>Harris Gelbard</td>
<td>Rochester (NY)</td>
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<td></td>
<td>Evan Y. Snyder</td>
<td>Boston</td>
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<td>1991</td>
<td>Kenneth J. Mack</td>
<td>Madison</td>
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<td>1992</td>
<td>Kelvin A. Yamada</td>
<td>St. Louis</td>
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<td>1993</td>
<td>Jeffrey J. Neil</td>
<td>St. Louis</td>
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<td>1994</td>
<td>Mia MacCollin</td>
<td>Boston</td>
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<td>1995</td>
<td>Adre J. du Plessis</td>
<td>Boston</td>
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<td>1996</td>
<td>Michael Rivkin</td>
<td>Boston</td>
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<td>1997</td>
<td>William A. Weiss</td>
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<td>1998</td>
<td>Joseph Gleeson</td>
<td>Boston</td>
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<td>1999</td>
<td>Amy Brooks-Kayal</td>
<td>Philadelphia</td>
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<td>2000</td>
<td>Stephen Back</td>
<td>Portland</td>
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<td>2001</td>
<td>Daniel J. Bonthius</td>
<td>Iowa City</td>
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<td>2002</td>
<td>Nigel Bamford</td>
<td>New York</td>
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<td>2003</td>
<td>Bradley Schlaggar</td>
<td>St. Louis</td>
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<td>2004</td>
<td>Terrie Inder</td>
<td>Melbourne</td>
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<td>2005</td>
<td>Mustafa Sahin</td>
<td>Boston</td>
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<tr>
<td>2006</td>
<td>Elliott Sherr</td>
<td>San Francisco</td>
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<tr>
<td>2007</td>
<td>Mirjana Maletic-Savatic</td>
<td>Stony Brook</td>
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<td>2008</td>
<td>Laura Jansen</td>
<td>Seattle</td>
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<td>2009</td>
<td>Jeffrey Neul</td>
<td>Houston</td>
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<tr>
<td>2010</td>
<td>Stephen Maricich</td>
<td>Cleveland</td>
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<td>2011</td>
<td>James Dowling</td>
<td>Ann Arbor</td>
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CNS LIFETIME ACHIEVEMENT AWARDS

2004  Jean Holowach Thurston  
       St. Louis, MO

2005  Robert Eiben  
       Cleveland, OH
       Arnold Gold  
       New York, NY

2006  Raymond Chun  
       Madison, WI
       Barry Russman  
       Portland, OR

2007  William Kennedy  
       Watertown, ME
       Gordon Watters  
       Montreal, Quebec

2008  Cesare Lombroso  
       Boston, MA

2009  Mary Anne Guggenheim  
       Helena, MT

2010  Russell Snyder  
       Albuquerque, NM

2011  Warren Grover  
       Dataw Island, SC

ARNOLD P. GOLD FOUNDATION HUMANISM IN MEDICINE AWARD AT THE CHILD NEUROLOGY SOCIETY

2010  Ruth D. Nass  
       New York, NY

2011  Shaul Harel  
       Tel Aviv, Israel
### BERNARD D’SOUZA INTERNATIONAL FELLOWSHIP
### AWARD RECIPIENTS

<table>
<thead>
<tr>
<th>Year</th>
<th>Name</th>
<th>City, Country</th>
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<tr>
<td>1989</td>
<td>Meral Ozmen</td>
<td>Istanbul, Turkey</td>
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<td>1990</td>
<td>Najoua Miladi</td>
<td>Tunis, Tunisia</td>
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<td>1991</td>
<td>Sergio A. Antoniuk</td>
<td>Curitiba, Brazil</td>
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<td>1992</td>
<td>Qin Jiong</td>
<td>Beijing, China</td>
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<td>1993</td>
<td>Anu Soot</td>
<td>Tartu, Estonia</td>
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<td>1994</td>
<td>Lai Choo Ong</td>
<td>Kuala Lampur, Malaysia</td>
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<td>1995</td>
<td>Nina Barisic</td>
<td>Zagreb, Croatia</td>
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<td>1996</td>
<td>Shan Wei Song</td>
<td>Beijing, China</td>
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<td>1997</td>
<td>Aleksandra Djukic</td>
<td>Belgrade, Yugoslavia</td>
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<td>1998</td>
<td>Ana Keleme</td>
<td>Novi Sad, Yugoslavia</td>
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<td>1999</td>
<td>Magda L. Nunes</td>
<td>Porto Alegre, Brazil</td>
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<td>2000</td>
<td>Brahim Tabarki-Melaiki</td>
<td>Brussels, Belgium</td>
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<td>Dimitrios Zafeiriou</td>
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<td>Vedrana Milic Rasic</td>
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<td>David Chkhartishvili</td>
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<td>Natalia A. Yermolenko</td>
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<td>Lusine Kirakosyan</td>
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<td>Gia Melikoshvili</td>
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<td>David E. Kombo</td>
<td>Dars Es Salaam, Tanzania</td>
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<td>Ikeolu Lagunju</td>
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<td>Uduak Mayen Offiong</td>
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<td>Parayil. S. Bindu</td>
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<td>Kyaw Linn</td>
<td>Myanmar</td>
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OUTSTANDING JUNIOR MEMBER AWARD RECIPIENTS

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

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

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

1999
- June Caruso
  Rhode Island Children’s Hospital
- Debra Holder
  Texas Children’s Hospital
- Carolyn Menache
  Boston Children’s Hospital

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

2001
- Marie Acosta
  Children’s National Medical Center
- Randa Jarrar
  Mayo Clinic
- Steven Miller
  UC San Francisco
- Jane Ness
  Children’s Hospital of Alabama

2002
- Tauen Chang
  Children’s National Medical Center
- Mirjana Maletic-Savatic
  SUNY Stony Brook
- Lauren Plawner
  Stanford University Medical Center
- Michael Seyffert
  University of Washington Med Ctr

2003
- Tauen Chang
  Children’s National Medical Center
- Yoshima Sogawa
  Schneider Children’s Hospital
- Ignacio Valencia
  St. Christopher’s Hospital
- Adeline Vanderver
  Children’s National Medical Center

2004
- Ignacio Valencia
  St. Christopher’s Hospital
- Brannon Morris
  Mayo Clinic
- Haim Bassan
  Boston Children’s Hospital
- William Benko
  Children’s National Medical Center

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
- Renee Shellhaas
  Children’s Hospital of Philadelphia
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

2007
- 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

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

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

2010
- Dawn Gano
  University of British Columbia
- Radhika Dhamija
  Mayo Clinic
- Patricia Musolino
  Massachusetts General Hospital
- Thitiwan Simasathien
  University of Alabama-Birmingham

2011
- Partha Ghosh
  Cleveland Clinic Foundation
- Andrea Pardo
  Cincinnati Children’s Hospital Medical Center
- Thitiwan Simasathien
  University of Alabama-Birmingham
- Sydi Seinfeld
  Virginia Commonwealth University

HIGH SCHOOL STUDENT NEUROSCIENCE PRIZE

1998  Karla Malloy
       Richmond, VA
1999  Nihar Gupta
       New York, NY
2000  Rishikesh Dalal
       Lenexa, KS
2001  Melanie Napier
       Laurelton, NY
2002  Corinna Zygoourakis
       Houston, TX
2003  Henry Marr
       Alhambra, CA
2004  Debashish Zircar
       Bronx, NY
2005  Max Christie
       Briarcliff Manor, NY
2006  Shoshana Tell
       Coral Springs, FL
2007  David Shiovitz
       Briarcliff Manor, NY
2008  Lauren Lisann
       Dix Hills, NY
2009  Inar Zhang
       Mercer Island, WA
2010  Pragya Kakani
       Jericho, NY
2011  Spencer Chan
       Forest Hills, NY
INTERNATIONAL VISITING PROFESSOR

2003  Kenton Holden  
       Mt. Pleasant, SC

       Anita Belman  
       Stony Brook, NY

2004  Robert Rust  
       Charlottesville, VA

2006  Vinodh Narayanan  
       Phoenix, AZ

       Peter Camfield  
       Halifax, NS

2008  Douglas Postels  
       East Lansing, MI

2010  John Bodensteiner  
       Phoenix, AZ

ASSOCIATION OF CHILD NEUROLOGY NURSES
CLAIRES CHEE AWARD FOR EXCELLENCE

2000  Jan Mims  
       Minneapolis, MN

2001  Claire Chee  
       Philadelphia, PA

2002  Rhonda Roell Werner  
       New Berlin, WI

2003  Elizabeth F. Hobdell  
       Chester Brook, PA

2004  Jane Meyer  
       Cottage Grove, WI

2005  Debbie Terry  
       Westerville, OH

2006  Amy Vierhile  
       Rochester, NY

2007  Elizabeth Tate  
       Springfield, IL

2008  Irene M. Elliott  
       Toronto, ON

2009  Christine O’Dell  
       Bronx, NY

2010  Julie Sprague-McRae  
       Fremont, CA

2011  Yolanda Harris  
       Birmingham, AL
THE CHILD NEUROLOGY SOCIETY
GRATEFULLY ACKNOWLEDGES
THE FINANCIAL SUPPORT OF

- Eisai, Inc.
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40th Annual Child Neurology Society Meeting
Scientific Program

Savannah, Georgia

October 26–29, 2011

Donna Ferriero, MD, President, CNS
Steven Miller, MDCM, Chair, CNS Scientific Selection and Program Planning Committee

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the Minnesota Medical Association and the 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 learning activity for a maximum of 27.25 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

PROGRAM

WEDNESDAY, OCTOBER 26

7:30 AM – 5:00 PM

Symposium I: Neurobiology of Disease in Children: Childhood Ataxia
Organizer: Bernie Maria, MD, MBA, Medical College of Georgia, Augusta, GA
Ataxia
Supported by the National Institutes of Health (NIH grant 5R13NS040925-09), the Child Neurology Society and the National Ataxia Foundation

7:30 AM – 7:40 AM
Opening Comments
Bernard L. Maria, MD., MBA., Principal Investigator
Medical College of Georgia, Augusta, Georgia
Story Landis, PhD, Director of NINDS Bethesda, Maryland

7:40 AM – 8:10 AM
Overview of Childhood Ataxia
Brent Fogel, MD, PhD
University of California Los Angeles

8:10 AM – 8:30 AM
Clinical Features of Friedreich Ataxia (FRDA)
Martin Delatycki, MBBS, PhD, FRACP
Bruce Lefroy Centre for Genetic Health Research

8:30 AM – 8:50 AM
Cardiomyopathy in FRDA
Mark Payne, MD
Indiana University School of Medicine

8:50 AM – 9:10 AM
Genetics of FRDA / Issues in Study of Rare Diseases
Jennifer Farmer, MS, CGC
Friedreich's Ataxia Research Alliance

9:10 AM – 9:30 AM
Question and Answer Session

9:30 AM – 9:45 AM
Coffee Break

9:45 AM – 11:45 AM
SESSION II: PROGRESS TO DATE—FRIEDREICH’S ATAXIA

Co-Director and Moderator: Christopher W. Gomez, MD, PhD
University of Chicago

9:45 AM – 10:10 AM
New Pathways
Massimo Pandolfo, MD
Free University of Brussels

10:10 AM – 10:35 AM
Epigenetic Controls
Joel Gottesfeld, PhD
The Scripps Research Institute

10:35 AM – 11:00 AM
Therapeutic Developments
Rob Wilson, MD, PhD
University of Pennsylvania Medical Center

11:00 AM – 11:25 AM
Clinical Trials Results
Susan Perlman, MD
University of California Los Angeles
11:25 AM – 11:45 AM
Question and Answer Session

11:45 AM – 1:00 PM
Lunch and Presentation by the National Ataxia Foundation

1:00 PM – 2:40 PM
SESSION III: NEW INVESTIGATIONS IN FRIEDREICH’S ATAXIA
Co-Director and Moderator: Susan Perlman, MD
University of California Los Angeles

1:00 PM – 1:20 PM
Clinical Measures
David Lynch, MD, PhD
Children’s Hospital of Philadelphia

1:20 PM – 1:40 PM
Insulin Resistance
Steve Willi, MD
Children’s Hospital of Philadelphia

1:40 PM – 2:00 PM
Cardiac Approaches
Subha Raman, MD
The Ohio State University

2:00 PM – 2:20 PM
Non-motor Investigations - Speech/Hearing
Gary Rance, PhD
University of Melbourne

2:20 PM – 2:40 PM
New Dilemmas in Diagnosis
Grace Yoon, MD
The Hospital for Sick Kids, Toronto

2:40 PM – 3:00 PM
Coffee Break

3:00 PM – 3:30 PM
EXECUTIVE SUMMARY OF THE DAY
Gihan Tennekoon, MD, PhD
The Children’s Hospital of Philadelphia

3:30 PM – 4:25 PM
SESSION IV: FUTURE DIRECTIONS PANEL DISCUSSION
Moderator: Katrina Gwin, MD NIH/NINDS

PANELISTS:
Tom Crawford, MD
Johns Hopkins University

Billie DiMauro, MD
Columbia University

Michio Hirano, MD
Columbia University

Kathy Mathews, MD
University of Iowa

George (Chip) Wilmot, MD, PhD
Emory University

Christopher Gomez, MD, PhD
University of Chicago

4:25 PM – 4:30 PM
Closing Comments and Thanks
Bernard L. Maria, M.D., MBA

Additional Wednesday Meetings/Sessions

8:00 AM – 4:30 PM
Association of Child Neurology Nurses
(NOT part of CNS CME programming)

2:00 PM – 5:00 PM
Professors of Child Neurology

6:00 PM – 8:00 PM
OPENING RECEPTION

8:00 – 10:00 PM
SIG Meetings (including Movement Disorders)

THURSDAY, OCTOBER 27

7:00 – 8:30 AM
CONTINENTAL BREAKFAST AND SEMINARS
Breakfast Seminar 1: Induced Pluripotent Stem Cells in Child Neurology: New Tools, New Hope?
Organizer: Kevin C. Ess, MD, PhD; Kennedy Center for Research on Human Development, Nashville, TN
Speakers: Excessive Generation of Human Neurons from TSC Derived Induced Pluripotent Stem Cells
Kevin C. Ess, MD, PhD
Modeling Autism Spectrum Disorders Using Human Neurons
Alysson Muotri, PhD, UCSD, San Diego, CA
Imprinting of Human Neurons Derived from Patients with Angelman Syndrome
Stormy Chamberlain, PhD; University of Connecticut Hlth Ctr, Farmington, CT

Breakfast Seminar 2: The Foregoing of Life Sustaining Treatment; Ethical Issues
Organizer: Leon Epstein, MD; Chicago Memorial Hospital, Chicago, IL
Speakers: The Foregoing of Life Sustaining Treatment: are futility policies ethical?
Geoffrey Miller, MD, Yale University, New Haven, CT
The Foregoing of Life Sustaining Treatment: value judgement is unavoidable, but not the tyranny of language
Joelle Mast, MD, PhD, Blythedale Children’s Hospital, New York, NY
Discussion
Pedro Weisleder, MD, The Ohio State University College of Medicine, Columbus, OH

Breakfast Seminar 3: Advances in MRI Imaging in Epilepsy
Organizer: Mohamad Mikati, MD; Duke University Medical Center, Durham, NC
Speakers: MRI Volumetrics: A Window to Brain Development and Function in Children with Epilepsy
Bruce Hermann, PhD; University of Wisconsin, Madison, WI

Functional Neuroimaging in Pediatric Epilepsy: new horizons
William Gaillard, MD; Children’s National Medical Center, Washington, DC

Diffusion Tensor Imaging of the Brain
Mohamad Mikati, MD

Clinical Utility of Advanced MRI Techniques in Specific Disorders and Directions for the Future
Harry Chugani, MD; Children’s Hospital of Michigan, Detroit, MI

9:00 AM – 9:10 AM CNS Lifetime Achievement Award: Warren Grover, MD, Dataw Island, SC

9:10 AM – 12:00 PM Symposium II: Presidential Symposium: A New Look at Neuroinflammation
Organizer: Steven P. Miller, MDCM, University of British Columbia, Vancouver, BC

Speakers: Inflammation and the Newborn Brain
Olaf Dammann, MD; Children’s Hospital of Boston, Boston, MA

Inflammation and Childhood Stroke
Heather Fullerton, MD; UCSF, San Francisco, CA

Is NF-1 an Inflammatory Disease?
David Ingram, MD; University of Indiana, Indianapolis, IN

Advances in Opsoclonus-Myoclonus Syndrome
Michael Pranzatelli, MD; Southern Illinois University School of Medicine, Springfield, IL

Autoimmune Encephalitis
Josep Dalmau, MD, PhD; University of Pennsylvania, Philadelphia, PA

11:30 AM – 6:00 PM Exhibits

12:00 – 12:30 PM CNS Business Meeting

12:30 – 1:30 PM Lunch, Exhibit & Poster Viewing

1:30 PM – 4:00 PM Symp III: Saving the Brain -- Opportunities in Pediatric Neurocritical Care
Organizer: Mark S. Wainwright, MD, PhD; Northwestern University Feinberg School of Medicine, Chicago, IL

Speakers: Continuous EEG Monitoring in the Pediatric ICU
Joshua Goldstein, MD; Northwestern University Feinberg School of Medicine, Chicago, IL

Biomarkers and Acute Neurological Injury
Michael Bell, MD; Children’s Hospital of Pittsburgh, Pittsburgh, PA

Cerebral Blood Flow and Vascular Reactivity
Monica S. Vavilala, MD; University of Washington School of Medicine, Seattle, WA

The End Justifies the Means: outcomes and chronic management following acute brain injury
Christopher C. Giza, MD; UCLA Brain Injury Research Center, Los Angeles, CA

The Neurologist’s Role in the Pediatric ICU: creating a neurocritical care service
Mark S. Wainwright, MD, PhD

4:00 – 6:00 PM Child Neuro News Break: Poster Walkaround/ Wine & Cheese Reception
Supported by a grant from Eisai, Inc.

FRIDAY, OCTOBER 28

7:00 – 8:30 AM CONTINENTAL BREAKFAST AND SEMINARS
Breakfast Seminar 4: An Update on Genetics for the Child Neurologist: new advances in the field and approaches to education
Organizer: Andrea Gropman, MD; Children’s National Medical Center, Washington, DC

Speakers: Importance of Genetics in Knowledge in Neurology Practice
Andrea Gropman, MD

Incorporation of Genetics into the Education of Neurology Trainees and Neurologists
Marc DiSabella, DO; Children’s National Medical Center, Washington, DC

Emerging Genetic Testing Technologies and Clinical Issues Encountered in Child Neurology Clinic: a case-based approach
Jodie Martin, MA, CGC; Children’s National Medical Center, Washington, DC

15 A Novel Web-based Targeted Education Program for Neurologists and Strategies for Education Evaluation
Emily Edelman, MA, CGC; Children’s National Medical Center, Washington, DC

Breakfast Seminar 5: Circadian Patterns to Pediatric Neurologic Disorders: novel approaches to diagnosis and therapy
Organizer: Sanjeev V. Kothare, MD; Children’s Hospital of Boston, Boston, MA

Speakers: Circadian Biology and Neurological Disorders of Childhood
Jonathan Lipton, MD, PhD; Children’s Hospital of Boston, Boston, MA
Circadian Patterns in Paroxysmal Pediatric Neurological Disorders
Tobias Loddenkemper, MD; Children’s Hospital of Boston, Boston, MA

Novel Circadian Chrono-therapeutic Approaches in Paroxysmal Neurological Disorders of Childhood
Sanjeev V. Kothare, MD

Breakfast Seminar 6: Managing Severe Pediatric Movement Disorders
Organizer: Rebecca K. Lehman, MD; Medical University of South Carolina, Charleston, SC
Speakers:
- Management Challenges in Juvenile Parkinsonism
  Toni Pearson, MD; Columbia University, New York, NY
- Management of Severe Dyskinesia in Childhood
  Erika Augustine, MD; University of Rochester, Rochester, NY
- When Your “Go-To” is Gone: management of severe Tourette Syndrome
  Rebecca K. Lehman, MD

Platform Sessions 1 & 2
8:45 AM – 10:45 AM

1. Autism and Agenesis of the Corpus Callosum (AgCC): Chromosomal Copy Number Variants (CNV) Point to Etiologic Linkage
   Elliott Sherr MD, PhD; San Francisco, CA

2. Regulation of ASTN1 Receptor Endocytosis and Trafficking by Nisch2 Reveals an Important Role for These Processes in CNS Neuronal Migration.
   Robert Fryer MD; New York, NY

3. Combination Treatment with Docosahexaenoic Acid (DHA) and Hypothermia Preserves Sensorimotor Function after Hypoxic-ischemic Brain Injury in Neonatal Rats
   JD Barks MD; Ann Arbor, MI

4. Restricted Diffusion in the Splenium of the Corpus Callosum in Neonates with Hypoxic-ischemic Encephalopathy, is a Predictor of Neurodevelopmental Outcome
   C Fons MD; Boston, MA

5. Elevated Concentrations of Inflammation-related Proteins in Postnatal Blood Predict Severe Developmental Delay at Two Years in Extremely Premature Infants
   Michael O’Shea MD; Winston-Salem, NC

   Yvonne Wu MD; San Francisco, CA

7. Effect of Prenatal MgSO4 on Head Ultrasound Imaging in Preterm Infants
   Deborah Hirtz, MD; Bethesda, MD

8. Early versus Late External Ventricular Drainage in Relation to Outcome in Preterm Infants with Posthemorrhagic Hydrocephalus
   Haim Bassan MD; Tel Aviv, Israel

8:45 AM – 10:45 AM

Platform 2

9. Lovastatin Normalizes the Brain Spontaneous Low-frequency Fluctuations in Children with Neurofibromatosis Type 1
   Marie Acosta MD; Washington, DC

10. Deep Brain Stimulation Demonstrates Partial Amelioration of Motor Dysfunction in a Mouse Model of Rett Syndrome
    Eric Arheart MD; Lebanon, NH

11. Everolimus Showed Long-term Efficacy and Safety in the Extension Phase of a Prospective, Open-label Phase I-II Study of Patients with Subependymal Giant-cell Astrocytomas Associated with Tuberous Sclerosis Complex
    Darcy Krueger MD; Cincinnati, OH

12. Excess Stroke Risk in Adult Survivors of Childhood CNS Tumors, Leukemia and Hodgkin’s Lymphoma: Results of the Childhood Cancer Survivor Study
    Sabine Mueller MD; San Francisco, CA

13. Therapeutic Hypothermia is Correlated with Seizure Absence in Perinatal Stroke.
    Mary Jo Harbert MD; San Diego, CA

14. Efficacy and Safety of Clobazam for Seizures Associated with Lennox-Gastaut Syndrome (LGS): Results of a Phase III Study
    Joan Conry MD; Washington, DC

15. Emergency Management of Febrile Status Epilepticus: Results from the FERSTAT Study
    Syndi Seinfeld MD; Richmond, VA

16. Answering Parents’ Important Questions after their Child has Status Epilepticus
    Peter Camfield MD; Halifax, NS

11:00 AM – 11:10 AM
Arnold Gold Humanitarian Award: TBA
Shaul Harel, MD, Tel Aviv, Israel

11:10 AM – 11:40 AM
Philip R. Dodge Young Investigator Award Lecture
Congenital Myopathies: Swimming toward treatments
James Dowling, MD, PhD; University of Michigan, Ann Arbor, MI

11:45 AM – 12:30 PM
Bernard Sachs Lecture
Adaptive Connectivity in Developing Brain
Laura Ment, MD; Yale University School of Medicine, New Haven, CT

11:30 AM – 4:00 PM
Exhibits

12:45 PM – 2:00 PM
Moderated Poster Session

Moderators:
Bradley Schlaggar, MD, PhD, Washington University, St. Louis, MO; Janet Soul, MD; Children’s Hospital of Boston, Boston, MA
17. Molecular Mechanisms Underlying Hypoxia-induced White Matter Injury during Early Post-natal Brain Development  
Andrea Pard MD; Cincinnati, OH

18. EEG Pattern Following Hypothermic Circulatory Arrest Predicts Subsequent Seizures  
Laurie Seltzer MD; Rochester, NY

19. Safety and Utility of Prolonged Video-EEG Monitoring in a Tertiary Pediatric Epilepsy Monitoring Unit  
Daniel Arrington MD; Phoenix, AX

20. Efficacy of the Ketogenic Diet for Lennox Gastaut Syndrome  
Monica Lemmon MD; Baltimore, MD

21. Neurofibromatosis Type 1 associated Cardio-Vasculopathy in Children: An Emerging Entity  
PS Ghosh MD; Cleveland, OH

22. Characterization and Clinical Correlates of Corpus Callosum Dymorphology in Smith-Lemli-Opitz Syndrome (SLOS)  
Ryan Lee MD; Baltimore, MD

23. Clinical Clues to Differentiating Genetic versus Non-Genetic Etiologies of Childhood Ataxias  
Ruba Benini MD; Montreal, QC

24. Can we Diagnose Pediatric Multiple Sclerosis (MS) After the First Event and the first MRI?: Retrospective Application of 2010 MS Diagnostic Criteria to a Pediatric MS cohort  
Thitiwan Simasthien MD; Birmingham, AL

12:45 – 2:00 PM: Lunch & Poster/Exhibit Walkaround

2:15 – 4:45 PM: Symposium IV: Muscle and Neuromuscular Junction Disease of Infancy: diagnosis and emerging treatments  
Organizer: Katherine Mathews, MD; University of Iowa, Iowa City, IA  
Speakers: Congenital Myopathies in 2011: from bedside to bench and back  
James Dowling, MD, PhD, University of Michigan, Ann Arbor, MI  
Congenital Myasthenic Syndromes: clinical and molecular understanding  
Duygu Selcen, MD; Mayo Clinic, Rochester, MN  
Congenital Muscular Dystrophies: recognition and diagnosis  
Katherine Mathews, MD  
Molecular Therapeutic Approaches to the Congenital Muscular Dystrophies  
Carsten Bonnemann, MD; NINDS, Bethesda, MD

Junior Member Seminar  
Organizer: Steven P. Miller, MDCM, University of British Columbia, Vancouver, BC

7:00 – 11:00 PM: RECEPTION AND BANQUET

SATURDAY, OCTOBER 29

7:00 – 8:30 AM: CONTINENTAL BREAKFAST AND SEMINARS  
Breakfast Seminar 7: Non-invasive Brain Stimulation in Children: neurophysiology and therapeutics  
Organizer: Adam Kirton, MD; Alberta Children's Hospital, Calgary, AB  
Speakers: Standard and Newer Applications of TMS in Children: an overview of TMS procedures and their applications, safety and tolerability  
Donald Gilbert, MD; Cincinnati Children's Hospital, Cincinnati, OH  
Measurement and Modulation of Developmental Plasticity in Pediatric Stroke Using TMS  
Adam Kirton, MD  
Update on TMS in Clinical and Experimental Epilepsy  
Alexander Rotenberg, MD; Children's Hospital of Boston, Boston, MA

Breakfast Seminar 8: Neurologic Sequelae of Pediatric Brain Tumors  
Organizer: Nicole Ullrich, MD; Children's Hospital of Boston, Boston, MA  
Speakers: Acute and Long-term Neurosensory Sequelae  
Roger Packer, MD; Children's National Medical Center, Washington, DC  
Brain Tumors and Epilepsy  
Elizabeth Wells, MD; Children's National Medical Center, Washington, DC  
Cerebrovascular Disease in Childhood Cancer Survivors  
Sonia Partap, MD; Stanford University, Stanford, CA  
Long-term Neurocognitive Outcomes in Survivors of Childhood Brain Tumors  
Nicole Ullrich, MD

Breakfast Seminar 9: Autism: a practical review for the practitioner  
Organizer: Ann M. Neumeyer, MD; Massachusetts General Hospital, Boston, MA  
Speakers: Autism: Clinical Phenotype and Medical Management  
Ann M. Neumeyer, MD
Autism Treatment Network Guidelines for Diagnostic Testing in Autism
Reet Sidhu, MD; Columbia University, New York, NY

Neurometabolic Disorders and Autism
Katherine Sims, MD; Massachusetts General Hospital, Boston, MA

Autism Research: current theories and evidence
Andrew Zimmerman, MD; Massachusetts General Hospital, Boston, MA

8:45 – 9:30 AM
Hower Award Lecture
Research that has Changed Clinical Practice in Child Neurology
Deborah Hirtz, MD; NIH/NINDS, Bethesda, MD

9:45 AM – 12:15 PM
Symposium V: Progressive Encephalopathies in Children: international perspective
Organizer: Kenneth Mack, MD, PhD; Mayo Clinic, Rochester, MN

Speakers:

- Neurologic and Neurobehavioral Complications in Children with HIV-1 Infection
  Jo Wilmshurst, FCPaed(SA), MD; University of Cape Town, Cape Town, South Africa
- Subacute Sclerosing Panencephalities: progressive and not so rare
  Professor Banu Anlar; Hacettepe University, Ankara, Turkey
- Progressive Encephalopathies Due to Lysosomal Storage Disease
  Marc Patterson, MD; Mayo Clinic, Rochester, MN
- An Approach to Vitamin/Cofactor-Responsive Encephalopathies
  Ingrid Tein, MD, FRCP(C); The Hospital for Sick Children, Toronto, ON

Questions and Panel Discussion
2011 ACNN CONFERENCE PROGRAM
Westin Savannah Harbor Golf Resort & Spa Savannah, GA
October 25–28, 2011

Tuesday October 25, 2011
7:00 pm–9:00 pm   ACNN Welcome Reception (Nurses only)

Wednesday October 26, 2011
7:00 am–8:00 am   Registration and Continental Breakfast
8:00 am–8:15 am   Welcome and Introduction
8:15 am–9:00 am   Janet Brucker Keynote Address Transition to Adult Care.
Rhonda Werner MS, RN, PCNS-BC
9:05 am–9:50 am   Consequences of Prolonged Febrile Seizures in Childhood.
Christine O’Dell RN, MSN; Kathryn A. O’Hara RN
9:50 am–10:05 am  Break
10:05 am–10:50 am  Botulinum Neurotoxin for the Treatment of Spasticity under
Rashida Brookins BS, RN; Robyn Neft CRNP
10:55 am–11:35 am  Anti-N-Methyl-D-Aspartate Receptor (NMDAR) Encephalitis:
Marian Kolodgie, MSN, CPNP
11:40 am–12:10 pm  Awards Presentation and Business Meeting
12:10 pm–1:00 pm   Lunch
1:00 pm–1:45 pm   Inflicted Traumatic Brain Injury: Child Abuse.
Gretchen Delametter, RN, MSN, CPNP-AC, CNS
1:45 pm–2:30 pm   Designing and Implementing a Trial in a Rare Disease:
Batten Disease as a Model. Amy Vierhile RN, MS, C-PNP
2:30 pm–2:45 pm   Break
2:45 pm–3:30 pm   Pediatric Neurological Trauma. Janet M. Brucker MS, RN
3:30 pm–4:15 pm   Take two of these and call me in the morning:
Dona Clarin MSN, FNP
Diagnosis and treatment of headaches in the pediatric population.
4:15 pm–4:30 pm   Wrap-up and Evaluations

Thursday, October 27, 2011
12:00 pm–12:30 pm  Roundtable Discussions and Lunch
12:30 pm–1:00 pm   Vitamin D Insufficiency in Children with Epilepsy.
Carole C. Atkinson MS, PNP-BC, CNRN
1:00 pm–1:30 pm   Psychogenic Nonepileptic Seizures: A Unique Model for Care.
Debbie Terry CNP
4:30 pm       5K Run/Walk fundraiser for ACNN/CNF Nursing Research Grant.

Friday, October 28, 2011
12:00 pm–1:30 pm   Lunch
The Ketogenic Diet: A Multicenter Perspective.
Maria Zak MN, NP-Peds and Panel - Eric Kossoff MD,
Elizabeth Donner MD, Claire Chee RN,
Cheryl Cahill RN, MSN, Valerie Chan RN, BScN, CNN(C)

Note: The ACNN conference program is geared for nurses, but all CNS meeting registrants are
welcome to attend any of the presentations. Nursing CE contact hours will be provided.
Platform Session 1: (#1–8)

1. Autism and agenesis of the corpus callosum (AgCC): chromosomal copy number variants (CNV) point to etiologic linkage

Sherr E (San Francisco, CA), Sajjan S (Seattle, WA), Fernandez L (San Francisco, CA), Gleeson J (Philadelphia, PA), Hakonarson H (Philadelphia, PA), Dobyns W (Seattle, WA)

Background & Objectives: One major causative mechanism hypothesized for autism is disruption of long-range cortical connectivity. AgCC is a common CNS malformation, for which autism or autistic symptoms are not infrequent and many patients have alterations in other major white matter tracts, suggesting global cerebral connectivity impairment. We hypothesized that AgCC patients would have a high burden of rare de novo CNVs and that these CNVs would overlap with those found for autism.

Methods: We identified and classified AgCC patients as part of an ongoing IRB approved study. Blood samples were obtained from proband and parents. DNA was extracted and run on an Illumina 610 Quad Chip array. Data were analyzed using PennCNV.

Results: 272 patient samples were run and high quality data were obtained from 96%. These data were compared against 1953 ethnically matched controls. We compared both CNVs binned by size and grouped by associated genes. Rare deletion CNV’s larger than 500 kb were significantly associated with AgCC patients as compared to controls (OR = 14.33; corrected p-value = 0.000016). We also analyzed the enrichment of genes within CNV’s previously associated with autism and found that CNV deletions in AgCC patients were significantly correlated with CNV duplications in autism (OR = 9.74; corrected p value = 0.0062).

Conclusions: Large CNV’s are commonly found in AgCC patients and there is a specific enrichment of autism genes with AgCC CNV’s. These data support a strong etiologic link between autism and AgCC and likely shared molecular and developmental pathways.

2. Regulation of ASTN1 receptor endocytosis and trafficking by Nisch2 reveals an important role for these processes in CNS neuronal migration.

Fryer R, Fang Y, Hatten MB (New York, NY)

Objective: Genes involved in receptor trafficking have recently been implicated in human brain malformations. Our objective is to characterize how Nisch2, a protein related to the sorting nexin family, regulates neuronal migration.

Methods: We used an in vitro migration assay with primary cultures of postnatal day 6 (P6) cerebellar granule neuron precursors (GNPs), and an in situ migration assay using P6 cerebellar slice cultures to evaluate the effects of Nisch2 gene dosage on neuronal migration. We transfected HEK293 cells with several different surface receptors and screened for an interaction with Myc-tagged Nisch2 by immunoprecipitation. Then, we used flow cytometry to measure surface expression of Astrotactin 1 (ASTN1) in HEK293 cells cotransfected with Nisch2 constructs. For live cell imaging of ASTN1 trafficking, we electroporated GNP's with ASTN1 tagged with a photoactivatable GFP, and followed its trafficking in the neuron after photoactivation.

Results: Gene dosage studies show that Nisch2 negatively regulates migration of GNP's in both in vitro assays and in cerebellar slice cultures. In HEK293 cells, overexpression of Nisch2 leads to an increase in surface ASTN1, suggesting that Nisch2 either enhances recycling of ASTN1 to the surface or inhibits its removal from the surface by endocytosis. Using the photoactivatable GFP reporter in neurons, we report that Nisch2 overexpression attenuates the internalization and trafficking of ASTN1.

Conclusions: Nisch2 is a novel gene that regulates ASTN1 receptor trafficking, allows for the correct positioning of neurons in the cerebellar cortex, and provides further evidence for the important role of receptor trafficking in neuronal migration.

3. Combination treatment with Docosahexaenoic Acid (DHA) and hypothermia preserves sensorimotor function after hypoxic-ischemic brain injury in neonatal rats

Barks JD, Berman DR, Mozurkewich E, Liu Y, Shangguan Y, Silverstein FS (Ann Arbor, MI)

Objective: Hypothermia is widely used for treatment of neonatal encephalopathy, but over 40% of treated neonates have poor outcomes; additional treatments are needed. DHA is a polyunsaturated fatty acid with neuroprotective properties in diverse experimental models. In rodents, maternal diets, enriched in DHA during pregnancy and lactation, confer resistance to neonatal hypoxic-ischemic (HI) brain injury in their progeny. Similarly, acute DHA injection, prior to HI lesioning, improves outcome in immature rodent models. This study evaluated combination post-HI treatment with DHA and hypothermia in a neonatal rodent HI brain injury model.

Methods: Seven-day-old (P7) rats (n=18/group) underwent right carotid artery ligation followed by 8% oxygen exposure (90 min). 15 min later, they received injections of DHA (2.5 mg/kg, complexed to albumin) or albumin (ALB). 1 hour (h) later, all underwent hypothermia (HT; 3h, 30°C). Sensorimotor function was assessed up to P28 with vibrissae-stimulated forepaw placement and grip strength measurements; without treatment, lesioning results in quantifiable left forepaw functional deficits.

Results: In the ALB+HT groups, left forepaw function was impaired; performance was close to normal in the DHA+HT groups (left forepaw placement scores on P21: 4.4/10±1.8 vs. 9/10±0.2; on P28: 4.2/10±1.8 vs. 9.6/10±0.5, p<0.001, ANOVA; left/right grip strength ratios: P21: 0.47±0.23 vs. 0.96±0.15, P28 0.5±0.09 vs. 0.92±0.23, p<0.001, ANOVA). The severity of right cerebral hemisphere brain damage was also reduced but to a lesser degree (by 12±3%, p<0.03, t-test).

Conclusions: DHA+HT combination treatment preserved sensorimotor function and modestly reduced brain damage. Early DHA treatment may augment hypothermic neuroprotection in neonates with hypoxic-ischemic encephalopathy.

4. Restricted diffusion in the splenium of the corpus callosum in neonates with hypoxic-ischemic encephalopathy, is a predictor of neurodevelopmental outcome

Fons C, MacLean A, Gregas M, Condie L, Soul J, Volpe J, Grant PE, Khwaja OS (Boston, MA)

Objective: To determine if early restricted diffusion in splenium of the corpus callosum (SCC) is related to poor neurodevelopmental outcome in newborns with hypoxic-ischemic encephalopathy (HIE). Analyze the risk factors and MRI injury pattern associated to SCC restricted diffusion.

Methods: Term newborns with clinical diagnosis of HIE and MRI including DWI performed < 1 week of life,
between 2006–2010, were selected. Outcome was assessed by Gross Motor Function Classification System (GMFCS) and Bayley-III Scales. Poor outcome was considered when Bayley cognitive and language composite scores <50, GMFCS scores = IV-V, and death. Statistical analysis was performed using binary logistic regression.

**Results:** 55 newborns with HIE were selected. Mean gestational age: 39 weeks and mean birth weight: 3.280 grams. Mean age at MRI was 4 days. SCC restricted diffusion was evident in 29 patients (52.7%). Neonatal seizures were significantly associated to SCC restricted diffusion (p=0.011) as were parietal, temporal, occipital, diffus cortex/subcortical white matter, and posterior watershed restricted diffusion (p<0.05). Treatment with hypothermia was associated to decreased risk of SCC restricted diffusion. Outcome in was good (31) and poor (24). Mean age at last follow-up was 17.39 months. Restricted diffusion in basal ganglia (p=0.003) and corticospinal tract (p=0.0040) were significantly associated with poor outcome but not SCC diffusion abnormalities.

**Conclusions:** Restricted diffusion in SCC is not correlated with poor outcome in HIE patients. Treatment with hypothermia decreases the risk of SCC diffusion abnormalities in this population. Vulnerability of SCC seems to be secondary to parietal, occipital and temporal white matter injury.

5. Elevated concentrations of inflammation-related proteins in postnatal blood predict severe developmental delay at two years in extremely premature infants

**Objective:** Perinatal inflammation is associated with neurological and developmental impairments. We hypothesized that elevated levels of inflammation-related proteins in early postnatal blood would predict impaired mental and motor development among extremely preterm infants.

**Methods:** We measured concentrations of 25 inflammation-related proteins in blood collected on postnatal days 1, 7, and 14 from 939 infants born before 28 weeks gestation. An elevated level was defined as a concentration in the highest quartile for gestational age and day of blood collection. We identified impaired mental and motor development at 24 months of age using the Bayley Scales of Infant Development. The primary outcomes were scores on the Mental or Motor Scale below 55 (more than 3 standard deviations below the mean).

**Results:** For 17 of the 25 inflammation-related proteins studied, one or more statistically significant associations (p < 0.01) was found between an elevated blood level of the protein and a developmental impairment. Protein elevations on multiple days were more often associated with developmental impairment than elevations present for only one day. More associations were found for protein elevations in day-14 blood than in day-7 blood. No associations were found for elevations in day-1 blood.

**Conclusion:** In extremely preterm infants, elevated levels of inflammation-related proteins in blood samples collected on postnatal days 7 and 14 are associated with impaired mental and motor development at age two years. Elevations of inflammation-related proteins, especially when persistent, appear to be involved in the pathogenesis of developmental impairments associated with extreme prematurity.

**Funding:** National Institute of Neurological Disorders and Stroke (U01 NS040069) and National Institute of Child Health and Human Development (P30 HD018655).

6. Genetic risk factors for cerebral palsy: a population-based study

**Objective:** To determine whether polymorphisms previously implicated in CP are associated with CP in a large California birth cohort.

**Design/Methods:** This case-control study is nested within a cohort of 334,333 infants born at ≥ 36 weeks gestation within Kaiser Permanente Medical Care Program, 1991–2002. We included only non-Hispanic whites. Case patients (N=138) were identified from medical records to have spastic or dyskinetic CP not caused by a developmental abnormality who had a neonatal blood spot available for study. Control patients (N=165) were randomly selected from the population. We genotyped 15 polymorphisms previously associated with elevated CP risk.

**Results:** The inducible nitric oxide synthase (iNOS) -231 polymorphism (OR 1.8, 95% CI 1.1–2.9) and the apolipoprotein E (apoE) ε4 allele (OR 1.7, 95% CI 1.04–2.8) were associated with increased CP risk. The association between the apoE ε4 allele and CP was evident only among patients with perinatal arterial stroke (OR 3.9, 95% CI 1.6–9.4). Heterozygosity at the MTHFR 677 polymorphism was associated with a reduced risk of CP (OR 0.4, 95% CI 0.2–0.9).

**Conclusions:** Most previous genetic associations with CP were not confirmed in our cohort. Variants in the iNOS and apoE gene may be associated with a modest increase in risk of CP, though these findings require further confirmation.

7. Effect of prenatal MgSO4 on head ultrasound imaging in preterm infants

**Objective:** To identify differences in neonatal head ultrasound (HUS) images between preterm infants exposed to magnesium sulfate (MgSO4) before delivery and unexposed controls.

**Methods:** As part of a clinical trial to evaluate whether MgSO4 given to mothers at risk of preterm delivery (< 32 weeks gestation) reduces the risk of CP in the offspring, HUS were done within the first week, at 21–28 days, and at 35–40 weeks projected gestational age. All images were independently reviewed centrally by 3 expert pediatric radiologists masked to clinical outcomes, and HUS abnormalities were quantified.

**Results:** 1832 infants had at least one HUS; 1519 had both an early and later HUS. 465/1832 (25.4%) had at least one of the following abnormalities: echodensity, echolucency, ventriculomegaly or intraventricular hemorrhage (IVH). MgSO4 was associated with fewer echodensities on HUS compared with placebo (1.7% vs 3.5%), O.R. 0.48 (0.26,0.89). These rates were almost identical to the rates of moderate to severe CP in the survivors. This effect was present whether examined for early (OR 0.45; 95% CI 0.21, 0.98) or later HUS (OR 0.39; 95% CI 0.16, 0.98). Echolucencies, ventriculomegaly and IVH were not different between the MgSO4 and the placebo treated groups.
Conclusions: Exposure to MgSO4 before premature birth decreased the occurrence of echodensities but did not affect other HUS abnormalities. This finding may underlie the mechanism of magnesium neuroprotection against the risk of CP.

8. Early versus late external ventricular drainage in relation to outcome in preterm infants with posthemorrhagic hydrocephalus

Bassan H, Eshel R, Levi L, Constantini S, Beni-Adani L (Tel Aviv, Israel)

Posthemorrhagic hydrocephalus (PHH) following intraventricular hemorrhage (IVH) is the most ominous complication after preterm birth. Early serial lumbar punctures failed to prevent long-term sequelae and intraventricular fibrinolysis decreased death or severe disability but increased the risk for secondary hemorrhage.

Objective: To delineate the impact of early versus late external ventricular drainage (EVD) on the neurodevelopmental outcome of preterm infants with PHH.

Methods: In premature infants with PHH who underwent early (<25 days) versus late (>25 days) EVD, we administered a neuromotor examination and assessed developmental outcomes (Battelle Developmental Inventory II; mean score: 100, standard deviation: 15).

Results: We studied 33 infants, born between 25 to 32 weeks at a mean age of 68±20 months. In comparison to infants managed with late EVD (n=23), infants managed with early EVD (n=10) had improved scores of cognitive (78.6±24.5 vs. 63±13.4), adaptive (79±22.6 vs. 60±8.64), communication (95.4±27.52 vs. 72.6±21.24) and personal social (91±26.03 vs. 71.1±18.9) functions (p<0.05 for all preceding variables). The incidence of low motor scores, cerebral palsy, need for ventriculoperitoneal shunt, and neurosurgical complications were equal between the groups. Subgroup analysis, based on severity of injury preceding the evolution of hydrocephalus, suggested that early EVD was beneficial in infants with IVH without parenchymal involvement (n=14, p<0.05) and had no effects in infants with prior parenchymal injury (n=19, p=NS).

Conclusion: Early (<25 days) EVD is associated with reduced rates of cognitive, communication and social disabilities in infants who had PHH without a preceding parenchymal injury.
Platform Session 2: (#9–16)

9. Lovastatin normalizes the brain spontaneous low-frequency fluctuations in children with neurofibromatosis type 1

Achira MT (Washington, DC), Chabernaud C (New York, NY), Mennes M (New York, NY), Kardel P (Washington, DC), Gaillard WD (Washington, DC), Kallel-Lefevre ML (Fairfax, VA), Van Meter JW (Washington, DC), Packer RI (Washington, DC), Milham MP (New York, NY), Castellanos FX (New York, NY)

Objectives: In the NF1 mouse model, lovastatin improves cognitive deficits. As part of a Phase 1 safety open label trial, seven participating children with NF1 underwent fMRI scans pre- and post-treatment. We present the examination of functional connectivity (FC) in Default Network (DN) architecture, which has been implicated in typical brain maturation.

Method: Participants underwent a 7-minute EPI scan at baseline and after treatment. Task-induced variance from the event-related data was removed leaving only “continuous resting-state” data. The task-related BOLD response was modeled to regress out the associated variance. Functional connectivity analyses were carried out on this “resting-state” signal using DN regions of interest. For each individual and age-matched healthy control, voxel-wise correlations were calculated for the time series of each seed, creating subject-level FC maps. Group-level analyses used a random-effects analysis.

Results: Lovastatin increased positive RSFC within DN regions along the anterior-posterior axis, with significant increase of long-range positive relationships between core regions along the anterior-posterior axis, with significant subject-level FC maps. Group-level analyses used a random-effects analysis.

Conclusions: Lovastatin administration in this sample appeared to normalize anterior-posterior and local FC within the DN. The pattern of results is consistent with normalization of developmental processes and apparent benefits in a mouse model. Interpretation is tentative because of the sample size; however, these results warrant that continued examination of the potentially beneficial effects of lovastatin in NF1.

10. Deep brain stimulation demonstrates partial amelioration of motor dysfunction in a mouse model of Rett syndrome

Arehart EJ, Leiter JC, Green AI (Lebanon, NH)

Objective: Rett syndrome (RTT) is a genetic disease that disrupts brain maturation leading to severe mental retardation and motor impairment in females. Neurotransmission imbalance is thought to play a critical role in pathogenesis. Recent work in animals suggests the process may be reversible. High frequency stimulation (HFS) of the brain modulates neural circuits and neurotransmitter release. We propose that HFS will reverse motor impairment in a mouse model of RTT, possibly by restoring balanced neurotransmission.

Methods: Deep brain stimulation (DBS) uses electrodes implanted in the brain and HFS to modulate neural circuits. Eighteen MECP-2 null mice underwent surgical bilateral electrode implantation in the striatum and were randomized to three treatment groups: six were treated with HFS for 15 min/day, six were treated with HFS for one hour/day, and six received surgery, but did not undergo HFS. Six MECP2 null mice and six WT mice did not undergo surgery and served as positive and negative controls. Animals were evaluated using the wire-hang test, open field test, daily weight and disability score.

Results: Mice treated with HFS as compared to litter-matched controls demonstrated improved neuromuscular performance (p<0.001), improved mobility (p<0.002), improved weight gain (p<0.002), a decrease in their general disability score (p<0.01), and increased survival (p<0.001). The performance improvements lasted for twenty-four hours after the period of DBS.

Conclusion: This work represents the first use of HFS to treat RTT and may eventually lead to clinical investigations of DBS in children with RTT to improve their long-term function and survival.

11. Everolimus showed long-term efficacy and safety in the extension phase of a prospective, open-label, phase I-II study of patients with subependymal giant-cell astrocytomas associated with tuberous sclerosis complex


Objective: To study long-term safety and efficacy of everolimus treatment in patients with subependymal giant-cell astrocytomas (SEGA) associated with tuberous sclerosis complex.

Methods: Long-term extension of a prospective, open-label, phase I-II trial in patients who received everolimus starting at 3 mg/m2/day for treatment of SEGA.

Results: Study cut-off was 31-Dec-2010, at which time 25 of 28 patients initially enrolled were still receiving everolimus. SEGA volume was reduced from baseline by 63% at 12 months, 79.2%, 64.7%, and 77.8% and by 80% in 50%, 41.2%, and 55.6% of patients at 24, 30, and 36 months, respectively. The performance improvements lasted for twenty-four hours after the period of DBS.

Conclusion: Everolimus showed long-term efficacy and safety in the extension phase of a prospective, open-label, phase I-II study of patients with subependymal giant-cell astrocytomas associated with tuberous sclerosis complex.

12. Excess stroke risk in adult survivors of childhood CNS tumors, leukemia and Hodgkin’s lymphoma: results of the Childhood Cancer Survivor Study

Mueller S (San Francisco, CA), Fullerton HJ (San Francisco, CA), Stratton K (Seattle, WA), Leisenring W (Seattle, WA), Weather RS (Houston, TX), Stovall M (Houston, TX), Armstrong GT (Memphis, TN), Goldby RE (San Francisco, CA), Packer RI (Washington, DC), Robison LL (Memphis, TN), Krall KR (Memphis, TN)

Objective: To assess predictors and long-term incidence rates of stroke in childhood cancer survivors.
Methods: The Childhood Cancer Survivor Study is a multi-institutional cohort study of childhood cancer survivors (alive ≥ 5 years after diagnosis), with a sibling comparison group. The age-adjusted incidence rates of self-reported first-stroke were calculated for brain tumor (n=1876), leukemia (n=4830) and Hodgkin's disease (HD) (n=1927) survivors, and compared to siblings (n=4023) using multivariable Poisson regression models. Multivariable Cox Proportional Hazards models were used to identify independent predictors of stroke.

Results: A total of 125 brain tumor, 71 leukemia and 44 HD survivors reported a stroke. The age-adjusted stroke rate per 100,000 person-years at age 22 was 279 (95% C.I. 199–391) for brain tumor survivors, 49 (95% C.I. 31–77) for leukemia, and 23 (95% C.I. 8–72) for HD, compared to 8.2 (95% C.I. 3–21) for siblings. Brain tumor survivors had 17.9% lifetime stroke risk (95% CI 17.1–20.1) after 10 years compared to 14.2% (95% C.I. 10.5–18.3) after 30 years.

Conclusions: Children with brain tumors, leukemia or HD have an increased stroke risk, and this excess risk persists for decades after diagnosis.

13. Therapeutic hypothermia is correlated with seizure absence in perinatal stroke.

Harbert MJ (San Diego, CA), Tam EWY, Glass HC, Bonifacio SL, Haeusslein LA, Barkovich AJ, Jeremy RJ, Glidden DV, Ferriero DM (San Francisco, CA)

Objective: We studied seizure occurrence, neurodevelopmental outcome, and the effect of therapeutic hypothermia in perinatal stroke presenting with encephalopathy.

Methods: A nested case-control study was performed within a single-center prospective cohort study of neonatal encephalopathy from 1994–2010. Cases of focal stroke were identified. Each case was matched on the basis of gender and degree of encephalopathy to two controls from the study cohort. The cumulative incidence of stroke in brain tumor survivors treated with 50+ Gy was 1.3% (95% C.I. 0.4–2.1) after 10 years compared to 14.2% (95% C.I. 10.5–17.9) after 30 years.

Conclusion: Children with brain tumors, leukemia or HD have an increased stroke risk, and this excess risk persists for decades after diagnosis.

14. Efficacy and safety of Clobazam for seizures associated with Lennox-Gastaut Syndrome (LGS): results of a Phase III study

Conry JA (Washington, DC), Ng YT (Phoenix, AZ), Drummond R, Stolle J, Owen JR, Weinberg MA (Deerfield, IL)

Objectives: To demonstrate the efficacy and safety of clobazam for LGS, we conducted a Phase III controlled trial.

Methods: Three oral dosages of clobazam were compared with placebo as adjunctive therapy for LGS. Following a 4-week baseline phase, patients who had ≥ 2 drop seizures per week were randomized to placebo or 1 of 3 dosages of clobazam (0.25, 0.5, 1.0 mg/kg/day), up to 40 mg/day maximum. Treatment included a 3-week titration, followed by a 12-week maintenance period. Primary endpoint was percentage decrease in mean weekly frequency of drop seizures during the maintenance phase (vs. baseline) for the modified intention-to-treat (mITT) population (all patients who had entered maintenance phase). Safety included physical examinations, laboratory evaluations, and AE information. Statistical significance was prespecified as p ≤ 0.01 for the primary endpoint.

Results: 301 patients were screened, 238 were randomized, 217 comprised the mITT population, and 177 completed the study. At baseline, patients' mean age was 12.4 years, and 60.5% were male. Demographics and clinical characteristics were similar between groups. There was a statistically significant decrease in mean weekly drop-seizure frequency for all three groups receiving clobazam vs. placebo: 68.3% for high dosage (p < 0.0001); 49.4% for medium dosage (p = 0.0015); and 41.2% for low-dosage (p = 0.0120), vs. 12.1% for placebo. Somnolence, lethargy, drooling, upper respiratory infections, and behavioral abnormalities were the most frequent treatment-emergent AEs reported for clobazam.

Conclusions: Clobazam 0.5 and 1.0 mg/kg/day statistically significantly decreased the weekly frequency of drop seizures associated with LGS. No new safety signals were observed vs. the Phase II study.

15. Emergency management of febrile status epilepticus: results from the FEBSTAT study

Seinfeld S (Richmond, VA), Pellock JM (Richmond, VA), Shinnar S (Bronx, NY), Sun S, Deng X (Richmond, VA), Hederffer D (New York, NY), O'Dell C (Bronx, NY), O’Hara K (Richmond, VA), Nordli D (Chicago, IL), Frank M (Norfolk, VA), Gallentine W (Durham NC), Moshe SL (Bronx, NY, FEBSTAT Study Team

Objective: To analyze pre-hospital and emergency department (ED) management of febrile status epilepticus (FSE).

Methods: Subjects were children age 1 month to 5 years who are part of a prospective, multicenter study of consequences of FSE which was defined as a febrile seizure or series of seizures without recovery in between lasting ≥ 30 minutes. We reviewed the emergency medical service (EMS) and ED management, including seizure recognition, medication administration and respiratory support. Preliminary data (93 of 200 patients) from two sites were analyzed. The remaining cases at the 3 other sites are currently being reviewed.

Results: EMS recognized a seizure on arrival 66% of the time. During EMS transport 92% of the patients had convulsions. The average time from seizure onset to initial dose of seizure medication by EMS or ED was 57 minutes. The mean seizure duration was 78 minutes when medication was administered prior to presentation to the ED and 99 minutes if no medication was administered (p value 0.12).
Seizure duration was longer in patients that received respiratory support (mean 115 vs 78 minutes, p-value 0.016).

**Conclusions:** FSE is a neurological emergency requiring prompt recognition and treatment. Seizure duration is related to the requirement of respiratory support. This study demonstrates a delay in FSE treatment. Studies of status epilepticus in adults have shown that early treatment reduces the need for respiratory support and ICU which emphasizes the urgency of early recognition and treatment. Supported by Grant NS 43209 (PI: S Shinnar MD PhD) from NINDS.

16. **Answering parents’ important questions after their child has status epilepticus**

_Camfield PR, Camfield CS (Halifax, NS)_

**Objective:** To answer 4 questions parents often ask about unprovoked status epilepticus.

**Methods:** The Nova Scotia Childhood Epilepsy Study (population-based) identified patients with ≥1 episodes of unprovoked status, focal epilepsy, normal intelligence and follow up ≥10 years.

**Results:** 156 cases had a mean follow up of 27±5 years with 1 death from status. 31 (20%) had ≥1 episodes of status. 15 had status as their first unprovoked seizure.

**Question 1. Will this happen again?** 20 (65%) had only 1 episode of status, 6 had 2, 5 had 3–10.

**Question 2. Will there be brain damage?** At onset 9/31 (29%) status patients and 27/124 (22%) non-status patients were clinically assessed to have learning disorders. At the end of follow up, 10 (32%) status and 41 (33%) non-status patients had learning disorders.

**Question 3. Will the epilepsy be harder to control?** As a proxy measure we assessed number of AEDs used throughout the clinical course – 14/31 (45%) status patients used ≤2 AEDs versus 76/124 (61%) non-status patients (p=0.1). The distribution of patients using 3–11 AEDs was similar.

**Question 4. Will the likelihood of remission be decreased?** Remission was defined as seizure-free without AEDs at the end of follow up. Excluding those with epilepsy surgery (3 status, 8 non-status) the remission rate for status patients was 15/28 (54%) versus 77/116 (66%) in non-status (p=0.2).

**Conclusions:** Despite its frightening and recurring nature, status epilepticus appears to have little influence on long term intellectual or seizure outcome of focal epilepsy in normally intelligent children. Parents may relax.
MODERATED POSTER SESSION

17. Molecular mechanisms underlying hypoxia-induced white matter injury during early postnatal brain development


Objective: White matter injury of prematurity (PWMI) is associated with a spectrum of neurological deficits ranging from mild cognitive and behavioral deficits to cerebral palsy. Previous studies have implicated impaired oligodendrocyte development as its primary cause, but the underlying mechanisms remain poorly understood. The goal of this study is to identify the molecular mechanisms for PWMI using a mouse model of hypoxia.

Methods: Postnatal (P) 7 mouse pups were exposed to hypoxia under two different conditions: 7.5% O2 for 60 minutes and 10% O2 for 180 minutes. We compared specification and differentiation of oligodendrocytes and subsequent myelin formation between hypoxia and sham animals at P9, P14 and P28 by examining the expression of key transcription factor regulators of oligodendrocyte differentiation, including Olig1, Olig2, Ascl1, Nkx2.2, and Sox10.

Results: During normal development, early postnatal (P0–P3) expression of Ascl1 defines the specification of oligodendrocyte progenitor cells, whereas the second peak of Ascl1 expression between P7 and P14 coincides with the induction of Nkx2.2 and cytoplasmic translocation of Olig1. These molecular events lead to terminal differentiation of oligodendrocytes and myelin gene expression in the white matter between P14 and P28. We found that hypoxia at P7 perturbs the second wave of Ascl1 expression, thereby delaying the subsequent progression of oligodendrocyte differentiation and myelin formation.

Conclusion: Our results suggest that Ascl1 is a target for hypoxic brain insult and its altered expression underlies impaired oligodendrocyte differentiation and hypomyelination in PWMI. Ascl1 could be a therapeutic target for prevention and treatment of PWMI.

18. EEG pattern following hypothermic circulatory arrest predicts subsequent seizures


Objective: To evaluate the pattern of recovery of electrical activity on EEG in neonates undergoing cardiac surgery and determine whether this pattern is predictive of short-term outcome.

Methods: A convenience sample of infants (n=40) >34 weeks gestation and ≤3 mo old who underwent cardiothoracic surgery at URMC 5/06-8/09. A baseline EEG was obtained, continuous video-EEG monitoring was started preoperatively and continued for 48 h after surgery. We qualitatively assessed electrographic patterns from the continuous video-EEG.

Results: Of these 40 infants, 19 patients had intraoperative EEGs that were isoelectric (110±41 min). All patients with isoelectric EEGs underwent deep hypothermic (20.95±2.05°C) circulatory arrest. Only 2 of the 40 infants had electrical seizures within 48 h postoperatively and both underwent deep hypothermic circulatory arrest. In both, their burst pattern during recovery had rhythmic, sharp components that were high amplitude and often asynchronous between the hemispheres. The time from development of the sharp burst pattern to onset of seizures was 29 h in one patient and 40 h in the second. This pattern was not seen during isoelectric recovery in infants who did not develop postoperative seizures. Patients without seizures had EEGs characterized by synchronous activity without sharp components.

Conclusion: The pattern of recovery on EEG from the isoelectric period in neonates undergoing cardiac surgery may be predictive of seizure development in the subsequent 48 h. The latency between recovery with sharp bursts to the onset of seizures is sufficient to consider preventative or neuroprotective treatment and can help in the management of infants during their recovery.

19. Safety and utility of prolonged video EEG monitoring in a tertiary pediatric epilepsy monitoring unit

Arington DK (Phoenix, AZ), Ng YT (Oklahoma City, OK), Troester MM, Kerrigan JF, Chapman KE (Phoenix, AZ)

Objective: Prolonged video-EEG (VEEG) monitoring is an invaluable tool. The adult literature demonstrates an increased risk of status epilepticus and injury during the examination. We review the safety and utility of our pediatric epilepsy monitoring unit (PEMU).

Methods: After IRB approval, we retrospectively reviewed 454 PEMU admissions over two years. Patient ages ranged from 11 days to 20 years. Demographic information, final event diagnoses, duration of events and medical complications were analyzed.

Results: 206 admissions (45.4%) captured epileptic seizures, 150 (33.0%) captured non-epileptic events (NEE), and 78 (17.2%) failed to capture any events. The average length of stay was 3.29 days. The patients had a mean age of 9.5 years with 213 males (47%). Medical complications included: one fall, one subdural fluid collection associated with grid placement, one patient with post-ictal psychosis, and one patient with hip pain following a seizure. No patients had any long-term complications; however, the patient with post-ictal psychosis significantly injured a nurse. Evaluating the rate of status epilepticus, defined as seizure lasting longer than 15 minutes, 10 patients had 12 episodes. This constituted 2.2% of all admissions and 4.8% of admissions with epileptic seizures. Evaluating the duration of events, the median was 26 minutes and the mean was 58 minutes. Two patients required transfer to the pediatric intensive care unit.

Conclusions: Compared to adult reports, our patients experienced a greater risk of status epilepticus but a lesser risk of medical complications. Overall, our study suggests that prolonged VEEG monitoring in the pediatric age group is a safe diagnostic procedure.

20. Efficacy of the Ketogenic Diet for Lennox Gastaut Syndrome

Lemmon ME, Terao NN, Rubenstein JE (Baltimore, MD), Ng Y (Phoenix, AZ), Knoff EH (Baltimore, MD)

Objective: The ketogenic diet (KD) is often used for children with Lennox-Gastaut syndrome (LGS) despite limited actual data specifically for that epilepsy syndrome. We analyzed both our center's experience treating this condition as well as the published literature.

Methods: The records of all children with LGS initiated on the KD at our institution from 1994-2010 were retrospectively reviewed. Inclusion criteria included the presence of 2-2.5 Hz spike-and-wave complexes on EEG, multiple seizure types, developmental delay, and age >1 year. In addition, we examined the published KD literature for cases of LGS and their outcomes.

Results: At our center, 71 children with LGS, age 1.5-18 years, were initiated on the KD. Children had been treated with a median of 7 anticonvulsants (range: 2-13). Using an intent-to-treat analysis, 53 children (75%) had >50% seizure reduction at 3 months; 20 (28%) reported >90% seizure reduction. At 6 months, 36 (51%) achieved...
>50% seizure reduction; 16 (23%) experienced >90% seizure reduction. Additionally, 30 (42%) were able to reduce concurrent AED use. Age, gender, presence of side effects, and history of infantile spasms were not predictive of >90% seizure reduction. In the literature, 94 (53%) of 176 reported children with LGS had >50% seizure reduction.

**Conclusion:** The ketogenic diet is efficacious in the treatment of LGS, with half of children responding within 6 months. These results confirm previous largely anecdotal clinical practice.

21. **Neurofibromatosis Type 1 associated cardiovasculopathy in children: an emerging entity**

Ghosh PS, Rotmier AD, Moodley M (Cleveland, OH)

**Objective:** Vasculopathy is a significant but under-recognized complication of Neurofibromatosis 1 (NF1). Its pathogenesis is poorly understood. The aim of our study was to recognize a complication of NF1.

**Objective:** Vasculopathy is a significant but under-recognized complication of Neurofibromatosis 1 (NF1). Its pathogenesis is poorly understood. The objective of our study was to recognize a complication of NF1.

**Methods:** Retrospective chart review of all patients with NF1 ≤ 18 years seen at the Cleveland Clinic over 10-year period. Patients were divided into 3 groups: (1) Cerebrovascular, (2) Cardiovascular (3) Other.

**Results:** Of 398 children with NF1, 26 (6.5%) had cardio-vasculopathy.

- Group 1: Ten (2.5%) had cerebrovascular abnormalities (mean age 12.8 years; 5 males), all had normal neurological examination. Presentation- headache (4), seizures (1), and asymptomatic (5).
- Group 2: Fifteen (3.7%) had cardiovascular abnormalities (mean age 6.6 years; 8 males). Presentation: hypertension (2), dyspnea (2), chest pain (1), syncope (1), murmur (6). Echocardiogram showed: pulmonary stenosis / occlusion of internal carotid artery -3, middle cerebral artery stenosis-2, posterior cerebral artery stenosis-1. Infarct noted in 1 on MRI brain. On follow-up (mean 5.2 years), 1 died of brain tumor, remaining 9 were neurologically intact. One with moyamoya disease underwent encephaloduroarteriomyosynangiosis.
- Group 3: Two girls had renal artery stenosis, both were hypertensive, 1 underwent surgical repair. In addition one had coarctation of aorta.

**Conclusions:** Children with NF1 should be carefully screened for cardio-vasculopathy so that timely and appropriate therapeutic and diagnostic interventions can be initiated.

22. **Characterization and clinical correlates of corpus callosum dysmorphology in Smith Lemli Opitz Syndrome (SLOS)**

Lee RWY, Yoshiha S, Mori S (Baltimore, MD), Gropman A, Baker EH, Porter FD (Washington, DC)

**Objective:** SLOS is a neurodevelopmental syndrome caused by mutations in 7-dehydrocholesterol reductase, resulting in excess 7-dehydrocholesterol (7DHC) and low cholesterol. Cholesterol is essential for embryonic hedgehog signaling, synaptogenesis, and axonal growth. Corpus callosum (CC) malformations are the most common neuroimaging abnormality in SLOS. This study is the first to characterize patterns of callosal morphology in SLOS, and hypothesizes that CC abnormalities correlate with biochemical and developmental measures.

**Methods:** 40 individuals with SLOS (20 males) between 0.20 and 25 years (mean 6.6 years; 8 males). Severity of dysgenesis was associated with higher SS and lower GMDQ, FMDQ and LQ (p<0.01).

**Results:** Significant correlations were found between CC area and 7DHC (p=0.53), GMDQ (p=0.38) and SS (p=0.33). CC length correlated with 7DHC (p=0.42), GMDQ (p=0.47), FMDQ (p=0.48), and LDQ (p=0.39).

**Conclusions:** For individuals with SLOS, CC area, length, and morphology correlated with levels of 7DHC, SS, and developmental delay in multiple domains. These findings suggest a relationship between biochemistry, CC morphology and developmental disability. Further studies will support biomarkers as predictors of neurodevelopmental outcome in SLOS.

23. **Clinical clues to differentiating genetic versus non-genetic etiologies of childhood ataxias**

Benini R, Ben Amor IM, Shevell M (Montreal, QC)

**Objectives:** Childhood ataxias are often categorized into inherited versus non-inherited etiologies. This study sought to identify what clinical features can help differentiate between these two etiologic groups at presentation.

**Methods:** A retrospective chart review analysis was conducted on 167 patients referred to neurology outpatient clinics for the evaluation of ataxia or ataxia-related symptoms. The frequency of clinical features, decided on a priori, was compared between the two etiologic categories.

**Results:** Out of the 167 cases, a larger proportion of patients were diagnosed with a non-genetic (89%, 148 patients) as opposed to an inherited cause (11%, 19 patients). The majority of patients in the non-genetic group (56%, 83/148) presented to medical evaluation earlier than 12 months from the onset of symptoms as opposed to those with inherited ataxias (31%, 6/19). In the genetic group, consanguinity (16% versus 4%) and a positive family history of first degree relative with similar symptoms (16% versus 2%) were more common. Symptoms of abnormal gait (95% versus 57%) and muscle weakness (47% versus 8%), as well as signs of abnormal muscle tone (63% versus 32%), abnormal reflexes (63% versus 16%), clonus (26% versus 9%), dysmetria (32% versus 5%), pes cavus (21% versus 1%), sensory deficits (16% versus 0%) and non-neurological musculoskeletal abnormalities (58% versus 19%) were more prevalent in patients diagnosed with inherited ataxia.

**Conclusions:** In conclusion, clinical features can help delineate between inherited and non-inherited causes of childhood ataxia and thereby guide physicians in the targeted evaluation of their patients.

24. **Can we diagnose pediatric Multiple Sclerosis (MS) after the first event and the first MRI? Retrospective application of 2010 MS diagnostic criteria to a pediatric MS cohort**

Simasathien T, Ness JM (Birmingham, AL)

In adults, early diagnosis of MS and implementation of disease modifying therapy (DMT) has been shown to reduce long term disability. 2001 McDonald criteria enabled serial cranial MRI (and revised in 2005 to include spine MRI) as a surrogate for dissemination in time and space after clinical
isolated syndrome (CIS). Revised 2010 MS diagnostic criteria now allows a single brain MRI with >1 T2 lesion in at least 2 regions and 1 enhancing lesion to fulfill dissemination in time and space. However, this streamlined diagnosis of MS has not been validated in pediatric demyelinating patients.

Objective: To determine the utility of revised 2010 MS diagnostic criteria in a pediatric MS cohort

Method: Retrospective chart review of MS patients <18 years who presented with CIS from 1998–2008 to assess whether the first MRI fulfilled 2010 MS diagnostic criteria

Results: The cohort consisted of 42 pediatric MS patients who presented with CIS (70% female, 40% African-American). Mean age at onset is 13.1 ± 0.5 years. Six patients presented with optic neuritis (5 unilateral, 1 bilateral). The rest presented with pyramidal or brainstem symptoms. No patients experienced encephalopathy. Applying 2010 criteria, 40% of this cohort (17/42) demonstrated dissemination in time and space on their initial MRI. There was no difference with respect to age, race or sex between patients fulfilling 2010 criteria and those who did not.

Conclusions: 2010 criteria could have allowed earlier diagnosis of MS in some patients. Further study is necessary to assess validity of these criteria in pediatric demyelinating patients.

POSTERS: Brain Tumors/ Oncology

B-1. Neurological complications of neuroblastoma

Objective: Describe the spectrum of neurological complications in neuroblastoma.

Method: We reviewed demographics and reasons for neurological consultation of patients with neuroblastoma (NB) seen between January 2006 and December 2010.

Results: Sixty-nine patients with NB (35 female; 48 stage 4; 27 MYCN amplified) had 71 consultations. Ages were 7 months to 27 years (median 37 months). Neurological manifestations prompted the diagnosis of NB in 18 patients: 8 with opsonoclousus-myxocluous syndrome (OMS) and 10 with epidural spinal cord disease (ESCD) and; identified relapse in 16 patients with central nervous system metastasis (CNSM). Nine patients with OMS had abnormal eye movement, limb tremor, ataxia and behavioral changes. Eighteen patients had ESCD; of these, 6 had paraparesis, 7 had parietal limb, 2 had painful limb and 4 had incidental finding on MRI (IF). Of fourteen patients with known brain metastasis 4 had headache, 1 had status epilepticus, 6 had focal deficit and 3 had IF. Of four patients with intracranial epidural metastasis 2 had headache and 2 IF. Of four patients with leptomeningeal disease 2 had headache, 1 had seizure and 1 was IF. Eleven patients were consulted for treatment complications: (6) metabolic encephalopathy, (3) headache, (1) femoral neuropathy and (1) leukencephalopathy. Ten had neurological conditions unrelated to cancer: (2) migraine, (2) febrile seizure and (8) others.

Conclusion: Our observations suggest ESCD and OMS are neurological manifestations present at initial diagnosis of NB while focal deficits and headaches in patients with known NB may indicate CNSM or treatment complications.

B-2. Morphological and neurocognitive sequelae following chemotherapy for leukemia in early childhood
Genschaft M, Hübner T, Plessow F, Krone F (Dresden, Germany), Ikonomidou V (Fairfax, VA), Abolmaali N (Dresden, Germany), Hofmann A (Chemnitz, Germany), Helfeld E (Cottbus, Germany), Vorwerk P (Magdeburg, Germany), Kramm C (Halé, Germany), Grubn Bi (Jena, Germany), Hernaiz-Driver P (Berlin, Germany), Sutter M, Hummel T (Dresden, Germany), Ikonomidou C (Madison, WI), Kirschbaum C, Smolka MN (Dresden, Germany)

The survival rate of patients with acute lymphoblastic leukemia (ALL), which comprises approximately 35% of pediatric cancers, is currently 80%. With improvement of survival rates we are increasingly faced with issues of therapy-related toxicity, including neurotoxicity. The goal of this investigation was to study long-term consequences of chemotherapy for ALL on the morphology of brain structures, cognitive functions, and smell.

We examined 19 ALL survivors and 19 age-matched controls, ages 15–22 years. All subjects in the patient group developed ALL prior to their 10th birthday and did not exhibit CNS involvement. They were treated with multiple intrathecal injections of methotrexate but did not receive radiation. Patients with recurrent disease were excluded from the study.

Based on T1 weighted magnetic resonance images (MRI) of the brain we analyzed changes of the volumes of grey and white matter. Volumes of subcortical structures were measured using FIRST (FMRIB’s integrated Registration and Segmentation Tool). Further comparisons were made using voxel-based morphometry (VBM). Investigations included neuropsychological assessment of hippocampus-dependent memory functions, executive functions, attention, and extensive tests of olfactory function.

Analysis revealed a significant reduction of the mean volumes of hippocampus, amygdala and the grey matter density in the putamen. Neuropsychological testing revealed significant impairments in verbal memory, ability to shield current action goals against distraction, sustained attention and increased impulsivity with continuous cognitive demand in the ALL group. No differences in olfaction were found.

These results suggest that ALL chemotherapy with intra-thecal methotrexate in patients younger than 10 years causes morphological and neurocognitive sequelae.

B-3. Headaches in children less than 8-years-old
Tarte CT, Zamarrripa AC, Rothner AD (Cleveland, OH)

Objectives: To determine the frequency of life-threatening headache etiologies in children less than 8-years-old and decide whether there is cause for concern in younger children with headache in the absence of an abnormal neurologic examination and/or evidence of increased intracranial pressure.

Methods: Charts of children less than 8-years-old, presenting with headache to the Cleveland Clinic from 2006–2008 were reviewed. Etiologies of headache in this age-group were compared to cohorts of young children previously published and presented.

Results: Our cohort included 100 children (male-to-female ratio 1:1; median age 5-years). Seventeen-percent of visits were to the emergency department, 27% to the general pediatric clinic and 53% to the pediatric neurology clinic. Nine children were excluded because of pre-existing neurologic conditions. Primary headache was diagnosed in 49/100, secondary headache in 41/100, and unknown cause in 1/100. Primary headache etiologies were migraine (28/49), non-classifiable headache (18/49), chronic-diary-headache (2/49), and tension-type headache (1/49). Secondary headache etiologies were viral or other non-life-threatening illnesses (37/41), brain tumor (2/41), concussion (1/41), and pseudotumor cerebi (1/41). Only 2/100 of children were diagnosed with life-threatening etiologies which were both brain tumors. One of these children had an abnormal
neurologic examination and the other had signs of increased intracranial pressure.

Conclusions: Based on our cohort and those reviewed in the literature, migraine is the most common headache type in children less than 8-years-old. The fear that headaches in young children are due to life-threatening etiologies is not supported without an abnormal neurologic examination or evidence of increased intracranial pressure.

B-4. Diminished ASL intracranial perfusion in children with Neurofibromatosis Type 1
Campen CJ, Rosenberg JK, Yeom KW (Stanford, CA)

Objective: Neurofibromatosis type 1 (NF1) a neurocutaneous syndrome affecting 1/3500 children is associated with moyamoya syndrome (MMS). However, no comparisons of cerebral perfusion in patients with NF1 and NF1-associated MMS to healthy controls exist. We hypothesize cerebral blood flow (CBF), as measured by magnetic resonance imaging (MRI) arterial-spin-labeled ASL, is diminished in children with NF1 compared to healthy controls, with the lowest levels seen in patients with NF1-associated MMS.

Methods: Twenty children aged 2-18 years with NF1, four with MMS, and 26 age-matched controls underwent ASL CBF on a 3T magnet. Pseudocontinuous-spin-echo-ASL technique was used. Measurements were taken bilaterally in cerebral cortical-subcortical regions, and the deep gray nuclei. Trends in measurements as a function of disease severity were evaluated with the Jonckheere-Terpstra test for ordered alternatives. A Bonferroni-adjusted p-value less than 0.0013 was considered significant.

Results: We identified 6/12 areas with significantly diminished ASL CBF (ml/100g/min) in patients with NF1 (midrange), and NF1-associated MMS (lowest) compared to healthy controls (highest). These included: the thalamus (left: p=0.0002, right: p=0.0004); superior/middle temporal lobes (left: p=0.0012, right: p=0.0009); temporopolar-occipital lobes (left: p=0.0006, right: p=0.0003); occipital poles (left: p=0.0009, right: p=0.0001); centrum semi-ovale (left: p=0.0022, right: p=0.0005); and left parietal lobe (p=0.0012).

Conclusions: Cerebral perfusion diminishes in a graded fashion in children with NF1 and NF1-associated MMS, particularly in the posterior circulation and the MCA-PCA posterior watershed zones. Future studies may demonstrate an important role for ASL in the presymptomatic diagnosis of cerebral vasculopathy, and the definition of NF1-related vasculopathy patterns.

B-5. Everolimus reduced seizure activity and altered the microarchitecture of CNS white matter in patients with tuberous sclerosis complex

Objective: Epilepsy is present in 70%-80% of patients with tuberous sclerosis complex (TSC). The current standard treatment for intractable epilepsy is surgical resection, effective in only 35%-45% of patients. A prospective, open-label, phase II trial (NCT00411619) of the selective mTOR inhibitor everolimus in patients with subependymal giant-cell astrocytoma (SEGA) associated with TSC assessed the effect of everolimus on seizure frequency and CNS white-matter microarchitecture as secondary endpoints.

Method: Patients aged ≥3 years (n=28) with documented SEGA growth received oral everolimus 3 mg/m²/day, titrated to achieve a target trough concentration of 5–15 ng/mL. Seizure activity was reported by patients at each clinic visit and by 24-hour video-electroencephalography (EEG) performed at baseline and at 6 months. Diffusion tensor imaging (DTI), used to assess change in the microarchitecture of brain white matter, was undertaken at baseline and after 12–18 months of everolimus therapy.

Results: Epilepsy data were available for 26 of the 28 patients enrolled in the study. At baseline 27% had daily seizures, which decreased to 8% and 4% after 6 and 12 months of everolimus therapy, respectively. EEG-recorded seizures (available for 16 patients) decreased from 6.30 seizures/24 hours at baseline to 2.75 seizures/24 hours at month 6 (P=0.022). DTI revealed increased fractional anisotropy and decreased radial and mean diffusivity in otherwise normal-looking white matter, indicating improved white matter integrity.

Conclusions: Seizure activity was decreased in patients with TSC receiving daily everolimus for ≥6 months. Everolimus was associated with significant changes to the microarchitecture of otherwise normal-appearing white matter.

B-6. Spectrum of neurological dysfunction in neurocutaneous melanocytosis
Ramaswamy V, Delaney H, Haque S, Marghoob A, Khakoo Y (New York, NY)

Objective: Neurocutaneous melanocytosis is a rare neurocutaneous syndrome defined by the presence of multiple congenital nevi and melanocytic deposits in the central nervous system. We sought to define the spectrum of central nervous system abnormalities in children with neurocutaneous melanocytosis.

Methods: Retrospective review of cases of neurocutaneous melanocytosis referred to the pediatric neurology service at our center between 2003–2010.

Results: Fourteen patients were identified, of which 8 are alive. Median age of death was 54 months (19–125 months), median age of survivors was 31 months (12–82 months) with one patient age 31 years lost to followup. Five out of 6 patients with diffuse leptomeningeal deposits died. Five patients were asymptomatic at last evaluation, and the mean age of presentation of neurological symptoms was 16.5 months (5 presented with epilepsy, 2 presented with hydrocephalus). One patient had normal neuroimaging however had focal seizures with focal epileptic discharges. Four patients presented to our center with leptomeningeal melanoma; three died and one was lost to followup. One patient had a Dandy Walker malformation. Three patients had dorsal holocord arachnoid cysts and one had a benign cervical spindle cell tumour. All three patients with dorsal arachnoid cysts were asymptomatic at a median age of 19 months (16–34 months), and had no progression on serial neuroimaging. Three patients had profound developmental delay; the other 11 patients were normal or had mild delay.

Conclusions: Children with neurocutaneous melanocytosis exhibit a wide range of intracranial and intraspinal abnormalities as well as a wide range of outcomes.

B-7. Cumulative cisplatin dose (CCD) does not correlate with event free (EFS) and overall survival (OS) outcomes in children with newly diagnosed average-risk medulloblastoma (ARMB) treated with cisplatin based adjuvant chemotherapy
Nageswara RAA (Washington, DC), Wallace D, Boyett J, Gajjar A (Memphis, TN), Packer R (Washington, DC)

Objective: Survival rates for children with medulloblastoma have risen over the past decade, in part due to the addition of cisplatin-containing post radiotherapy adjuvant chemotherapy. However, cisplatin is often associated with significant hearing loss related to the total cumulative dose. The
total dose of cisplatin required for optimal treatment in unknown. This study evaluated the association of survival outcomes and cumulative cisplatin dose (CCD) in children with newly diagnosed ARMB.

Methods: The study included 363 patients with ARMB, between 3 and 21 years of age, enrolled in a prospective study and treated with craniospinal radiation and cisplatin-based adjuvant chemotherapy.

Results: Eight-year EFS for all patients was 78.2±2.6%. Only 73 patients received the protocol specified CCD of 600 mg/m², primarily due to mandated cisplatin toxicity-related dose reductions. The median CCD given in those without relapse or death was 487.5 mg/m². Median follow-up for 306 patients alive at last follow-up is 8.9 years. Cox proportional hazards model showed that CCD, as a time-dependent covariate, was not associated with EFS (p=0.54). The 343 patients who did not fail during chemotherapy treatment were categorized according to CCD into four groups (N=10; 0–150 mg/m²), (N=26; 151–300 mg/m²), (N=113; 301–450 mg/m²), and (N=194; 451–600 mg/m²). There were no statistically significant differences in EFS (p=0.53) or OS (p=0.49) among these four groups.

Conclusions: Cumulative cisplatin dose does not correlate with EFS and OS. This study suggests that lower doses of cisplatin can be incorporated into future medulloblastoma protocols, possibly reducing toxicity without affecting survival outcomes.

B-8. Predicting recurrence in pediatric central nervous system low grade gliomas: the role of MRI surveillance in asymptomatic children
Utaka Y, Yeh-Nayre L, Levy M, Crawford J (San Diego, CA)

Objective: To determine clinical features associated with relapse or progressive disease in children diagnosed with primary CNS low-grade gliomas.

Background: Pediatric low-grade gliomas are the most common brain tumor of childhood. Little information is known with regards to clinical predictors of recurrent disease and optimal magnetic resonance imaging surveillance.

Methods: Retrospective analysis of 102 consecutive patients diagnosed at Rady Children’s Hospital San Diego between 1994–2010 with low-grade glioma exclusive of a diagnosis of Neurofibromatosis was performed. Clinical information with regards to tumor location, age, gender, and symptomatology were correlated with disease recurrence.

Results: Forty-four of 102 children diagnosed with low-grade glioma had evidence of recurrent or progressive disease between 2 months and 11 years (mean 27.3 months). Gross total resection was associated with improved progression free survival (p=0.012). Location of tumor (p=0.26), age at diagnosis (p=0.69), duration of symptoms (p=0.72), histologic subtype (p=0.74), gender (p=0.53) or specific chemotherapeutic treatment regimen (p=0.24) had no significance in predicting recurrence or progression. Sixty-four percent of children with progressive disease were asymptomatic and were diagnosed by surveillance MRI imaging alone. All patients diagnosed at less then 2 years of age were asymptomatic at recurrence (p=0.04).

Conclusions: The majority of children in our series were asymptomatic at the time of low-grade glioma recurrence. In particular, all children less than 2 years of age were diagnosed with recurrent or progressive disease by MRI surveillance imaging alone. Our study demonstrates the need for routine neuroimaging even in the case of gross total resection, especially in younger children.

B-9. TrkB and BDNF promote the survival of glioma cells
Blockus H, Song H-R (New York, NY)

Object: Neurotrophin receptor signaling pathways are critical in neurodevelopment. Expression of tropomysosin receptor kinase B (TrkB) has been implicated in the pathogenesis of a number of neuronal and non-neuronal tumors, however significance of this expression has not been determined in glioma. Here we examined the effect of brain-derived neurotrophic factor (BDNF) and its high-affinity receptor, TrkB, in the survival of glioma cells.

Methods: The expression of TrkB receptors was examined by RT-PCR, Western blotting, and immunostaining in glioma cells (U251), neurospheres derived from human glioblastoma, and primary human glioblastomas. Glioma cells were incubated in the presence or absence of BDNF with or without various concentrations of K252a. Cell lysates were analyzed for the expression of TrkB and BDNF and phosphorylation of Akt and MAPK by western blotting. Cell survival was evaluated using MTT assay.

Results: TrkB is expressed highly in human glioblastomas, glioma cells, and glioma neurospheres we examined. Stimulation of glioma cells with BDNF activates signaling proteins Akt and mitogen-activated protein kinase (MAPK). Glioma cells treated with BDNF promotes survival, while treatment with K252a, a Trk tyrosin kinase inhibitor, diminishes the ability to grow in culture in a dose dependent manner. Further, addition of BDNF protects from cell death induced by K252a and enhances the survival of glioma cells.

Conclusions: We demonstrate that BDNF activation of TrkB increases the survival of glioma cells in culture, suggesting that BDNF-TrkB signaling may be a potential therapeutic target in gliomas.
POSTERS: Case Studies

CS-1. What is the best way to treat immune mediated chorea encephalopathy?
Qureshi JS, Pereira AP, DeSousa C (London, UK)

Objective: Immune Mediated Chorea Encephalopathy Syndrome (IMCES) is a self-limiting condition, believed to have a post infection autoimmune cause, whereby all children make full recoveries with no recurrences. Since 2002, several more children have presented with the condition in the UK and internationally. Typical presentation includes an acute onset of choreiform movements, fever and behavioural change. Abnormal investigations show slow wave electroencephalography (EEG), oligoclonal bands in the cerebrospinal fluid and recently anti-N-methyl-D-aspartic acid (NMDA) receptor antibodies.

The aim was to determine treatment practices for IMCES in Great Ormond Street Hospital and ascertain a defined treatment protocol to encourage rapid recovery of patients.

Method: Patients included were up to 16 years of age. Data was obtained retrospectively by searching through the neuroscience discharge summary database from 2002.

Results: A total of 10 patients were found. Females were more likely to suffer from the condition than males with 70% and 30% respectively. Average age of onset was 5.1 years with a recovery time of 8.2 months. Only 1 patient was anti-NMDA receptor antibody positive. Patients given corticosteroids or intravenous immunoglobulin (IVIg) both took 18 months to recover while those without took just 6.7 months.

Conclusion: Only one patient has been tested to date for anti-NMDA receptor antibodies. It appears neither corticosteroids or IVIg are helpful in accelerating the recovery of patients. Symptomatic relief and supporting the patients in a psychosocial manner, appears appropriate. If a relationship between IMCES and anti-neuronal antibodies is established, then other treatment such as plasmapheresis could be trialled.

CS-2. Raised intracranial pressure: an unusual presentation of Pycnodysostosis with patent sutures
Alladi SK, Rittey C, Bahl A, Sinha S (Sheffield, UK)

Objectives: Pycnodysostosis is a rare autosomal recessive skeletal dysplasia caused by absence of active cathepsin K, that plays a role in degrading the organic matrix of bones. Intracranial hypertension represents a rarely reported life threatening complication. We describe two children with pycnodysostosis who presented with raised intracranial pressure.

Methods: We present clinical features, investigations and management conundrums of two children with pycnodysostosis.

Results
Case 1
A 6 year old Pakistani girl presented with visual deterioration, headache and papilloedema. Intraparenchymal pressure monitoring revealed raised pressure. CT revealed patent anterior and posterior fontanelles and lambdoid sutures. MR venography demonstrated narrowing of distal transverse and sigmoid sinuses.

Case 2
A 2½ year Pakistani boy presented with visual deterioration and papilloedema but no headache. ICP monitoring revealed raised intracranial pressure. CT scan showed fused sutures close to the base of skull. The cranial aspect of the lambdoid, coronal, metopic and sagittal sutures appeared open. Anterior fontanelle was widely patent. MRI showed a large left transverse sinus and small right transverse sinus without venous occlusion. Ventriculoperitoneal shunt was inserted. Following this papilloedema decreased and visual acuity improved.

Conclusion: Raised intracranial pressure is a rare complication of pycnodysostosis. The mechanism is uncertain as both widened cranial sutures and craniosynostosis can occur in this condition.

Management is challenging due to uncertainty about mechanism of raised intracranial pressure in the face of small ventricles and open fontanelle. Further research is required into the interplay between intracranial vault abnormalities, raised intracranial pressure and role of cathepsin.

CS-3. Microarray as a first genetic test in global developmental delay: a cost-effectiveness analysis
Trakadas Y, Shevell M (Montreal, QC)

Background: Microarray technology has a significantly higher clinical yield than karyotyping in patients with Global Developmental Delay (GDD). Despite this, it has not yet been routinely implemented as a screening test due to the perception that this approach is more expensive.

Methods: To address this, we evaluated the cost-effectiveness of array-CGH (aCGH) compared to karyotyping by retrospectively analyzing the cost of work-up in a cohort of 114 children representing a consecutive series of children diagnosed with GDD.

Results: The average increase in cost if aCGH had been performed instead of karyotyping as a first test was $442 per patient when performed by a private company (98% CI: $238-604). In contrast, $106 (98% CI: -$17; - $195) would have been saved if aCGH was done locally in a lab already possessing the required technology. The Incremental Cost per additional diagnoses was estimated to be $12,874 if aCGH was performed in a private lab, but less than $1,379 if performed locally.

Conclusion: aCGH would be cost-effective as a first genetic test in the clinical evaluation of patients with GDD.

CS-4. High resolution mapping of cat like cry in a subject with 5p terminal deletion
Young IR, Eun HC (Gwangju, South Korea)

We report on a five-year-old girl with speech delay referred for cytogenetics study. Karyotyping revealed terminal 5p deletion. Expectedcri du Chat syndrome’s features like facial dysmorphism and the signature cat like high pitched cry were not present. High resolution microarray analysis using cytogenetics whole genome 2.7M array (Affymetrix) showed terminal 8.9 Mb deletion of 5p. Previous studies have produced inconsistent results concerning the precise location associated with the manifestation of cat like cry. The controversial results are likely due to the limitation of analytical techniques used to assess the genotype. The Affymetrix 2.7M array provides whole genome backbone coverage of 1kb with the highest density of 2.7 million markers to enable superior resolution. Our finding suggested that the critical region for cat-like high pitched cry is located distal to 8.9 Mb region from the terminal of 5p.

CS-5. Does the absence of an abnormal imaging study define a specific cerebral palsy subtype?
Benini R, Dagenais L, Shevell M (Montreal, QC)

Objectives: Up to 16% of cerebral palsy (CP) children may have normal or non-specific neuroimaging.
Methods: A population-based registry (REPACQ) was used to identify what clinical factors could differentiate these patients from those with abnormal imaging.

Results: Of the 213 patients, 126 had MRI imaging available and were included in this study. 90 patients (51 males, 39 females) had abnormal imaging whereas 36 patients had normal/nonspecific findings (17 males, 19 females). Normal/non-specific imaging was more prevalent (p=0.001) in children with dyskinetic CP (72.7%, 8/11 patients) versus other CP variants (24.4%, 28/115 patients). In contrast, normal/non-specific MRI findings were less likely (p=0.002) in spastic hemiplegic CP (37.2%, 32/86 patients) versus other CP variants (10%, 4/40 patients). There were no significant differences (p>0.05) with respect to the prevalence of perinatal or postnatal clinical features nor clinical outcomes. Furthermore, 42% (15/36) of CP patients with normal/non-specific neuroimaging exhibited a high level of functional disability (GMFCS IV-V) as compared to 33% (30/90) patients with abnormal imaging.

Conclusions: Apart from confirming that normal/non-specific imaging is more prevalent in dyskinetic CP, no clinical features were identified to set these patients apart from those with abnormal imaging. This raises the question of whether more refined imaging techniques are needed in the evaluation of patients with normal/non-specific findings and whether genetic rather than gross structural lesions underlie the pathophysiology of CP in this subset. Furthermore, the high proportion of functional disability underlines the importance of continuous follow-up even in the absence of abnormal imaging.

CS-6. A case of idiopathic isolated hypoglossal nerve palsy in a Korean child
Lee JH (Changwon, Korea), Kim SK (Seoul, Korea), Choi KL (Changwon, Korea)

Hypoglossal nerve palsy (HNP) is an uncommon neurological abnormality and can provoke characteristic clinical signs, including unilateral atrophy of the tongue musculature. We present a case of a healthy 13-year-old Korean male who was admitted to the outpatient department of our institution with acute onset dysarthria, tongue fasciculations, and right-sided tongue weakness upon awakening. His evaluation included a virology work-up, neck CT, brain MRI and ENT consultation; all tests were normal and showed no evidence of inflammation. Fifteen days after the onset of symptoms, the patient recovered completely. Herein, we report a case of idiopathic isolated HNP in a Korean male.

CS-7. Clinical characteristics of children with isolated reversible lesion in the splenium of the corpus callosum
Kim YC (Cheonan, Korea), Moon HK (Daegu, Korea)

Purpose: To clarify the clinical characteristics of an isolated lesion of splenium of corpus callosum(SCC) on MR imaging in children.

Methods: Ten patients with the lesion of SCC on MRI were identified between January 2000 and July 2009. Their clinical, radiologic, laboratory and EEG data were reviewed.

Results: The ages ranged from 25 months to 14 years old, and Male:Female ratio was 7:3. Their clinical diagnoses were diverse; 7 acute gastroenteritis including 4 rotaviral gastroenteritis (70%), 1 upper respiratory infection(URI) (10%), 1 meningocencephalitis (10%), 1 meningitis (10%).

The most frequent symptoms were seizures which occurred in 90% of patients. There was no definite correlation between clinical manifestations and the splenial lesion. The cerebrospinal fluid findings were normal in 8 patients with gastroenteritis and URI. Other laboratory findings including CBC, electrolytes, liver function tests, and EEG were unremarkable in all patients. The MR imaging revealed an ovoid lesion in the SCC with a decreased apparent diffusion coefficient values. It was hypointense on T1-weighted images, and hyperintense on T2-weighted and diffusion weighted images without gadolinium enhancement. The splenial lesion disappeared completely after 1 - 4 weeks. All patients were recovered without any sequelae.

Conclusions: In this study the most prevalent clinical diagnosis associated with the splenial lesion was gastroenteritis, especially by rotavirus. The prognosis was good whatever the clinical diagnoses were.

CS-8. Pantothenate kinase-associated neurodegeneration in Korea: Recurrent R440P mutation in PANK2 and outcome of deep brain stimulation
Lim BC (Seoul, Korea), Kim SH (Seoul, Korea), Kim HM (Seoul, Korea), Kim KJ (Seoul, Korea), Cha JH (Seoul, Korea), Hwang YS (Seoul, Korea), Jeon BS (Seoul, Korea), Paek SH (Seoul, Korea)

Objective The purpose of this study was to evaluate the mutation status of PANK2 among Korean patients with pantothenate kinase-associated neurodegeneration (PKAN) and to document the outcome of pallidal deep brain stimulation (DBS).

Methods: Direct sequencing and deletion/duplication analysis of PANK2 were conducted in 12 patients (11 unrelated) with PKAN, diagnosed on the basis of extrapyramidal dysfunction and the ‘eye-of-the-tiger sign’ on brain magnetic resonance imaging. Pallidal DBS was conducted in three patients and the outcomes were measured using the Burke–Fahn–Marsden Dystonia Rating Scale.

Results: A PANK2 mutation was identified in both alleles in all patients. The most prevalent mutation was c.1319G>C (p.R440P) in 8/22 mutated alleles (36%). An intragenic deletion ranging from exons 2 to 4 was found in one allele (1/22, 4.5%) by deletion/duplication analysis. The outcome of pallidal DBS was favorable in two patients with atypical PKAN and moderate severity of dystonia. However, one patient with typical PKAN and relatively severe symptoms responded poorly.

Conclusions: The c.1319G>C. (p.R440P) mutation appears to be a founder genotype among Korean patients with PKAN. Furthermore, this study provides additional data for the recent international effort to evaluate the efficacy of pallidal DBS in the treatment of patients with PKAN.

CS-9. Occupational therapists as providers of cognitive behavioral therapy for Tourette Syndrome
Rowe J, Dure L (Birmingham, AL)

Recent studies directed at treatment of tics and Tourette syndrome indicate a role for habit reversal. This strategy, Cognitive/Behavioral Intervention for Tourette Syndrome (CBIT), utilizes awareness training and the identification of premonitory urges to ultimately craft competing responses that can be used to minimize tic expression. Although published studies exist, it is unclear how adaptable this strategy is to other practices. To that end, we hypothesized that a
program could be developed under the auspices of an occupational therapy clinic.

Patients were referred primarily from a single movement disorder clinic at the University of Alabama at Birmingham, and were selected on the basis of distress related to tics, but a desire to avoid medical management. 24 children were enrolled from January, 2010 through January, 2011, and data is presented on 17 who have completed the program. Mean age of participants was 11.5 years with 12 males and 5 females. Baseline tic frequency and interference were assessed, as was global anxiety throughout the 10 weeks of therapy.

Of the children with complete data (n=17), all reported improved function on the Short Child Occupational Profile (parent) and the Child Occupation Self Assessment (child). At entry, almost 30% exhibited clinically significant anxiety on the Multi-Dimensional Anxiety Scale for Children (MASC-10), and at the end of the study, MASC-10 scores had declined to non-pathologic ranges.

The study indicates that CBIT can be effectively used in an occupational therapy paradigm, and suggests a novel avenue for treatment for children with Tourette syndrome.

CS-11. Globus Pallidus DBS for DYT1 dystonia in young children
Mink JF, Catone J, Augustine EA (Rochester, NY)

Objective: To determine if bilateral globus pallidus pars interna (GPI) deep brain stimulation (DBS) is effective for treatment of DYT1 dystonia in children. GPi DBS is increasingly used to treat primary dystonia in adult patients with inadequate benefit from medications. Few prior reports of GPi DBS in dystonia included children.

Methods: We report four patients with DYT1 dystonia who have been treated with bilateral GPi DBS. All four had incomplete benefit from treatment with trihexyphenidyl and baclofen, and had dose-limiting side effects. Patient 1 had onset of dystonia at age 8 and DBS surgery at age 11. Patient 2 had onset of dystonia at age 8 and DBS surgery at age 14. Patient 3 had onset of dystonia at age 6 and DBS surgery at age 8. Patient 4 had onset of dystonia at age 7 and DBS surgery at age 9. Dystonia severity was rated with the Burke-Fahn-Marsden dystonia rating scale (BFMDRS).

Results: All 4 patients had greater than 50% improvement on the BFMDRS; one is now asymptomatic. All have been able to reduce their oral medication doses with concomitant improvement of side effects. Two of the patients had complications from infection that required removal and subsequent reimplantation of the DBS systems. Three had dystonic storms in the week after surgery requiring hospitalization.

Conclusion: Bilateral GPi DBS appears to be effective in young children with DYT1 dystonia. Complications are common but are self-limited. The benefit appears to substantially outweigh the risk.

CS-12. Siblings with continuous spike wave in sleep syndrome: a case report
Martyanyan A, Wirrell E, Nickels K (Rochester, MN)

Objective: Report on a sibling pair with continuous spike wave in sleep syndrome (CSWS).

Methods: Through a comprehensive search of the Medical Index and EEG reports, all patients with ESES seen at the Mayo Clinic from 2007–2009 were identified. Their charts were reviewed to identify sibling pairs.

Results: One sibling pair with CSWS was identified. MK presented at age 8 years with developmental regression, a history of global developmental delay since infancy, and a seizure disorder since age four years. Overnight EEG demonstrated electrical status epilepticus in slow wave sleep (ESWS), consistent with CSWS. His younger brother developed normally until age 6, when presented with a seizure disorder and developmental regression. Overnight EEG also demonstrated ESWS and he was diagnosed with CSWS. Family history was significant for maternal grandmother with a seizure disorder and documented bilateral mesial temporal sclerosis. Both boys were successfully treated high dose oral prednisone for ESWS. They have been successfully maintained on lamotrigine with remission of CSWS and improvement in language and development.

Conclusion: Continuous Spike Wave in Sleep Syndrome (CSWS) is a rare but treatable seizure syndrome of childhood. It is defined by developmental regression and electrical status epilepticus in slow wave sleep (ESWS). At present, the pathophysiology of CSWS is unknown, and most cases are sporadic. This case of two siblings suggests a potential genetic component to CSWS. While most CSWS is sporadic, a subset may be inherited.

CS-13. A large prospective study of children with Cyclic Vomiting Syndrome
Moses J, Keilman A, Rothner A, Radbakerman K, Parikh S (Cleveland, OH)

Objective: Cyclic Vomiting Syndrome (CVS) is a chronic disorder of unknown etiology characterized by
repeated stereotypical vomiting episodes accompanied by debilitating nausea and/or headaches. We examined the presentation, evaluation and management of our CVS patients and determined whether they had associated abnormalities.

**Methods:** 100 consecutive patients less than 21 years of age seen from 2007 to 2010 were included. Information regarding anthropometrics, medical history, laboratory and radiological studies, medications and treatment outcomes was collected.

**Results:** The mean age at diagnosis was 8.9 ± 5.0 years. Patients reported cycles with median duration of 24 hours, 18 vomiting episodes per cycle and a peak of 5 emesis per hour at 4-week intervals. Episode triggers were noted in 66%, including intercurrent illness in 35%. A family history of migraines was seen in 71%. Prodromal symptoms occurred in 63%. Autonomic symptoms were seen in 25%. Amitriptyline was helpful in 58% of patients; Ciproheptadine in 49%. Neuroimaging showed new intra-cranial abnormalities in 12% of the patients, none which accounted for the CVS. Abdominal ultrasound showed abnormalities in 21% of patients. 61 patients had an upper gastrointestinal series (UGI); all were normal. Metabolic abnormalities were seen in 35%, with 29% of the total having findings consistent with mitochondrial dysfunction.

**Conclusions:** The characteristics of our patients are consistent with previous reports. Neuroimaging, UGIs and endoscopy were of low clinical yield. One-third of our patients had abnormalities suggesting mitochondrial dysfunction. Additional evaluation of these patients is needed and being planned at our institution.

**CS-14. Electroencephalography can be a good modality for evaluation of cerebral hemodynamics in pediatric moyamoya disease**

Chee JH, Lim BC (Seoul, Korea), Park HJ (Daejeon, Korea), Kim HM, Kim SH (Seoul, Korea)

**Objective:** The clinical value of electroencephalography (EEG) in pediatric moyamoya disease has been underestimated, though the characteristic patterns are well known. We undertook this study to evaluate the clinical value of EEG as a diagnostic and post operative follow-up modality in pediatric moyamoya disease.

**Methods:** We retrospectively reviewed the pre- and post-operative EEG with effective hyperventilation in 127 pediatric moyamoya patients and compared their patterns with hemodynamic images.

**Results:** One hundred and two patients (80.3%) showed abnormal EEG findings before revascularization surgery. The typical build-up phenomenon was observed in 82 (64.6%) and localized build-up in 32 (25.2%) without any significant clinical ischemic events. The build-up was observed more frequently in younger age groups (less than 13 years) and Suzuki stages III. The location of the build-up distribution was consistent with the area showing hemodynamic abnormalities on single photon emission computed tomography (SPECT) and/or perfusion magnetic resonance imaging (MRI). Post-operative follow-up EEGs were performed in 41 patients. Six patients with remaining build-up in post-operative follow-up EEG showed poorer postoperative clinical outcomes.

**Conclusion:** This study may reappraise EEG as an easy, safe and valuable diagnostic and post-operative follow-up modality for evaluation of hemodynamic status at least before further more aggressive examination, especially in children.

**CS-15. Clinical analysis of the pediatric patients with neurologic disorders in the emergency department**

Chae SA, Park SW, Yoon SW, Yoo BH (Seoul, Korea), Kim DW (Goyang, Korea)

**Objective:** Pediatric emergencies with seizure, change of consciousness may cause severe complications without early proper management. In the context the distribution rate of neurological disorders may be different according to the various conditions, it would be valuable to evaluate the recent data of the disorders mentioned above in Korea.

**Methods:** Patients who had neurological problems and below 18 years old were defined as case. 1,058 (5.6%) cases who visited the emergency department of Chung-Ang University Hospital from January 2006 to December 2009 were analyzed. The patients were also divided into four age groups: age 1 year or younger, preschool children (2–5 years), middle childhood group (6–10 years), and adolescent group (11–18 years).

**Results:** The male to female ratio was 1.5:1. Most children were between 2 to 5 years old (mean age = 3 years). Febrile convulsion is the most common neurological disorder among infant and preschooler, meningitis among middle childhood, epilepsy and headache among adolescent. Main initial presentations were seizure followed by fever, headache and vomiting. Febrile convulsion was the most common neurological disorders in addition to epilepsy and meningitis. The admission rate of patients with neurological disorders was higher than one of total emergent patients.

**Conclusions:** Neurological disorder is increasing as the cause of pediatric emergencies and has contributed to highest admission rate. The prevalence of the disease differs according to the age. In addition, the disease of this type contains the seizure disorder such as febrile convulsion and epilepsy and the infectious disease of CNS such as meningoencephalitis.

**CS-16. Exacerbation of aberrant cardiorespiratory regulation in response to pain in girls with Rett syndrome**

O’Leary H, Barnes K, Khwaja O (Boston, MA)

**Objectives:** To determine the pattern of cardiorespiratory dysregulation in wakefulness, sleep and during painful procedures in girls with Rett syndrome.

**Methods:** We used simultaneous video recording, continuous ECG, and non-invasive respiratory inductance plethysmography (BioCapture®, CleveMed, Cleveland, OH) during rest, sleep, active wakefulness, during venipuncture and lumbar puncture in patients with a clinical and genetic diagnosis of Rett syndrome.

**Results:** The lowest respiratory and heart rate variability was observed during sleep. There was an increase in respiratory variability during periods of wakefulness and the cardiorespiratory coupling was decreased; however, the most significant changes were observed during painful procedures. There was a 17% increase in heart rate, a 30% decrease in respiratory rate, the number of breathholds increased, there was up to a 3-fold increase in respiratory variability, an increase in parasympathetic activity, and a decrease in cardiorespiratory coupling when periods of painful procedures were compared to subject baselines.
Conclusions: Patients with Rett syndrome demonstrate dramatic worsening of baseline cardiorespiratory and autonomic dysregulation during painful procedures.

CS-17. Lateralizing findings on neurological or neuropsychological exam are associated with correlating abnormalities on MRI
Carullo MP, Urion D (Boston, MA)

Objective: To determine the prevalence of MRI findings on a clinic-referred population with learning disabilities that has lateralizing findings on neuropsychological or neurological examination.

Methods: 1587 consecutive cases referred to a tertiary-hospital-based multi-disciplinary learning disabilities program were reviewed. 127 (8%) had lateralizing findings on neurological or neuropsychological examination. 87 of these had clinical MRI at the hospital: 52 on a 1.5 Tesla machine, 35 by 3.0 Tesla. Reports were reviewed and scans re-examined for abnormal findings which correlated with exam focialty.

Results: 37 scans had abnormalities correlating with the focal findings (42.5%). Of the 1.5 Tesla scans, 16/52 (31%) had findings correlating with the examinations; of the 3.0 Tesla scans, 21/35 (60%) had findings correlating with the examinations.

Conclusions: Previous studies have shown that on 1.5 Tesla MRI, 21% children with focal epilepsy have a correlating abnormality. Using 3.0 Tesla machines, this increases to 71%. Other studies have shown that the experience of the neuroradiologist interpreting the study (one familiar with the clinical entity in question) and the sequence protocol used can shift the detection rate from 40% to 90%. Studies have shown that 1/3 of children with development language disorders and focal examinations had abnormal 1.5 Tesla MRI scans. Our population with learning disabilities follows a similar pattern: focal findings speak to focal anatomic abnormalities. This can improve our understanding of the origin of learning disabilities. Future inquiry using more powerful tools such as DTI protocols may help us better understand the nature of learning disorders.

CS-18. Anti-N-Methyl-D-Aspartate (NMDA) receptor antibody encephalitis: a case series of pediatric patients
Borrero-Meiias C, Berger B, Schusse C, Williams K, Bodenstein J (Phoenix, AZ)

Objectives: Anti N-Methyl-D-Aspartate (NMDA) Receptor Antibody Encephalitis is a recently described disorder that is more common in young women with teratomas of the ovary, but also reported in men and children with or without associated tumors. Since its recognition, several cases have been reported in the literature but few of them describe this entity in children. In this series we describe five cases of children with Anti-NMDA Receptor Antibody Encephalitis that were treated in our institutions.

Methods: This is a multi-center, retrospective, observational study. We reviewed medical records of patients with a confirmed diagnosis of Anti-NMDA-Receptor Antibody Encephalitis that were cared for in two tertiary centers in Phoenix, AZ.

Results: There were 2 male and 3 female patients. All were Hispanic. Ages ranged from 8 to 17 years with a mean of 13.2 years. Interval between onset of symptoms and diagnosis was 3 to 16 weeks. They all had psychiatric symptoms, encephalopathy, hypoventilation or autonomic instability, dyskinesias and seizures. All were found to have the antibody confirmed by ELISA testing and were treated with immunomodulating therapy. All but one showed slow, gradual improvement.

Conclusions: The characteristic clinical presentation of Anti-NMDA Receptor Antibody Encephalitis in children is similar to what has been reported in the adult literature. This potentially fatal entity should be considered when managing children who present with psychiatric symptoms, movement disorders and/or refractory seizures. We underscore the importance of investigating the possibility of ovarian teratomas or other neoplasms, given the potential for effective treatment if identified.

CS-19. Selective serotonin reuptake inhibitors as prophylactic medication for cyclic vomiting syndrome
Babineau S, Chiriboga C (New York, NY)

Introduction: Cyclic vomiting syndrome (CVS) is characterized by stereotypic periods of intense vomiting interspersed with periods of wellness and is considered a migraine variant. The refractory nature of CVS, safe side effect profile of selective serotonin reuptake inhibitors (SSRIs) and co-morbidity of migraine and CVS with depression or anxiety prompted us to determine whether SSRI administration has a role in refractory CVS. We report a case series of 3 patients treated with SSRIs.

Objective: To determine whether SSRIs are effective treatment of children with refractory CVS.

Methods: We treated with SSRIs children with CVS refractory to traditional treatment that presented to our hospital between 2009–2010. Indication for treatment was lack of response to at least one CVS-related medication.

Results:

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age of Onset</th>
<th>Number of Prior Medications</th>
<th>Age Treated</th>
<th>Baseline Episode Frequency Prior to SSRIs</th>
<th>Response</th>
<th>SSRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>5 months</td>
<td>2</td>
<td>2 years</td>
<td>Monthly</td>
<td>No events $\times$ 1 year</td>
<td>fluoxetine</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>4 months</td>
<td>5</td>
<td>6 years</td>
<td>Monthly</td>
<td>No events $\times$ 1.5 years</td>
<td>citalopram</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>3 days</td>
<td>2</td>
<td>20 months</td>
<td>Bimonthly recurrences</td>
<td>Unchanged</td>
<td>fluoxetine</td>
</tr>
</tbody>
</table>
Discussions: Serotonin is involved with both the central and peripheral circuits involved in vomiting and is also involved in activation of nociceptive pathways in migraine and CVS. The results of this case series suggest that SSRIs may be effective in treating CVS in children, especially girls. We noted no side effects associated with SSRIs.

Conclusion: SSRIs appear to be safe and effective in treating CVS in children.

CS-20. Neurologic complications following pediatric hepatic transplant: A single center experience
Ghosh PS, Hybertz V, Ghosh D (Cleveland, OH)

Objective: We studied neurologic complications (NCs) after hepatic transplantation (HT) in children.

Methods: Retrospective review of HT patients ≤21 years. NC classified as early (<3 months post-HT), delayed (>3 months).

Results: Of 65 children with HT, 20 (30.7%) had NCs; age 11.8 ± 5.9 years, 16 females. Early complications - 9 (45%): Seizures (7); 1 posterior reversible leukoencephalopathy syndrome (PRES), 1 intracerebral hemorrhage (ICH) requiring hemiecranietomy, others due to metabolic derangements; altered mental status (2). Neuroimaging: PRES (1), ICH (1), mild cerebral edema (1) and bilateral basal ganglia T1W hyperintensities (1). Follow up: 3 deaths (2 within 3 months, 1 after 2 years, unrelated); 1 with ICH had residual left hemiparesis who received long-term antiepileptic-drugs (AED). Others had normal neurological examination. Late complications- 11 (55%): Seizures (4) - nodular heterotopia (1), hypoxic-ischemic/metabolic encephalopathy (1); Headache (4) - aseptic meningitis (1), migraine (1) chronic daily headache (2); Paresthesias (2); C20 cervical disc disease (1) and possible small fiber neuropathy (1); 2 had altered mental status (1 had seizure, in addition). Neuroimaging: bilateral subependymal heterotopias (1), hypoxic-ischemic encephalopathy (1), encephalomalacia due to old hemorrhage (1), FLAIR hyperintensity of posterior periventricular white matter (1), developmental venous anomaly (1), and degenerative cervical disc disease (1). Follow-up: all survived, 2 had abnormal neurological examination - papilledema with secondary optic atrophy requiring optic nerve sheath fenestration (1), diffuse hyperreflexia (1). One needed long-term AED.

Conclusions: NCs are common in children after HT, seizures being the commonest. Early detection and appropriate management of NC is important.

CS-21. EEG and seizure characteristics in patients with primary cerebral folate deficiency
Steele SL, Veerapandian A, Smith EC, Gallentine WB (Durham, NC), Hyland K (Atlanta, GA), Mikati MA (Durham, NC)

Objective: Analyze the electroencephalographic (EEG) and clinical findings of four patients with Primary Cerebral Folate Deficiency (CFD).

Methods: Inclusion criteria: Decreased cerebrospinal fluid 5-methyltetrahydrofolate with normal serum/RBC levels; development delay/learning disorder not fully attributable to other etiologies; marked clinical improvement on folic acid therapy in all other patients. EEGs and clinical charts were retrospectively reviewed.

Results: (a) 5-year-old male with microcephaly and developmental delay who developed infantile spams, tonic, clonic, and myoclonic seizures as of the age of 3 months. Interictal EEGs: hypsarrhythmia. Ictal EEG: electrodecremental fast discharges. (b) 4.5-year-old male with secondarily generalized tonic clonic seizures beginning at 9 months of age. Video EEG: Electrographic status epilepticus (ESE) of bilateral continuous spike slow waves with concurrent epilepsy partialis continua (EPC) of left arm/leg. (c) 7-year-old male born prematurely with neonatal course complicated by suspected encephalitis developed seizures after a left occipital ventriculoperitoneal shunt at 4 months of age. His seizures included infantile spasms, partial seizures, and ESE during sleep. (d) 20-year-old female with mild seizures as of the age of 2 months subsequently regressed to severe developmental delay as of age 6 years and had frequent generalized tonic clonic seizures. EEG: Slow background with frequent bursts of shifting spike wave discharges.

Conclusions: We describe the following novel manifestations in CFD: (a) West Syndrome, infantile spasms with hypsarrhythmia; (b) ESE in wakefulness and in sleep with or without EPC; (c) Coexistence of CFD with preexisting cerebral injury; (d) Developmental regression and seizure worsening years after an initial mild presentation.

CS-22. Predictors of Vitamin D levels in northern climates
Holler YE, Gothard MD, McBride MC (Akron, OH)

Objective: Maintaining adequate Vitamin D (VitD) levels is an important aspect of promoting bone health in non-weight-bearing children or those on antiepileptic medications (AEDs). Our aim was to determine if VitD levels have seasonal variation and whether typical dietary intake of VitD is sufficient to maintain a normal level in our area of Northeast Ohio (latitude 38).

Methods: From January 2009 to January 2011 medical and dietary information was collected on 193 children at the time their VitD level was ordered.

Results: The mean VitD level was 34.0 ± 13.17 ng/ml (range 6–70); 49% were ≤32 ng/ml and 80% were below 45 ng/ml. VitD levels were higher in the summer (June – August) than the rest of the year (40.6 vs. 31.7, p < .001). Estimated daily VitD intake based on history of milk/formula and vitamin consumption correlated positively with VitD level (R = .35, p < .001). Based on this regression every additional 100 International Units (IU)/day of VitD was associated with an increase in level of 2 ng/ml. Enzyme inducing AED therapy had no effect on VitD levels in our sample.

Conclusion: In northern climates many children have suboptimal VitD levels, especially during the non-summer months. Clinicians interpreting a VitD level should consider the month in which it was drawn. Our data suggest that an additional 500 IUs of VitD may be needed to increase a level by 10 ng/ml.

CS23. Use of aspirin for stroke prevention in sickle cell disease
Nwosu ME, Panepinto J, Amlie-Lefond C (Milwaukee, WI)

Objective: Aspirin may prevent stroke through its antithrombotic and anti-inflammatory effect, but is currently not routinely recommended for use in sickle cell disease (SCD) due to concerns about intracranial hemorrhage. We describe current practice of aspirin use for adjuvant primary and secondary stroke prophylaxis in children and young adults with sickle cell disease.

Methods: With IRB approval, a retrospective single institution chart review was performed on patients with SCD and stroke or cerebrovascular accident in aspirin therapy for adjuvant stroke prophylaxis.
Results: Aspirin was recommended in 27 patients, of whom 20 reported compliance. Of these 20, 8 had a history of stroke, 8 had confirmed cerebrovascularopathy, 2 had both, and 1 had a history of transient ischemic attack (TIA). The 20 patients ranged in age from 4 to 43 years (mean 17 years). Seventeen were on chronic transfusion. Exposure to aspirin therapy ranged from 2 – 64 months (mean 37). Doses ranged from 0.8 to 5.4 mg/kg/day (mean 2.3).

One patient developed a bleeding duodenal ulcer on aspirin. Due to recurrent TIA's, aspirin was resumed, along with lansoprazole, with no further complications. No other complications were reported.

Conclusion: Although chronic transfusion has been shown to markedly reduce the risk of stroke in children with SCD, patients continue to have an increased risk of both hemorrhagic and ischemic stroke. As hemorrhagic stroke is not associated with previous ischemic stroke or moyamoya, it may be that the benefits of low dose aspirin outweigh the risk in patients with cerebrovascularopathy and previous arterial ischemic stroke.

CS-24. Periodic limb movements of sleep, serum-ferritin levels, and sleep fragmentation on polysomnogram in Autism Spectrum Disorder

Youssef JN, Huntington N, Gregas M, Lodenkemper T, Becker R, Kothare SV (Boston, MA)

Objective: Children with autism spectrum disorders (ASD) experience a range of sleep disturbances; exact mechanisms are not well characterized. This study investigates the association of serum-ferritin and sleep-fragmentation on polysomnograms (PSG).

Methods: We conducted a retrospective chart-review of children with ASD seen in a tertiary-care center between 1990–2010. Inclusion criteria were availability of PSG-data and ferritin-levels. The following variables on PSG characterized sleep fragmentation: arousal-index, presence of alpha-intrusions, reduced sleep-efficiency, and apnea-hypopnea-index.

Results: Of 9791 children with ASD identified, 511 had a ferritin level, 377 had PSG-data, and 53 had both ferritin and PSG-data. Median age was 8y (range 5–13). Median ferritin level in the entire ASD population: 35ng/mL (23–73); the study population: 27ng/mL (18–49); ASD subjects with PLMS: 24ng/mL (17–47); and controls: 86ng/mL (35–264) (P < 0.01). The prevalence of periodic limb movements of sleep (PLMS) in the entire ASD population: 27%, compared to 8% in controls (p < 0.01)1.

A marker of sleep-fragmentation was observed in 40% of subjects with ASD. Median ferritin levels were significantly lower in patients with poor sleep-efficiency (7ng/mL: 3–19) compared to those with normal sleep-efficiency (29.1ng/mL < 51, p = 0.011). Trends for females to have alpha intrusions (p = 0.060) and lower sleep efficiency (p = 0.07) were observed.

Conclusion: Children with ASD had an eight-times higher prevalence of PLMS compared to controls. Our preliminary observations, which have not been described before, need to be validated in further multicenter prospective studies.

CS-25. An atypical presentation of BECTS

Hughes I, Lysenko L, Erba G, Kwon JM (Rochester, NY)

Objective: The seizures associated with Benign Epilepsy with Centrotemporal Spikes (BECTS) have characteristic semiology often allowing clinical diagnosis by description of the events alone. We describe a case of BECTS initially presenting as a kinesiogenic movement disorder prior to progression to more typical seizures.

Methods: We review the case of a healthy 5yo boy who presented with insuppressible myoclonic jerks of his right arm, and sometimes leg. The jerks occurred when awake, and were associated with movement of the limb or with intention to move, lasting throughout the action and several minutes into resting. His family provided more than an hour of accumulated video footage of his movements occurring in a variety of settings, with no alteration in consciousness. An initial EEG performed when he was asymptomatic showed left centrotemporal spikes with an otherwise normal background. His symptoms resolved for several months. When the same symptoms returned there were additionally new episodes of sustained rhythmic right face and right arm twitching with interruption in speech lasting several minutes that occurred when he was fatigued.

Results: A repeat EEG confirmed the presence of centrotemporal spikes with clinical correlation of EEG findings with arm movements. The patient was started on levetiracetam with immediate cessation of myoclonic movements while awake, as well the seizures. Family history revealed a similar childhood history of jerking movements precipitated by action in the patient’s father.

Conclusion: This case demonstrates that BECTS can present as an apparent paroxysmal movement disorder in children without clear seizure activity.


Marks W, Honeycutt J, Acosta F, Bailey L, Reed MA, PomyFair A, Mercer M (Fort Worth, TX)

Objective: Compare the early response to pallidal deep brain stimulation (DBS) in children with cerebral palsy or DYT-1 dystonia (Dyt-1).

Background: DBS is accepted therapy for Dyt-1. We have shown that some children with dystonia due to cerebral palsy (CP) respond favorably to DBS. There is no direct comparative data for DBS response rates in children with CP and Dyt-1.

Methods: A confidential IRB approved database is maintained on all patients undergoing DBS at Cook Children's Medical Center. All patients less than age 16 years with cerebral palsy or Dyt-1 were included in this analysis. Motor outcome was determined using the Burke-Fahn-Marsden Motor (BFMDS-R-M) and Disability (BFMDS-R-D) scores and the Barry-Albright Scales (BAS). General Linear Modeling-Repeated Measures (significance 0.05) was used to evaluate changes.

Results: Since January 2008, 8 patients with CP and 6 with Dyt-1 have undergone at least 6 months of bilateral pallidal stimulation. Mean subject age was 10.83 +/- 2.88 years and was similar between groups. Patients with CP had greater motor disability at baseline (BFM-M: 58.89 v 22.25; BFM-D: 20.56 v 7.75); BAS: 17.44 v 9.75). Both groups showed general improvement at 6 months (BFM-M: 39.39 v 22.00; BFM-D: 17.00 v 9.25; BAS: 15.67 v 6.25). Statistical significance was seen for the entire group on the BFM-D (13.57%; p = 0.05). Small sample size precludes intergroup comparisons.

Conclusions: The early response of children with dystonia due to cerebral palsy appears comparable to those with...
CS-27. Evaluation of neuroinflammation in children with infantile spasms using \(^{11}\text{C}\)-PK-11195 positron emission tomography

Ajay K, Chugani HT (Detroit, MI)

Objective: The efficacy of ACTH for infantile spasms (IS) raises the possibility of underlying neuroinflammation in its pathogenesis. In this pilot study, we used PET scanning with \(^{11}\text{C}\)-PK-11195 (PK-PET), which binds to activated microglia, to detect potential neuroinflammation in children with IS.

Methods: Three female children (age: 0.6–1.9 years) with IS underwent dynamic PK-PET imaging. Binding potential (BP: measure of receptor-ligand binding) was calculated in different brain regions using reference tissue model and compared with normal adult values (n=11; mean age: 27±7.7 years; 5 males).

Results: Focal cortical areas of increased PK-binding were seen in all three children with increased tracer binding in ipsilateral caudate nucleus in one, in ipsilateral caudate and lentiform nuclei in the second, and in ipsilateral caudate and lentiform nuclei, bilateral thalami and brain stem in the third child (TABLE). Our findings suggest increased activated microglial cells in focal cortical regions and basal ganglia in children with IS, suggesting underlying neuroinflammation in these specific areas. The present findings are consistent with previous studies indicating an important interactive role of basal ganglia and cortex in the pathophysiology of IS.

Conclusions: Our findings suggest increased activated microglial cells in focal cortical regions and basal ganglia in children with IS, suggesting underlying neuroinflammation in these specific areas. The present findings are consistent with previous studies indicating an important interactive role of basal ganglia and cortex in the pathophysiology of IS.


Objective: Recent research has focused on mitochondrial (mt) dysfunction in Autism Spectrum Disorders (ASD). Deficiencies in mt enzymes in biopsied skeletal muscle have been reported in isolated cases, most commonly in respiratory chain complex (RCC) I and IV, although complex III and V defects have also been described. A recent small-scale study using lymphocytes demonstrated mt abnormalities in 6/10 autistic children (Giulivi et al, JAMA 2010;304:2389). Assessment of mt dysfunction in biopsied muscle in children with mt disorders (MD) is expensive and invasive. In our experience, buccal swab analysis from MD patients can sensitively assess complex I and IV activities, highly correlated with similar evaluations in muscle. The aim of this study is to investigate RCC defect prevalence in children and adolescents with ASD.

Methods: We studied 39 consecutive patients, 28M/11F, ages 3–15 years, fulfilling DSM-IV-TR diagnostic criteria for ASD, and 63 age-matched controls, using combined microspectrophotometry and enzyme immunocapture techniques.

Results: RCC deficiencies, defined as activity values<2 SD from controls’ mean, were found in 21/39 (54%) patients: 4 complex I, 12 complex IV, and 5 both. Moreover, complex I/IV activity ratio was significantly increased in a subset of 10 cases with severe phenotypes (p<0.05 vs. not severe).

Conclusions: This is the largest cohort of ASD patients, so far studied for mt dysfunction, demonstrating a high prevalence of RCC defects. Buccal swab analysis is a non-invasive technique that may allow the assessment of mt dysfunction in large populations of ASD patients. Ultimately, this may help to better understand ASD pathogenesis.
micro-motion with 13 results from an attention task. Patients meeting the DSM-IV criteria for ADHD were treated and reassessed in 1–2 weeks.

**Results:** Of the 35 children included in this series, 15 (43%) achieved normalized motion and attention metrics at the time of the second assessment; 5 (14%) achieved normalized motion control, but excessive inattention remained; 2 (6%) achieved normalized attention, but excessive hyperactivity remained; and 13 (37%) had excessive hyperactivity and inattention. 5 of the 15 patients with normalized motion and attention scores at the time of the second test, were previously treated, but not well controlled at baseline.

**Conclusions:** It is feasible and practical to implement an objective measurement of hyperactivity and analysis of shifts in attention state using the Quotient ADHD Test in a community care setting. Follow-up studies are needed to determine the time to optimal medication management compared to rating scales, and the impact on compliance, adherence and patient satisfaction.

**CS-30. Does ADEM present with only brainstem lesion?**
**Objective:** Isolated brainstem lesions in patients presenting with acute neurological findings create a major diagnostic dilemma. Differential diagnosis include acute demyelination, CNS inflammation secondary to rheumatologic disorders, brainstem encephalitis, or brainstem glioma. Although brainstem is frequently involved in acute disseminated encephalomyelitis (ADEM), solitary brainstem lesions are rare and not well defined. The study goal was to describe the neuroimaging features, underlying diagnoses and clinical outcome in children with isolated brainstem inflammation.

**Methods:** We included patients who presented with a lesion confined to brainstem and had ADC/DWI sequences available. Clinical findings, serial MRIs, and prognosis at last visit were reviewed.

**Results:** Six children were identified with isolated brainstem lesions. Lesions involved medulla (n=4) and pons (n=2), and enhancement was seen in only two. Infectious etiology was unlikely based on the CSF results, negative cultures and viral serology. Two children were diagnosed lupus and localized scleroderma. Both patients had incomplete recovery with residual neurological findings. Other four children remained with uncertain diagnosis; in one child drug ingestion was considered and acute demyelination was suspected in three. Initial characteristics of the lesions were rare and not well defined. The study goal was to describe the neuroimaging features, underlying diagnoses and clinical outcome in children with isolated brainstem inflammation.

**Conclusions:** Although ADEM is typically a multifocal disease, it rarely presents with demyelinating lesions confined to the brainstem.

**CS-31. Two unrelated males with novel MECP2 deletions and the Preserved Speech Variant form of Rett syndrome**
**Ho E, Markowitz J, Barnes K, O'Leary H, Khwaja O (Boston, MA)**

**Objective:** To describe two unrelated boys with novel exon 4 deletions in the MECP2 gene with features of the Preserved Speech (Zappella) Variant of Rett syndrome (PSV-RTT).

**Methods:** Clinical and genetic description of neurological and developmental symptoms and signs in 5 year old and 12 year old boys with deletions in Xq28 identified by chromosome microarray analysis.

**Results:** Sequencing analysis in probands and siblings and/or parents identified novel hemizygous deletions in the MECP2 gene. The deletion in exon 4 extending to the 3' untranslated region (3'UTR) was identified in PSV-RTT patients. The deletion is predicted to result in a frameshift and a truncated protein with altered splicing. The deletion in PSV-RTT patients is associated with a milder phenotype even in males.

**Conclusion:** Late exon 4-3' UTR deletions in the MECP2 gene in males are associated with features of the preserved speech variant of Rett syndrome. These findings suggest that these deletions are potentially hypomorphic causing a milder phenotype even in males.

**CS-32. Mitochondrial respiratory chain complex deficiencies and DNA deletions assessed by buccal swab in patients with epilepsy**

**Objective:** Diagnosis of mitochondrial disease (mtD) usually requires invasive techniques like muscle biopsy. Our laboratory has demonstrated the reliability of buccal swab in identifying respiratory chain complex (RCC) I and IV deficiencies in children with suspected mtD. The objective of this study is to describe the RCC findings and mitochondrial DNA (mtDNA) analysis in 3 patients with epilepsy and mtD using this technique.

**Methods:** Buccal swabs processed in extraction buffer were assessed for complex I activity by immuno-capture methodology (Mitosciences™) and complex IV and citrate synthase (CS) activities by micro-spectrophotometry. RCC values were normalized relative to CS activity, and expressed as ratios (i.e., I/CS and IV/CS). Analysis of large-scale deletions (i.e., the 5 and 7.4 kb deletions) and 15 pathogenic point mutations was performed in mtDNA extracted from patients’ buccal swabs, with relative abundance of each deletion gauged using semi-quantitative analysis.

**Results:** Three out of 10 children with epilepsy studied for mtD, had significant RCC deficiencies (one in complex I, one in complex IV, and one in both), and harbored mtDNA deletions. Their I/CS ratios were 0.07, 0.06, and 0.17 (controls: 0.32±0.1, n=82) and their IV/CS ratios 3.6, 1.8, and 0.8 (controls 6.3±1.9, n=82). Detectable levels of large-scale mtDNA deletions (the 5 and/or the 7.4 kb deletions) were found in all three patients. They did not have any of the tested pathogenic mtDNA point mutations.

**Conclusion:** Buccal swab is a non-invasive technique useful to evaluate mitochondrial RCC and mtDNA abnormalities in patients with epilepsy and suspected MD.
CS-33. Reversible peri-ictal MR imaging changes in pediatric epilepsy.
Osorio MJ, Lindsey J, Zuccolli G (Pittsburgh, PA)

Objective: Describe reversible MR imaging changes in pediatric patients presenting with seizures.

Methods: Retrospective study of 4 patients with frequent seizures or status epilepticus and brain MR imaging with evidence of transient changes mimicking structural lesions.

Results: Series of 4 male patients, mean age 7.5 years. 2 patients presented in status epilepticus and 2 presented with frequent focal seizures. Only one patient had prior history of epilepsy. MR was obtained within 24–72h after the last seizure and demonstrated focal restricted diffusion in 2 patients and increased diffusion in the other 2 patients. Areas involved included focal lesions of the left parietal lobe in 2 patients, the right frontal basal region in 1 patient, and left hippocampus in 1 patient. Repeat MR in 1 week to 6 months showed reversibility of either cytotoxic or vasogenic edema. EEG within 24h of the last seizure demonstrated abnormalities ipsilateral to the neuro-imaging findings, including focal slowing in all patients, focal electrographic seizures in 2 patients, and focal inter-ictal sharp waves in 1 patient.

Conclusion: Our study of 4 pediatric patients with frequent seizures or status epilepticus demonstrated MR signal changes, which initially mimicked structural lesions with either associated cytotoxic or vasogenic edema. These signal abnormalities were reversible on repeat imaging, suggesting a peri-ictal phenomenon. The electroencephalographic findings were ipsilateral to the MR imaging changes, again also suggesting a peri-ictal phenomenon. This is the first case series demonstrating reversible peri-ictal radiologic abnormalities in a pediatric population.

CS-34. Pursuit, saccade and vestibule ocular reflex eye movements in autism
Osorio MJ, Furman J, Minshew N (Pittsburgh, PA)

Objective: The purpose of this study is to assess the functional status of different brain regions in high-functioning autistic children and adults by studying pursuit, saccadic and vestibular eye movement testing in the same cohort.

Methods: 79 high functioning autistic (HFA) individuals and 62 matched controls with ages between 5 and 52 years were included. All subjects had IQ scores above 70. Ocular-motor screening included assessment of horizontal saccadic eye movements and horizontal smooth pursuit. For vestibular testing, earth vertical axis rotation was performed in darkness and in lighted visual surround with a fixation target.

Results: There were significant differences between the two groups in saccade latency and pursuit gain but not in saccade accuracy and velocity. Vestibular testing revealed increased visual-vestibulo-ocular reflex gain in HFA but no differences in the remaining vestibular variables. A regression analysis showed a similar effect of age in all variables in both groups.

Conclusions: The increased saccade latency and decreased pursuit gain suggests dysfunction in frontal, prefrontal, parietal and cingulate areas, all areas known to be involved in these tasks. The normal saccades accuracy and vestibular testing, tasks mainly controlled by the cerebellum and brainstem (with the exception of visual-vestibulo-ocular reflex gain, that also involves occipital cortex control), do not support the idea of functional cerebellar abnormalities in autism. Our results suggest a broad abnormality in the autism brain, involving the cerebral cortex, that is likely to be better explained by abnormal cortical connectivity.

CS-35. The trajectory of recovery following arterial ischaemic stroke in childhood: the first six months
Gordon AL, Anderson VA, Monagle P, Mackay M, Ditchfield M, Coleman L, Hunt R (Melbourne, Australia)

Objective: To describe the nature and trajectory of recovery across multiple domains of health in the six months after diagnosis of arterial ischaemic stroke in children.

Methods: A consecutive sample of twenty-seven children, aged between term neonates to 16 years admitted to a single tertiary centre were recruited upon diagnosis of first arterial ischaemic stroke. Detailed neurological examination during the acute phase was followed by screening assessment of motor, language, social-emotional, cognitive skills and adaptive behaviour at one and six months following diagnosis. Diversity of outcome was anticipated given wide range of age and brain injury characteristics.

Results: Neonates and older children were analysed separately, with findings compared with population norms, changes over time and differences between age groups examined. Severity of overall neurological impairment decreased over time however nature of impairments changed with more cognitive and language impairments evident later. The older children show wider variation in scores and across the group with some improvement between one and six months. Language, cognitive and social-emotional screening showed no significant deficits for either age group. Adaptive behaviour screening at six months reveal 5/27 children had adaptive impairments across the domains of communication, socialization and self-care.

Conclusions: Neurological impairments change in nature and severity over the first six months after stroke. While impairment findings suggest impairments are most prevalent in motor domains, adaptive behaviour sequelae are evident in multiple areas of function at six months.

CS-36. Withdrawn

CS-37. Open label trial of Taurine in SSADH deficiency
Pearl PL (Washington, DC), Theodore WH (Bethesda, MD), McCarter R (Washington, DC), Drinnings IM (Washington, DC), Gihon KM (Houghton, MI)

Objective: SSADH deficiency is an autosomal recessive defect in GABA degradation leading to increased endogenous GABA and GHB. Taurine, a neuromodulator which interacts with GABA-A and -B receptors, has shown survival benefits in the SSADH null mouse. Following a case report of improvement in a 2-year-old boy with SSADH deficiency, we conducted an open label trial in SSADH.

Methods: Subjects are titrated weekly from 50mg/kg/day until reaching a target of 200mg/kg/day to a maximum of 16 grams/day. The Adaptive Behavior Assessment Scale-II (ABAS-II) is administered at baseline and following six and twelve months of therapy.

Results: Twelve patients have been recruited: 6M/6F; age at enrollment 13y mean; range 5-28y. One patient had a
serious adverse event on 16 grams/day (hospitalization for hypersomnia). This led to a dose lowering paradigm with a new maximum dose of 10 grams. The taurine has been otherwise well-tolerated. Six subjects have completed the trial; 3 withdrew early due to perceived lack of efficacy. There have been no significant changes between pre- and Rx-composite scores in general adaptive, conceptual, practical, or social skills.

Conclusions: Taurine is an aminosulfonic acid sold as a dietary supplement and has neuromodulatory, osmoregulatory, and tropic roles. It may have a protective role against retinal toxicity associated with vigabatrin, an irreversible inhibitor of GABA-transaminase leading to elevated GABA levels. Taurine has shown benefit in the SSADH deficient mouse model. This open-label pilot trial of taurine in patients with SSADH deficiency did not lead to demonstrable improvement in adaptive neurobehavioral functioning.

CS-38. Use of carbamazepine in stimulus induced drop attacks associated with Coffin-Lowry syndrome
Bay MJ, Accardo JA, Belcher HM (Baltimore, MD)

Objective: Up to 20% of patients with Coffin-Lowry syndrome (CLS) have stimulus induced drop attacks (SIDAs). SIDAs are often difficult to treat non-epileptic movement disorder. We report a case of an adolescent with CLS, who responded to carbamazepine with dramatic decrease in SIDAs.

Methods: Descriptive report of carbamazepine treatment outcome of a patient with CLS and SIDAs.

Results: This sixteen-year old boy was clinically diagnosed with CLS by a geneticist at age 10 years. He has severe intellectual disability, classical CLS characteristic dysmorphisms, and family history of x-linked inheritance intellectual disability. Subject had multiple normal electroencephalograms and normal brain MRI. His drop attacks were characterized by brief loss of lower-extremity tone without loss of consciousness, sometimes induced by auditory stimuli. Drop attacks began at two years of age and increased in frequency over the years. He had a prior medication treatment history of lamotrigine at 11 years and valproic acid at 14 years, with development of adverse effects and no clear improvement. He presented to our clinic at age 16 years with multiple drop episodes, averaging five times daily. The subject was started on carbamazepine 200 mg twice daily and increased to 400 mg twice daily. At one-month follow-up, his drop attacks had nearly ceased. At six-month follow-up, he reported having occasional episodes, ranging from zero to at most two episodes per week.

Conclusions: We report a decrease in drop episodes in a youth with CLS following carbamazepine initiation. There is limited literature regarding efficacious treatment of this handicapping condition.

CS-39. Clinical, neuroradiologic and genetic findings in mild Canavan Disease
Victorio MC, Kurczynski T, Naffaa L (Akron, OH)

Objective: To describe cases of mild form of canavan disease (CD).

Methods: A case report and literature review on the clinical presentation, neuroradiologic and genetic findings in patients with mild CD were done.

Results: A 2 1/2 year old girl with history of mild developmental delay presented with complex partial seizures. She had a normal neurologic examination and head circumfer-

ence. EEG showed epileptiform discharges in bifrontal and left parietal regions. Brain MRI revealed symmetric hyperintensities in bilateral putamen, caudate nuclei and pons. Metabolic work-up showed elevated N-acetylaspartic acid (NAA). Molecular studies showed compound heterozygosity for a 914C>A mutation and 770C>G novel variant in the ASPA gene.

A review of the literature identified ten similar mild cases with developmental delay and elevated NAA; three had seizures and only two were macrocephalic. Predominant brain MRI findings were bilateral involvement of lentiform and caudate nuclei, thalamus and pons. MRS indicated elevated NAA in 9/10 cases. Majority had low to undetected aspartocylase activity in cultured fibroblast. Eight had molecular testing. 7/8 had compound mutations of the ASPA gene; two 863A>G/884T>G; one 637A>G/914C>A; two 914C>A/212G>A; one 863A>G/914C>A; one -2A and 3C deletion of exon 3 /863A>G. One had 212G>A/212G>A mutation.

Conclusions: CD, a devastating leukodystrophy, can exist in a mild form. Symmetric basal ganglia hyperintensities with minimal white matter involvement is a common finding in mild CD. The presence of certain mutations in CD may result in mild disease.

CS-40. A role for magnetization transfer images in diagnosis of Tuberous Sclerosis Complex
Frelich ER, Vezina G, McClintock WM (Washington, DC)

Objective: Tuberous Sclerosis Complex (TSC) is a genetically inherited neurocutaneous disorder of multiple organ systems including the brain. Diagnosis of TSC is based on clinical and radiographic findings. The most frequent lesions found in the brain are cortical tubers, subependymal nodules, subependymal giant cell astrocytomas, and white matter lesions. Magnetization Transfer (MT) images are known to increase the sensitivity of conventional MR. We present three patients with TSC where diagnosis would not have been made without the use of MT images.

Methods: MR images were obtained on 1.5 Tesla GE scanner using standard pediatric epilepsy protocol.

Results: Two patients with localization-related epilepsy, and one patient with cardiac rhabdomyoma underwent MR imaging, with typical findings of TSC noted only on MT images; conventional sequences showed nonspecific T2 changes or nothing (Figure 1). Diagnosis of TSC was made based on radiologic findings and confirmed by further evaluations and/or gene testing.

Conclusions: MT images have an important role in diagnosis of TSC due to increased visualization of common brain findings, and should be considered in all new onset epilepsy patients, not only those with clinical suspicion of TSC.

CS-41. Sleep problems in children with Tourette Syndrome
Ghosh D, Rajan PV, Das D, Datta P, Rothner AD, Erenberg G (Cleveland, OH)

Objective: To determine the frequency, nature of sleep problem and its impact in children with Tourette Syndrome (TS) to address its possible inclusion as a co-morbidity.

Background: Sleep problem in TS is not well studied. It is thought to be related to comorbid Attention Deficit Hyperactivity (ADHD).

Design/Methods: Single center, prospective, questionnaire study of patients with a confirmed diagnosis of TS,
FIGURE 1: A) Patient 1 with refractory epilepsy and mild MR: multiple cortical tubers noted on MT (Left), nonspecific T2 changes noted on FLAIR (Right). B) Patient 2 with epilepsy and typical development: subcortical and transmantle linear lesions on MT (Left), not visualized on T2 FSE (Right). C) Patient 3 with cardiac rhabdomyoma: cortical tubers noted on MT (Left) not noted on T2 FSE (Right).
21 years, conducted over 3 years after IRB approval. A standard questionnaire was administered directly to the child and legal guardian at the end of the clinic visit by one of the investigators. Each completed questionnaire was then reviewed by the first author. Data were tabulated in Excel spreadsheet, simple statistics applied to find out frequencies.

**Result:** N = 129, 2 groups (Gp): A- without ADHD (50); B- with ADHD (79). Sleep initiation problem: 48% Gp-A & 55.7% Gp-B; sleep onset time was 1.2 & 1.7 hours, respectively. Sleep maintenance problem: 28% (A) & 47% (B). Abnormal sleep behavior: Ritualistic behavior before sleep 28% in each Gp; Periodic leg movement in sleep (PLMS) 22% & 34%, sleep walking 22% & 18%, sleep talking 50% & 70%, vivid nightmares 18% & 27% of Gp A & B, respectively. Impact: In each Gp 50% had difficulty in waking up, 65% felt unrefreshed after sleep, 54% experienced excessive day time sleepiness.

**Conclusion:** Sleep problem is common in children with TS irrespective of associated ADHD. The impact of this problem is high, thus necessitating its inclusion as a co-morbidity in TS.

**CS-42. Posterior reversible encephalopathy syndrome in pediatric patients**

Schreiber J, Carpenter J, Kaulas H (Washington, DC)

**Objectives:** The aim of this study was to describe the clinical features in pediatric patients with posterior reversible encephalopathy syndrome (PRES).

**Methods:** Patients diagnosed with PRES from 6/1/2008 to 4/1/2011 were identified through a prospective pediatric neurology ICU database and a neurology log of inpatients and consults.

**Results:** Fifteen patients were identified. Mean age was 11.7 years (range, 5–17) and 73% were girls. All patients except one were found to be hypertensive (mean 25/11 mmHg above the 99th percentile for those taking immunosuppressive agents vs. 43/20 mmHg). 53% percent had renal disease, three who were also taking immunosuppressive therapy. Five were status post bone marrow or stem cell transplant and were on immunosuppressive treatment. The one patient without hypertension was receiving Tacrolimus for bone marrow transplant. One patient had recurrent PRES (3 episodes separated in time). Presenting signs/symptoms of each episode in order of decreasing frequency were acute encephalopathy (16), seizures (13), headache (12), subjective vision changes (9), status epilepticus (4), and focal neurologic findings (2). Most with seizures (10/13) were treated with short term antiepileptics. One patient developed new onset complex partial epilepsy. Follow-up neuroimaging was normal or improved in all 7 patients where repeat neuroimaging was obtained.

**Conclusions:** Patients affected with PRES were commonly hypertensive and/or taking immunosuppressive agents including Tacrolimus and cyclophosphamide. Seizures were a frequent presenting symptom but epilepsy was uncommon in short term follow up.

**CS-43. Preschool diagnostic process and changes in diagnosis of autism spectrum disorder**

Gabis VL, Maayan M, Rivka S, Aya S-H, Marcy Y (Tel Hashomer, Israel)

**Objective:** During early development autism spectrum disorders (ASD) share features common to other disorders and characterized by a wide range of comorbidity. Diagnostic process should be based on information from several sources and social contexts. Coordinated collaboration between professionals from various disciplines and structured measurements, may lead to a comprehensive diagnosis of ASD and comorbidity. A diagnostic kindergarten set-up for children may facilitate a multidisciplinary diagnosis, integrated with a “family centered” intervention process.

We examine the changes in children diagnoses after one year of observation and treatment in a special education set-up, and assessed common/comorbidity, differential diagnosis and subsequent placement recommendations.

**Methods:** Seventy-six diagnoses of children, age 18–42 months at admission, attended the “diagnostic preschool” at Weinberg Center during the last decade. Changes in the frequencies of ASD diagnoses were calculated prior and after discharge as well as frequencies of comorbid disorders.

**Results:** Pre admission diagnoses changed in almost half of children (44.7%) of after one year of treatment. From children admitted with other developmental diagnoses, 14.2% were diagnosed with ASD at the end of the year. In contrast, children admitted with ASD in 25% diagnosis changed and was removed. Language disability, was present in 76%. Comorbid disorders were present in 66% of cases. Subsequent to one year of treatment, a less intensive special education program or a regular kindergarten was recommended in half of children.

**Conclusions:** Diagnosis of ASD in childhood is dynamic and requires a multidisciplinary diagnostic process combined with intervention.
POSTERS: Developmental/ Degenerative Disorders

DD-1. The influence of a multi-sensory intervention for preterm infants, provided by parents, on developmental abilities and on parental stress levels

Objectives: Preterm infants are at increased risk of neurodevelopmental impairments. There are only few theory-based, “parent-focused intervention” programs which start at an early stage during Neonatal Intensive Care Unit (NICU) stay, and their influence on child’s development. We designed a multisensory intervention based on NITCAP theories, to be provided by parents during NICU hospitalization of their preterm infants. We assessed developmental and parental stress outcome after 2–3 years.

Methods: A multi-sensory intervention program on preterm infants hospitalized at the NICU was implemented, including parental training. The study included 21 subjects as intervention group, and 20 subjects as control group. Since the intervention involved changes of general NICU setup, control group were recruited prior to intervention. Five different developmental areas: Cognitive, Language, Motor, Social-Emotional and Adaptive Behavior using the Bayley III scale were evaluated, as well as parental stress.

Results: We found a positive intervention effect on the toddlers’ language and motor skills’ development. We could not find any significant differences between groups in cognitive and adaptive behavior outcomes, nor in head circumference growth. In addition, we found a marked influence of the intervention in social-emotional scores. Gender, twinning and level of prematurity were found as significant variables.

Conclusions: A multi-sensory intervention program for preterm infants may improve language and motor outcomes at 2–3 years. We speculate that intervention program focused on positive parent-infant interactions and identification of the infant’s needs, enhanced the infant’s abilities. These findings support the impact of early intervention involving parents on neurodevelopmental outcomes of prematurity.

DD-2. Altered neural activation in ornithine transcarbamylase deficiency during working memory: An fMRI study

Objectives: Ornithine transcarbamylase deficiency (OTCD) an X-linked inborn error of metabolism, is the most common of the urea cycle disorders. Deficient protein metabolism results in hyperammonemic (HA) episodes which confer substantial injury to the brain’s white matter. Additionally, it has been shown that “asymptomatic” OTCD is associated with deficits in an array of cognitive subdomains, despite normal global IQ. These include impaired working memory, executive cognition and reaction speed, and contribute significantly to disability in OTCD. Aim: To test for differences in BOLD signal activation between OTCD patients and healthy controls during a working memory task.

Methods: Nineteen OTCD patients and 21 healthy controls participated in a case-control study at Georgetown University Medical Center. An N-back working memory task was performed in a block design using 3T functional magnetic resonance imaging.

Results: In OTCD patients, we observed increased BOLD signal within the right superior frontal gyrus and decreased signal in the basal ganglia bilaterally, relative to healthy controls.

Conclusions: Activation patterns in OTCD patients point to disorganized activation of the working memory network in these patients. Overall, these findings offer preliminary evidence that brain injury conferred by biochemical dysregulation in OTCD may impact the functional neuroanatomy serving working memory processes. OTCD patients show relatively higher DLPCF activity and reduced basal ganglia activity, suggesting a pattern of prefrontal inefficiency and impairment in manipulation and noise-regulation pathways. Further investigation at higher cognitive load is required to further interrogate these neurocognitive differences between OTCD patients and healthy subjects.

DD-3. Sex differences in clinical progression and quality of life in Juvenile Neuronal Ceroid Lipofuscinosis

Objectives: Juvenile Ceroid Lipofuscinosis (JNCL, Batten disease) is a childhood onset neurodegenerative disease, characterized by vision loss, seizures, dementia and premature death. Overall severity of JNCL disease does not seem to differ between males and females; however, some aspects of the disease trajectory may differ.

Methods: We investigated six age-related factors determined by administration of the Unified Batten Disease Rating Scale (UBDRS), patient registry and a QoL survey. Age at which subjects had loss of ambulation, un intelligible speech and inability to perform ADLs was determined by UBDRS scores and plotted as a Kaplan-Meier curve. Age at symptom onset, QoL and age at death were compared between males and females with parametric statistics.

Results: Among 228 individuals with JNCL, who died at 30 years or younger (128 females, 98 males; age at death 13–30 years), the average age at death for females was lower than for males (females mean = 20.9 years, SD=4.5; males mean= 22.2; SD = 4.2; t=-2.17, p=0.03). Evaluation of age of onset showed that females experience first symptom onset at least one year later than males (females mean=6.24 years, SD= 1.2; males mean= 5.16 years, SD= 0.88). Using a parent-rated QoL instrument, females QoL related to physical function was significantly lower than males, with similar trends noted for other QoL domains.

Conclusion: These data suggest that the disease course for females may unfold more rapidly and that the impact of the disease on QoL is greater for females than for males.

DD-4. Tract based spatial statistics of DTI color-coded orientation map in Angelman Syndrome

Objectives: In the present study, we sought to determine whether abnormal regional white matter architecture in
Angelman Syndrome (AS) children could be detected by a sensitive TBSS based whole brain approach using DTI color-coded orientation map.

**Methods:** Using tract based spatial statistics (TBSS) of DTI color-coded orientation map, the fraction of fibers that are oriented in anteroposterior (AP) and mediolateral (ML) directions were determined in the whole brain white matter in 7 children with Angelman Syndrome (AS, mean age, 70 ± 25.78 months, five males) and 7 children with typical development (TD, mean age, 79.8 ± 17.25 months, four males).

**Results:** Children with AS had a significantly lower AP component than the TD group in 10 clusters (4 bilateral and 2 unilateral). Bilateral clusters were located in inferior fronto-occipital (IFO), cingulate, anterior thalamic radiation (ATR) and arcuate fasciculus (AF) regions. Unilateral clusters involved left brainstem and right uncinate regions. Similarly, children with AS had significantly lower ML component than TD group in 5 clusters (2 bilateral and 1 unilateral). Bilateral clusters were located in corpus callosum and cingulate regions while the unilateral cluster was located in left ATR region.

**Conclusions:** AS patients have global impairment of white matter integrity including both AP and ML components in whole brain suggesting a potential problem with axon guidance mechanisms during brain development possibly due to loss of UBE3A gene expression.

**DD-5. Angelman syndrome: genomic imprinting overlaps maturational EEG patterns**
Youn MS, Lee EH, Kim JH, Ko TS, Yoo HW (Seoul, Korea)

**Objective:** Angelman syndrome is a neurogenetic disorder caused by a lack of UBE3A gene expression from the maternally inherited chromosome 15 due to various 15q11–q13 abnormalities. In addition to having microcephaly, severe developmental delay, gait ataxia, speech impairment, and happy demeanor, over 90% of these patients have epilepsy and its distinctive electroencephalographic changes. Epilepsy predominates in childhood, but may persist or reappear in adulthood. The seizure types may be quite varied and sometimes difficult to control.

**Methods:** We retrospectively reviewed and analyzed data of 30 patients with genetically confirmed AS at Asian Medical Center.

**Results:** When we analyzed 47 EEG records from 16 patients, we found that slow background patterns were significantly associated with refractory periods of epilepsy and that spike discharges tended to change from notched delta at young age, shifting from posterior to anterior head regions.

**Conclusions:** Children with Angelman syndrome follow general developmental patterns, with specific patterns of EEG reflecting the maturational pattern of the brain and epileptic activity.

**DD-6. Disruption of CNS connectivity following developmental hypoxic injury**
Bonkowsky J, Stevenson T, Kogelchatz C, Trinh T, Fujimoto E (Salt Lake City, UT)

Hypoxic injury to the developing human brain is a major cause of both acute and chronic neurodevelopmental impairment. The effects of chronic hypoxia on the developing brain are poorly understood, despite the long-term adverse neurological problems that can result including mental retardation, epilepsy, autism, and ADHD. Using a small vertebrate model, we have found that developmental hypoxic injury leads to impaired pathfinding of forebrain commissural axons, and is not caused by apoptosis or changes in overall brain patterning. Hypoxia only induces the pathfinding deficits during the period of axon extension, and is due to a failure of commissural axons to cross the midline. Further, the pathfinding defects are due to activation of the hypoxia-inducible transcription factor hif1α pathway, and can be mimicked by chemical inducers of the hif1α pathway or by expression of a constitutively active form of hif1α. Using a candidate gene approach, we have determined that the cell-surface ligand ephrinB2a mediates the pathfinding defects. Misexpression of a dominant-negative form of ephrinB2a, or knock-down of ephrinB2a, can rescue the pathfinding defects, through a reverse signaling mechanism. These studies offer the potential for developing a small vertebrate model in which to perform drug screens to rescue effects of hypoxia.

**DD-7. Congenital malformations in Cerebral Palsy: a distinct subset**
Self L, Dagenais L, Shevell (Montreal, QC)

**Objective:** A subset of individuals with cerebral palsy also have concomitant congenital malformations in non-CNS organ systems.

**Methods:** In this study a population-based cerebral palsy registry (REPAQ) was used to compare those children with cerebral palsy with and without an associated congenital malformation.

**Results:** A total of 240 children in whom complete information was available included were included in REPAQ over a 6-year inclusive (1999–2002) birth interval. Fifteen percent (n=36) had an associated congenital malformation. These children did not differ from those without an associated congenital malformation in terms of neurologic subtype, gross motor severity (GMFCS Level) or co-morbidity, with the exception of a statistically significant higher frequency of cognitive impairment in the context of an associated congenital malformation. Furthermore there did not appear to be any difference between the two groups regarding prenatal or perinatal factors recognized as potential antecedents for either cerebral palsy or congenital malformations.

**Conclusions:** Children with cerebral palsy and an associated congenital malformation do not appear to represent a distinct phenotype of this heterogeneous symptom complex.

**DD-8. Cost-benefit analysis of early childhood development intervention programs**
Veerapandiyam A (Durham, NC), Alderman H (Washington, DC), Steele S, Mikati MA (Durham, NC)

**Background:** Early childhood developmental interventions (ECDIs) aim to improve long term cognitive outcome, but need to be cost effective.

**Objective:** Determine the cost-effectiveness of ECDIs.

**Methods:** Comprehensive and systematic review and analysis of the relevant worldwide literature to determine, on a percent per capita gross national product (PCGNP) comparative basis: i) duration of ECDIs and their yearly costs, ii) impact of interventions on cognitive outcomes, and iii) impact of improved cognitive outcome on expected later individualized PCGNP. We subsequently performed a

**Results:** Using a conservative analysis we found that preschool ECDIs (ages 3 through 5 years) result in an average increase of IQ of 8.05 points (range 4–12, mean follow-up: 6 years) and that a higher IQ is associated with higher income (each single IQ point is associated with a 0.9% increase in PCGNP/year, lifelong). Projected income accumulation versus accumulation of the value of initial costs revealed a break-even point at the age of 33 years with a resultant gain of 3,567% of PCGNP (equivalent to $1,179,650 in 2008 in the USA) at retirement age 65. Low estimate of effect of intervention resulted in a break-even point at the age of 45 years (gain of 1,106% PCGNP; $365,894), and a high estimate in a break-even point at the age of 29 years (5,966% PCGNP; $1,973,014).

**Conclusions:** ECDIs have long-term cost-effective benefits. However, these benefits are recuperated well into the future.

**DD-9. Infantile spasms in Trisomy 21: EEG characteristics and response to treatment**

**Objective** Describe clinical and EEG characteristics of infantile spasms (IS) in Trisomy 21 and assess treatment response and long-term outcomes.

**Methods** Medical records and EEG’s from 1991–2008 for children with IS and trisomy 21 were reviewed. Treatment response was defined as clinical cessation of spasms and absence of hypsarrhythmia on prolonged video-EEG. Long-term epilepsy and developmental outcome data were also collected.

**Results** We identified 12 children with trisomy 21 and IS accounting for 5% of cases of IS. Median age of onset was 6 months and at admission 11 months. Of 12 children, 11 still had clinical spasms on admission and one had responded to clonazepam initiated elsewhere. Eleven of 12 (92%) had classic hypsarrhythmia, 9/10 with clinical spasms had an electrodecremental ictal pattern and 3/12 (25%) had continuous focal slowing on interictal EEG. Ten of 11 infants with clinical spasms on admission were treated with Adrenocorticotropic Hormone and 7 had a full response (no spasms and no hypsarrhythmia). Three (43%) subsequently relapsed and all responded to another course of treatment. At last follow-up (mean 4.5 years), 9/12 (75%) were seizure free with or without medication. Two non-responders had intractable epilepsy and profound retardation. Developmentally, five of six who could be assessed met criteria for autistic spectrum disorder.

**Conclusions** The EEG characteristics, treatment response and long-term epilepsy outcomes in children with IS and trisomy 21 were more similar to those seen in cryptogenic than symptomatic IS. However, IS in trisomy 21 is associated with a high rate of autism.

**DD-10. A sensitive diffusion tensor imaging quantification method to identify language pathway abnormalities in developmentally delayed children**
Gopal SP, Tiwari VN, Venstra AL, Kumar A, Behen ME, Chugani HT, Sundaram SK (Detroit, MI)

**Objective** One of the neurologic substrates of impaired language in developmentally delayed children (DD) is the poor development of perisylvian language networks such as arcuate fasciculus. In the present study, we sought to determine whether abnormal regional white matter architecture in the broader perisylvian region could be used as a sensitive quantitative method to identify language abnormalities DD children.

**Methods** We performed Diffusion tensor imaging (DTI) in 15 DD subjects (age: 61.1±20.9 months) and 15 age-matched typically developing (TD) children (age: 68.4±19.2). Using DTI color-coded orientation map, we quantified the fiber orientation distribution in perisylvian region (Fig.1) through which the arcuate fasciculus passes. The fraction of fibers in the region that are oriented in anteroposterior (AP) and mediolateral (ML) directions were determined and their ratio was calculated. These measures were subsequently correlated with Vineland adaptive behavior scores.

**Results** The AP/ML ratio was more sensitive than tracography in characterizing perisylvian regional abnormalities in DD children. The AP/ML ratio of the left perisylvian region was significantly lower in DD children compared to TD children (p = 0.03). The ML component of bilateral perisylvian regions was significantly higher in DD children compared to TD children (p=0.01 (left) and p=0.004(right)). A significant negative correlation of the ML component with Vineland communication skills was observed (r = -0.657, p = 0.011).

**Conclusions** We observed regional white matter architectural abnormalities in perisylvian region in DD children. It can be used as a sensitive quantitative method to identify language abnormalities in these children.
subpopulations of individual corticostriatal synapses. By returning the synapse to a more stable, normalized state, this synaptic plasticity encodes learned experiences and fosters compulsive and automatic behaviors that control motor movements and emotions, with aberrant function related to dystonia, tics and co-morbid neuropsychological diseases.

DD-12. Is hemimegalencephaly a fetal tauopathy?
Sarnat HB, Flores-Sarnat L (Calgary, AB), Crino PB (Philadelphia, PA), Hader W, Bello-Espinosa L (Calgary, AB)

Background: Upregulation of abnormally phosphorylated tau protein is a feature of many adult neurodegenerative diseases, but is not reported in fetuses or infants. Abnormal tau during development potentially can interfere with growth, differentiation and migration of neuroblasts and glioblasts by microtubular disruption, resulting in dysgenesis and hamartoma. Several reports have identified enhanced glioblasts by microtubular disruption, resulting in dysgenesis and hamartoma. Multiple reports have identified enhanced mTOR cascade signaling in hemimigalencephaly (HME), an hamartomatos malformation associated with refractory epilepsy. mTOR pathway also was studied.

Methods: We examined surgical resections for epilepsy of brains of 3 infants with HME. One case died postoperatively of complications and autopsy was performed promptly, providing opportunity to examine other brain structures. Multiple immunocytochemical cell markers, mildly phosphorylated tau antibody and α-B-crystallin were examined, as well as ultrastructural examination. The mTOR pathway also was studied.

Results: Overexpression of tau protein was demonstrated in the hippocampus and neocortex. Antibodies against α-synuclein, ubiquitin and TDP45 were nonreactive, but α-B-crystallin was positive. Many dysmorphic cells showed mixed neuronal/glial lineage and expression of nestin and vimentin. Resident stem cells in the dentate gyrus were proliferated. EM exhibited lipidoic degeneration of many hippocampal neurons. The contralateral hemisphere, by contrast, did not show tau overexpression, except in rare, scattered dysmorphic neurons, and none in subcortical structures. Robust immunolabeling for the phosphorylated isoform of S6 protein, a marker of activated mTOR signaling, was identified in the dysmorphic cells.

Conclusions: Abnormal tau expression may be a factor in the pathogenesis of HME by disrupting microtubule assembly through the mTOR pathway during cellular growth and differentiation. It represents a fetal tauopathy.

DD-13. Endothelial alterations in mitochondrial cytopathies of early infancy
Sarnat HB, Flores-Sarnat L, Khan A (Calgary, AB)

Background: Electron microscopy is a reliable method of diagnosing mitochondrial disorders in striated muscle biopsy; histology and even biochemical analysis are not always diagnostic in infancy. Ultrastructural alterations are seen not only in mitochondria of myofibres, but also in capillary endothelium.

Methods: Quadriceps muscle biopsies of 3 infants and 2 toddlers, ages 23 days to 3.5 years, were performed for clinical, MRI and metabolic serum markers suggestive of systemic mitochondrial disease. Pathological studies included histochemistry, EM and biochemical assay of respiratory chain enzymes.

Results: EM demonstrated frequent severe ultrastructural alterations of mitochondria in capillary endothelial cells more than in myofibres. Changes included stacking of cristae and paracrystallin structures, including within long, looped villi. Mitochondrial alterations of myofibres were fewer and less severe, without paracrystallin structures.

Conclusions: Mitochondrial ultrastructural alterations in young infants and toddlers with mitochondrial cytopathies are more frequent in the endothelium than in myofibres in muscle biopsies. This distribution may explain the frequent lack of prominent histochemical changes and biochemical abnormalities in homogenates of muscle biopsies of young patients. Endothelial involvement in the brain may contribute to epilepsy and neuronal death by ischemia and impaired transport of molecules and toxic metabolites.

DD-14. Parent-reported benefits of flupirtine in Juvenile Batten Disease (CLN3) are not supported by quantitative data

Objective: Juvenile neuronal ceroid lipofuscinosis (JNCL; CLN3 disease; Batten disease) is an autosomal recessive neurodegenerative disease of childhood characterized by vision loss, cognitive decline, motor dysfunction, seizures, and behavior problems. No therapy has been shown to slow the progression of disease in JNCL patients. Flupirtine has been shown in vitro to reduce apoptosis in CLN3 lymphocytes. Based on that preclinical study, several children with JNCL have been given flupirtine by their parents. The purpose of this study was to determine if there was evidence of attenuated disease progression in any JNCL symptom domain.

Methods: We administered a survey to parents of JNCL children to qualitatively assess flupirtine efficacy. We used the Unified Batten Disease Rating Scale (UBDRS) to investigate quantitatively three age-related factors: loss of independent ambulation, loss of intelligible speech, and loss of independence in activities of daily living (ADLs). UBDRS scores for the physical, behavior, and capability subscales were determined in flupirtine-exposed subjects and compared to age-, sex-, and genotype-matched subjects who had never taken flupirtine.

Results: Twenty-one percent of survey responders reported administering flupirtine to their JNCL child, and 56% of these families perceived beneficial changes that they attributed to flupirtine. However, our quantitative, prospectively obtained data did not show any change in JNCL disease severity or progression that could be attributed to flupirtine.

Conclusions: We were not able to demonstrate that flupirtine slowed disease progression at a quantitatively detectable rate in this sample of JNCL subjects. This study highlights the need for prospective experimental therapeutic research.

DD-15. Feasibility and reliability of teledicine administration of the unified Batten Disease Rating Scale: a powerful tool for rare disease clinical research

Objective: Juvenile Neuronal Ceroid Lipofuscinosis (JNCL; CLN3 disease; Batten disease) is an inherited rare fatal neurodegenerative disease of childhood characterized by vision loss, cognitive decline, motor dysfunction, seizures, and behavior problems. No therapy has been shown to slow the progression of disease in JNCL patients. Flupirtine has been shown in vitro to reduce apoptosis in CLN3 lymphocytes. Based on that preclinical study, several children with JNCL have been given flupirtine by their parents. The purpose of this study was to determine if there was evidence of attenuated disease progression in any JNCL symptom domain.

Methods: We administered a survey to parents of JNCL children to qualitatively assess flupirtine efficacy. We used the Unified Batten Disease Rating Scale (UBDRS) to investigate quantitatively three age-related factors: loss of independent ambulation, loss of intelligible speech, and loss of independence in activities of daily living (ADLs). UBDRS scores for the physical, behavior, and capability subscales were determined in flupirtine-exposed subjects and compared to age-, sex-, and genotype-matched subjects who had never taken flupirtine.

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Conclusions: We were not able to demonstrate that flupirtine slowed disease progression at a quantitatively detectable rate in this sample of JNCL subjects. This study highlights the need for prospective experimental therapeutic research.
loss, seizures, dementia, behavioral difficulties, and motor impairment. The Unified Batten Disease Rating Scale (UBDRS) is a reliable research tool designed for in-person evaluation to quantify disease progression. We sought to determine if remote administration of the UBDRS physical subscale was reliable and feasible across a broad range of disease severity.

**Methods:** For the initial telemedicine evaluations, a trained rater performed the exam and rated the subjects while a second trained rater simultaneously rated the subjects via live video. For the other sessions, a non-physician examiner performed the exam while a trained rater scored the subjects via live video. Within 30 minutes of the evaluation, a second trained rater conducted an in-person evaluation and separately rated the subjects. Reliability was determined by Intra-class Correlation Coefficient (ICC).

**Results:** Subjects (N=13) represented a wide range of disease severity. Remote administration of the UBDRS physical subscale had high inter-rater reliability in all rated subjects (ICC = 0.94). When only the subjects (N=10) who had been examined by the untrained rater and rated remotely were included in the analysis, the reliability was essentially unchanged (ICC = 0.95). Telemedicine administration of the UBDRS took no more time than did in-person administration.

**Conclusions:** The UBDRS physical subscale is reliable and feasible for telemedicine administration. These results have important implications for enhancing the feasibility of rare disease research.

**DD-16. Seizures are associated with a marked worsening of dementia in Down syndrome**

Doran E, Tournay A, Movsesyan N (Orange, CA), Nguyen V, Gillen D (Irvine, CA), Lois IT (Orange, CA)

**Objective:** While seizures are known to be associated with Alzheimer disease (AD) type dementia in Down syndrome (DS), it is unclear how they affect the rate of cognitive decline.

**Methods:** During a treatment trial for dementia in DS (NIH-AG021912), we became aware that subjects with a seizure history showed rapid neurological decline to the point of being untestable. Estimates of associations were obtained from the Continuation Ratio Model for performance-based measure outcomes (Severe Impairment Battery; Brief Praxis Test) and the Linear Mixed Effects Model for informant-based measure outcomes (Dementia Questionnaire for Mentally Retarded Persons; Vineland Adaptive Behavior Scales). In addition to seizure status, we also adjusted for age, gender, APOE e4 allele status and baseline cognitive impairment level.

**Results:** The seizure cohort comprised 24 of 53 total participants (45%). For the performance measures, the estimated odds ratios were 9.53 (95% CI: 2.32, 39.07) and 12.58 (95% CI: 2.18, 72.70), ratios that were significantly different from 1 (p<0.05), indicating that the seizure group reached “inability to test” earlier than the non seizure group. For the informant measures, point estimates and 95% CIs revealed significantly higher scores, indicating more severe impairment in the seizure group. None of the other covariates were associated with a significant odds ratio.

**Conclusions:** Co-occurring seizures are associated with an accelerated progression of dementia in adults with DS and AD. In these patients, the occurrence of seizures appears to have a worse prognosis than seizures occurring in early childhood.

**DD-17. Cell proliferation and oxidative stress response mediated by Nrf2 pathways are modified in fibroblasts from Sturge-Weber syndrome patients**

Kadam S (Baltimore, MD), Guck M (Bethesda, MD), Cole R, Watkins P, Comi A (Baltimore, MD)

**Objective:** Sturge-Weber syndrome (SWS) results in a facial port-wine birthmark, brain vascular malformation, and neurologic symptoms including seizures and stroke-like episodes. Sturge-Weber syndrome occurs sporadically and the etiology is unknown; a causative somatic mutation is hypothesized and we aimed to study resulting protein expression changes.

**Methods:** Early passage fibroblast cell lines were derived from affected and unaffected skin punch biopsies from 4 individuals with SWS. We employed isobaric tags for relative and absolute quantification (iTRAQ-8plex) based LC-LC MS/MS approach to identify differentially expressed proteins expression between port-wine-derived fibroblasts and normal skin-derived fibroblasts, reported as ratios.

**Results:** Proteins were identified that were significantly up- or down-regulated (i.e., ratios >1.2 or <0.8) in 2 or 3 pairs of samples (n=30) and their associated p values reported. Biological functional analysis using the Ingenuity Pathway Analysis (IPA) tool showed significant alterations in cell growth and proliferation. The disease disorders that figured prominently in the Top biological functions in 3 of pairs were Cancer, and Skeletal and Muscular Disorders. In all four pairs, Oxidative Stress Response Mediated by Nrf2 was listed in the top toxicologic pathways. Consistently the individual up-regulated proteins were associated with pathways that support cell proliferation and down-regulated proteins control proliferation.

**Conclusion:** Protein analysis of fibroblast cell lines derived from normal and SWS port-wine skin suggest that the putative somatic mutation may impact the Nrf2 oxidative stress response pathway and cellular proliferation.

**DD-18. Escitalopram improves mood, anxiety and motor function in adolescent girls with Rett syndrome**

Barnes K, O'Leary H, Khwaja O (Boston, MA)

**Objective:** Adolescent girls with Rett syndrome (RTT) are at risk of developing mood disorders, anxiety frequently associated with a worsening of extra-pyramidal symptoms. There have been anecdotal reports of improvements in mood and anxiety with escitalopram oxalate treatment. We aim to study the effects of escitalopram on mood, anxiety and motor function in RTT.

**Methods:** This was a retrospective, open label, non-placebo controlled study. Subjects were diagnosed as having deterioration in mood and worsening of anxiety in the preceding six months. In addition all subjects clinically had worsening extrapyramidal symptoms. Primary outcome measure was the Clinical Global Impression Improvement scale. Secondary outcome measures were the Unified Parkinson Disease Rating Scale (Motor), the Screen for Anxiety-Related Emotional Disorders, Children's Depression Rating Scale-revised and subscales of the Aberrant Behavior Checklist.

**Results:** 19 subjects aged 9–18 years were treated with a mean escitalopram dose of 12 mg for at least 12 weeks. 12 of 19 subjects had a CGI-I score ≤ 2 (much improved or
very much improved). Significant improvements were also seen in motor symptoms and on the SCARED, CDRS and subscales of the ABC. These improvements were more marked in the 12 patients defined as responders based on CGI-I scores. There were no major adverse events and no effect on the QTc interval.

Conclusions: Escitalopram appears to have efficacy in the treatment of adolescent girls with RTT with mood or anxiety disorders and motor dysfunction.

Results: Out of fifty-eight SWS patients with brain involvement that were started on aspirin, fifty reported no significant side-effects and eight patients reported various side-effects. Out of the patients reporting complications, five reported only experiencing minor side-effects (nosebleeds, bruising). Three patients reported serious side-effects including allergic rash, hematemesis, and subdural hematoma. Aspirin was stopped in six of the eight patients due to side-effects or complications.

Conclusion: This study reviews aspirin use in a large population of SWS patients. While available data suggests efficacy, use in such a young population brings up issues regarding safety. In this study, only a minority of patients experienced side-effects, suggesting that aspirin should not be withheld due to concerns about complications. Future studies will further evaluate clinical efficacy of aspirin in SWS in order to better assess the risks and benefits.
Objective: While child neurology resident education includes teaching on various etiologies of neurodevelopmental diseases, exposure to evidenced based guidelines and cost of the diagnostic evaluation for global developmental delay (GDD) may be lacking. This study aims to assess the effect of a resident developed quality improvement project developed to improve resident knowledge on evidenced based guidelines on the evaluation of GDD and the cost of diagnostic tests.

Methods: 12 child neurology residents at Children’s Hospital Boston were surveyed on knowledge based questions relating to the current guidelines of evaluation of GDD and cost of commonly ordered diagnostic tests. The curriculum was offered to the child neurology residents and highlighted the American Academy of Neurology (AAN) Practice Parameters on global developmental delay (GDD), the current cost of commonly ordered diagnostic tests, and the cost-benefit of these tests for GDD evaluation. Two months later, residents were re-tested and pre- and post- curriculum results were compared using a two-tailed, paired student-t-test.

Results: Significant improvement in knowledge of the evidenced based guidelines on the evaluation of GDD was noted, \( P = 0.01 \). There was no significant improvement on residents’ knowledge about the cost of the diagnostic GDD evaluation, \( P = 0.25 \).

Conclusion: While the curriculum was helpful in improving resident knowledge of an evidenced based evaluation of GDD, it was not an effective way in improving residents’ knowledge on cost of this work-up. This study highlights the need to incorporate evidence based guidelines and cost of care into resident education in a more continuous way.

DD-23. Neurodevelopmental status in children with extraventricular obstructive hydrocephalus
Kuwatk A, Laughlin S, MacGregor D, Moharir M (Toronto, ON)

Objectives: Extraventricular Obstructive Hydrocephalus (EVOH) is a relatively common neuroimaging finding in infants and young children who are investigated for macrocephaly. These children typically have non-progressive enlargement of ventricular and extra-axial subarachnoid spaces. Literature concerning the clinical implications of these findings in the context of macrocephaly is scarce and controversial as diverging opinions exist regarding the neurodevelopmental outcome. The objective is to study the developmental status of children with macrocephaly and EVOH at presentation and assess the long term neurodevelopmental outcome.

Methods: A retrospective study of children with macrocephaly and radiologically confirmed EVOH (January 2000 to July 2009) was performed by chart review completed by a developmental pediatrician and neuroimaging review by a pediatric neuroradiologist. All children with a clear comorbid neurological, developmental and genetic condition were excluded. Neurodevelopmental status was established by neurometabolic clinical examination conducted by a pediatric neurologist.

Results: Ninety-three children (73 male, mean age; 10 months, range; 3 months-3 years at presentation) were analyzed. Thirty (32%) had mild to moderate neurodevelopmental deficits. No significant association was found between the developmental outcome and the degree of ventriculomengry or extra-axial space enlargement.

Conclusion: Children identified with macrocephaly and EVOH should be followed with regular developmental assessment to provide prognosis about the neurodevelopmental outcome for children who will need timely interventions.

DD-24. Biochemical and molecular diagnosis in children with Leigh syndrome in Korea
Lee YM, Kang HC, Lee JS, Kim HD (Seoul, Korea)

Objective: Deficits of the mitochondrial respiratory chain is reported to be the major cause of Leigh syndrome. This study compared the aspects of biochemical and molecular diagnosis of mitochondrial respiratory chain complex (MRC) defect in Leigh syndrome, using methods of biochemical enzyme assay and molecular genetic analysis.

Methods: We included total number of 82 patients who satisfied the clinical criteria of Leigh syndrome. All patients underwent muscle biopsy. We performed biochemical enzyme assay to analyze MRC enzyme and molecular genetic analysis of muscle tissues to search for the presence of specific, known mtDNA mutations of Leigh syndrome and SURF1 mutation. Clinical aspects of cases without mutation were compared with those of the cases with mutation.

Results: MRC defect was found in 47 (57.3%) out of 82 patients. MRC I defect was seen in 23 (28.0%) cases and MRC IV defect in 15 (18.3%) following it. There were 12 with mutation including 9 with confirmed mtDNA mutation, 3 with SURF1 mutation and 35 patients without mutation. Continuous ventilator care and perinatal asphyxia were reported significantly more often in mutation(+) group. In brain MRI, the percentage of multiple lesion, brain stem and thalamus lesion were significantly higher in mutation(+) group. Statistically higher proportion of mutation(+) patients had combined MRC defect.

Conclusions: Further gene analysis on more extended group of patients will enable us not only to improve diagnostic precision but to understand Leigh syndrome better by revealing the correlation between its phenotypes and genotypes.

DD-25. Severe postnatal progressive microcephaly and brain atrophy in the Caucasus Jewish ethnic group.
Kaufmann R (Petrov Tikva, Israel), Strausberg R (Petrov Tikva, Israel), Mandel H (Haifa, Israel), Fattal-Valevski A (Tel-Aviv, Israel), Ben-Zeev B (Ramat-Gan, Israel), Naarnati A (Jerusalem, Israel), Saggi A (Jerusalem, Israel), Zeviri S (Jerusalem, Israel), Koenen O (Petrov Tikva, Israel), Mimouni-Bloch A (Petrov Tikva, Israel), Dobyhns WB (Chicago, IL, USA), Edvardson S (Jerusalem, Israel), Pines O (Jerusalem, Israel), Elpeleg O (Jerusalem, Israel)

Objectives: Postnatal Primary microcephaly is a feature of many neurological disorders, mostly associated with mental retardation, seizures, and spasticity, and it typically carries a grave prognosis.

Methods: We represent a new autosomal recessive syndrome exclusively seen in four families, with five siblings, of Caucasian Jewish origin. It includes: onset in early infancy with rapid neurologic deterioration, progressive postnatal microcephaly, atrophy and hypomyelination affecting the cerebrum, cerebellum and pons, profound mental retardation, spastic quadriplegia and generalized seizures. All patients, except one, are still alive at the time of this report, aged 5 months to 16 yrs.

Results: A search for a common homozygous region revealed a 2.28 Mb genomic segment on chromosome 11 that encompassed 16 protein-coding genes. A missense mutation in one of them, MED17, segregated with the disease state in the families and was carried by four of 79 anonymous Caucasian Jews. A corresponding mutation in the homologous S.cerevisiae gene SRB4 inactivated the
protein, according to complementation assays. Screening of MED17 in additional patients with similar clinical and radiologic findings revealed four more patients, all homozygous for the p.L371P mutation and all originating from Caucus Jewish families.

Conclusions: We conclude that the p. L371P mutation in MED17 is a founder mutation in the Caucus Jewish community and that homozygosity for this mutation is associated with infantile cerebral and cerebellar atrophy. Screening for the mutation is warranted among Caucus Jewish couples, which would enable a better estimation of the carrier rate and identify couples at risk.

DD-26. Long-term safety and efficacy of Clobazam for Lennox Gastaut syndrome (LGS): 2-year results of an open-label extension (OLE) study

Ng YT (Phoenix, AZ), Conry JA (Washington, DC), Paolicchi JM (Nashville, TN), Kernitsky L (Richmond, VA), Mitchell WG (Los Angeles, CA), Drummond R, Austin SA, Weinberg MA, Owen JR (Deerfield, IL)

Objective: We assessed long-term safety and efficacy of open-label clobazam for drop seizures associated with LGS.

Methods: In an ongoing OLE (OV-1004), LGS patients who had completed 1 of 2 RCTs — OV-1002 (Phase II) or OV-1012 (Phase III) — received clobazam if ≤14 days had elapsed since their last doses. Most patients initially received 0.5 mg/kg/day (≤40 mg/day). Dosages were then managed based on safety/efficacy, with a maximum of 2.0 mg/kg/day (80 mg/day). Visits were at Day 1, Week 1, Months 1, 2, 3, 6, 9, and 12, and every 6 months thereafter. During the week preceding each visit, parents/caregivers maintained seizure diaries.

Results: 267 of 306 patients from OV-1002 or OV-1012 entered the OLE. As of July 1, 2010, 213 (79.8%) remained: 189 had received clobazam for ≥1 year, 128 for ≥18 months, and 94 for ≥2 years. Median percentage decreases (vs. RCT baseline) in average weekly drop-seizure rate were 71.1% and 91.6% at Months 3 and 24. Dosages decreases (vs. RCT baseline) in average weekly drop-seizure rate were 71.1% and 91.6% at Months 3 and 24. Dosages were then managed based on safety/efficacy, with a maximum of 2.0 mg/kg/day (80 mg/day). Visits were at Day 1, Week 1, Months 1, 2, 3, 6, 9, and 12, and every 6 months thereafter. During the week preceding each visit, parents/caregivers maintained seizure diaries.

Conclusions: Neurodevelopmental abnormalities in children with PHACE syndrome include gross motor and language delay, hypotonia during infancy, and abnormalities speech. Brain structural abnormalities did not predict outcomes, although this study may have been underpowered to detect an association.

DD-28. Feasibility, reproducibility, and clinical validity of the Pediatric Anxiety Rating Scale (PARS) in Fragile X syndrome

Russo N (Chicago, IL) Yeinsky J (Chicago, IL), Hessl D (Sacramento, CA), Berry-Kravis E (Chicago, IL)

Objective: A core feature of fragile X syndrome (FXS) is anxiety, yet a valid outcome measure for anxiety in FXS is lacking. Given numerous impending targeted pharmaceutical trials directed at underlying biological defects and core symptoms in FXS, this study sought to evaluate the feasibility, reproducibility, and clinical validity of the Pediatric Anxiety Rating Scale (PARS), a clinician administered anxiety scale, as a potential outcome measure.

Methods: The PARS was administered twice (T1, T2; 4–8 weeks between sessions) to parents of 42 (age range 5–35, 26M, 25 participants<18 years) individuals with FXS. At T1, parents also rated their children on an established anxiety checklist (Anxiety, Depression and Mood Scale [ADAMS]). A Clinical Global Impression-Severity scale (CGI-S) for anxiety was obtained independently from the treating physician (EBK). Inter-rater reliability (IRR) for two non-physician clinical raters, intraclass correlation coefficients (ICC) for test-retest reproducibility, and correlation with other clinical measures were analyzed for the PARS.

Results: The PARS was successfully administered to all participants with high IRR (Symptoms Checklist r=0.862, Total Severity Index r=0.987). Number of Symptoms endorsed and Severity Scores showed excellent test-retest reproducibility (ICC =0.879 and 0.882, respectively). For the full cohort, Severity Scores correlated with CGI-S for anxiety (r=0.574, p<0.001), the ADAMS General Anxiety score (r=0.661, p<0.001) and multiple ADAMS subscores. Similar results were observed for gender and age subgroups.

Conclusions: The PARS shows promise as a feasible, reproducible measure of clinically-relevant anxiety in FXS for use in clinical trials.

DD-29. Attention deficit hyperactivity disorder in epileptic children with developmental delay

Kim GH, Eun SH, BL, Byeon JH (Ansan-si, Korea)

Objective: It is known that the attention deficit hyperactivity disorder (ADHD) is more frequent in children with epilepsy than in the general pediatric population. The aim of this preliminary study was to investigate whether the
prevalence of ADHD in epileptic children is higher even for people with well controlled epilepsy and without a significant developmental delay.

**Methods:** Epileptic children, aged 6 to 12 years, who visited for 6 consecutive months were included in the study. Among them we included only those without significant developmental delay as well as being seizure-free for over 3 months. We utilized parent questionnaires based on DSM-IV criteria to diagnose ADHD and Korean version of Child Behavior Checklist and Child Depression Inventory.

**Results:** We enrolled 56 patients (mean age, 9.6 ± 2.3) including 27 boys and 29 girls. Twelve (21.4%) were diagnosed with ADHD (9 combined, 3 inattentive types; 6 boys, 6 girls). The number of ADHD patients vary by epilepsy types: childhood or juvenile absence epilepsy (42.8%, 3 of 7); cryptogenic focal epilepsy (20.8%, 5 of 24); generalized epilepsy (20.0%, 2 of 10); benign rolandic epilepsy (13.3%, 2 of 15).

**Conclusions:** The results indicate that the prevalence of ADHD can be higher even for children with well controlled epilepsy and without significant developmental delay. And the most predominant type of ADHD is the combined type, which is the same as in the general pediatric population.

**DD-30. A multicenter trial of oxcarbazepine oral suspension monotherapy in children with partial epilepsy: clinical and cognitive evaluation**

**Eun SH** (Seoul, Korea), **Kim HD** (Seoul, Korea), **Chung HJ** (Ilsan, Korea), **Kang HC** (Seoul, Korea), **Lee JS** (Seoul, Korea), **Kim JS** (Daegu, Korea), **You SJ** (Seoul, Korea), **Moon HK** (Daegu, Korea), **Lee YM** (Seoul, Korea), **Kim DW** (Ilsan, Korea), **Sub ES** (Seoul, Korea), **Kim JY** (Seoul, Korea), **Lee JY** (Seoul, Korea), Eun BL (Seoul, Korea)

**Objective:** We conducted a prospective multicenter open-label trial to evaluate the effectiveness of oxcarbazepine oral suspension (OXC) in newly diagnosed pediatric partial epilepsy patients.

**Methods:** Children between the ages of 4–16 were eligible for the study if they had been diagnosed with partial epilepsy and experienced two or more partial-onset or generalized tonic-clonic seizures during the preceding 6 months. OXC was introduced as monotherapy to previously untreated children and was titrated over 2–4 weeks to effective target doses, followed by maintenance phase for another 6 months and the change in cognition and behavior from screening to the end of the maintenance phase. Efficacy of OXC was compared in intellectually normal versus impaired children (IQ < 70).

**Results:** We enrolled 171 patients (mean age, 9.18 ± 2.69) including 99 boys and 72 girls. Maintenance dose of OXC was 24.92 ± 8.02 mg/kg/day. Out of the 171 patients enrolled, 122 completed the study and 91 patients (53.2%) became seizure-free after using the OXC treatment. In comparing the efficacy of OXC for intellectually normal and impaired patients, 76 (53.5%) of 142 intellectually normal patients and 15 (51.7%) of 29 intellectually impaired patients became seizure-free (P = 0.779). After treatment, the perceptual organization, picture completion, and attention and concentration subtests were improved in intellectually normal patients (p < 0.05), but no significant difference was seen between intellectually normal and impaired children.

**Conclusions:** OXC is effective and well tolerated as monotherapy in children with partial epilepsy. There is no difference of the effectiveness between intellectually normal and intellectually impaired children.

**DD-31. Ketamine plus Midazolam for sedation-analgesia during lumbar puncture in autistic children**


**Objective:** To assess safety and efficacy of ketamine plus midazolam as a sedation-analgesia protocol during lumbar puncture in autistic children.

**Methods:** As part of a diagnostic workup for the clinical trial CAST (Corticosteroids for Autism — A Scientific Trial), male autistic children from three to seven years of age underwent a lumbar puncture. The sedation protocol consisted of oral midazolam, 1mg/Kg (maximum, 20mg) before admission to the procedure room, and either intramuscular or intravenous ketamine, 3–5mg/Kg or 1–3mg/Kg respectively. All subjects also received atropine, 0.01mg/kg, and ondansetron, 0.15mg/kg. Patients’ vital signs and O2 saturation were monitored from procedure onset until full recovery. The rate of side effects/complications and vital sign variability were compared between the two groups.

**Results:** Ten patients received IM ketamine (group 1), while six patients received IV ketamine (group 2). Comparison of the two groups showed that neither age nor body weight showed any statistically significant difference (p = 0.89 and 0.15). Average ketamine dosage was 3.4 mg/kg for group 1 and 1.7 mg/kg for group 2. Lumbar puncture was successful in all subjects, and time from sedation administration to full recovery did not differ significantly between the two groups. Side effects included drooling (4 children) and vomiting (1 child). Complications: one patient from group 1 had laryngospasm, and one patient from each group displayed symptoms of post-procedure intracranial hypotension.

**Conclusions:** Ketamine plus midazolam were safe and effective as a sedation-analgesia protocol for lumbar puncture in autistic children. Side effects and complications were uncommon and easily managed.


**Lieberet F** (Evry, France), **Amiet C** (Evry, France), **Couchon E** (Cambridge, MA), **Carayol J** (Evry, France), **Rio Frio T** (Evry, France)

**Objective:** Autism is a highly heritable complex neurodevelopmental disorder with a 4.5:1 male:female ratio and a 10% sibling recurrence-risk ratio. We explored the predictive ability of a single-nucleotide polymorphisms (SNPs) based test to evaluate autism risk in siblings of children with autism.

**Methods:** SNPs associated with an increased risk of autism were identified by performing gender-based genome-wide association studies on 544 multiplex families which included 964 children with autism and 304 unaffected siblings. Identified SNPs were prioritized using relevant biological data. We then assessed the ability of gender-specific genetic scores (GS), the sum of individual risk-associated alleles, to discriminate siblings with or without autism.

**Results:** A total of 87 autism associated SNPs were identified. 51 SNPs were associated with autism in both males and females, 17 SNPs associated with autism in males only and 19 SNPs in females only. GSs were constructed by combining these SNPs with 8 previously identified autism-associated SNPs. The results indicate that the prevalence of autism in siblings of children with autism is higher even for people with well controlled epilepsy and without a significant developmental delay.
SNPs. For males, the area under the receiver operator characteristic curve (AUC) was 0.82 (95%CI:0.78–0.86); a GS ≥ 74 was associated to a 89% specificity (95%CI:83–95), a 52% sensitivity (95%CI:48–56), and a 48% (95%CI:36–66) Positive Predictive Value (PPV). For females, the AUC was 0.86 (95%CI:0.82–0.90); a GS ≥ 73 was associated to a 93% specificity (95%CI:89–97), a 53% sensitivity (95%CI:46–60), and a 24% PPV (95%CI:17–40).

Conclusions: A gender-specific genetic score based on the presence of multiple risk-associated markers allows for the identification of siblings of children with autism who have a significantly high risk to develop autism.

DD-33. Expressive language sampling as an outcome measure for interventions in Fragile X syndrome
Berry-Kravis E, Doll E (Chicago, IL), Sterling A, Kover ST, Schroeder SM, Abbeduto L (Madison, WI)

Objective: There are numerous impending clinical trials of targeted therapeutic and pharmaceutical interventions for fragile X syndrome (FXS) and thus, a great need for valid outcome measures of functional improvement. This project sought to determine the feasibility, reproducibility, and clinical validity of expressive language sampling utilizing a standardized narrative and conversation task as a potential outcome measure of language function.

Methods: A 20-minute narrative–plus-conversation task was administered to 36 verbal males (N=29) and females (N=11) with FXS (age 5–36). Alternate versions were used with randomized task order at 2–3 week intervals in a test-retest design. Audio recordings of sessions were transcribed and analyzed with SALT, a computer program that analyzes specially prepared transcripts. Dependent measures reflected talkativeness, utterance planning, articulation, vocabulary and syntactic ability. Reproducibility of measures between sessions was evaluated with intraclass correlation coefficients (ICC).

Results: The task was feasible for all 36 participants. Coded data thus far analyzed for both sessions (N=15 subjects, age 10–35; 11M) has shown excellent reproducibility with Pearson correlations significant at p<0.01 for all measures, and ICCs >0.8 for all measures (Table below).

<table>
<thead>
<tr>
<th>Language characteristic</th>
<th>Measure</th>
<th>ICC</th>
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</thead>
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<td>Talkativeness</td>
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<td></td>
<td>Utterances/minute</td>
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<td>Utterance planning</td>
<td>Proportion utterances</td>
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<td>Articulation</td>
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<td></td>
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<td></td>
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<tr>
<td>Syntax</td>
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</tr>
</tbody>
</table>

Conclusions: This expressive language sampling task shows good promise as a highly reproducible measure of functional expressive language outcome in FXS clinical trials.

DD-34. Bone mineral density in children and adults with epilepsy and cerebral palsy
Maytum JC, Wical B, Sheridan KJ (St Paul, MN)

Objective: Chronic treatment with antiepileptic drugs (AEDs) is associated with reduced bone mineral density (BMD) as is inability to bear weight. Our study evaluates BMD in patients with co morbid epilepsy requiring long-term treatment with AEDs and cerebral palsy (CP).

Methods: Charts of patients with epilepsy and CP who also had a bone density study (DXA scan) were reviewed for age, gender, DXA scan results, type of CP, gross motor classification scores (GMFCS), type of epilepsy, AEDs used, fracture history, and levels of vitamin D.

Results: DXA scans were obtained in 61 patients; BMD was ascertained in 59. Ages ranged 5 to 62 years; 37 (62.7%) were < 21. All were on AEDs; 88% had quadraparetic CP. Forty-five patients (76.3%) were non-ambulatory, with GMFCS scores of 4 or 5; 15 (25.4%) had GMFCS scores of 1–3. Fractures occurred in 44.3%. Only 8 had Vitamin D levels assessed. None were deficient (<20ng/mL); 2 were insufficient (20–29ng/mL).

BMD was found to be low or very low in 54/59 (91.5%) of patients in whom BMD was able to be determined. No differences were found among epilepsy types. Normal BMD was found in 4/16 (25%) ambulatory patients. Only 1 non-ambulatory patient had normal BMD.

Conclusions: In this highly selected group of patients, abnormal BMD was extremely common. Patients with epilepsy and quadraparetic CP are at very high risk for impaired BMD. Screening for and recognition of low BMD in this population should be part of the comprehensive care of these vulnerable patients.

DD-35. Executive function impairment in children with ADHD in Bogota, Colombia.
Vélez-van-Meerbeke A, Talero-Gutierrez C, Guzman G, Figueroa B, Zamora I (Bogota, Colombia)

Objective: To determine the association of executive function impairment in children from a school sample in Bogota, Colombia with Attention deficit and hyperactivity disorder.

Methods: Sample cases (n=117) were selected from children with positive symptoms of ADHD (DSM IV) of public and private schools from low and medium socioeconomic level. Diagnosis of ADHD was confirmed by the Behavior Assessment System for Children scale. All cases were evaluated by the WISC- R test in order to exclude those with cognitive deficits. Control group (n=85) was composed by children from the same school level but without symptoms of ADHD. Afterwards, they were assessed on six executive functions (EF) measures. Statistical analysis was conducted to realize comparisons between variables, a multivariate study (MANCOVA) and a logistic regression analysis.

Results: 117 ADHD and 85 controls children with age between 6 and 12 years were studied. When controlled by gender, age and type of school, children with ADHD were significantly more impaired in measures of EF than controls (p<0.001, MANCOVA). Graphic fluidity and Rey–Osterreith Complex Figure appeared to be the most compromise subtests. When ADHD groups were compared, results were similar in the attention deficit and combined deficit children; in hyperactive-impulsive cases we found only impairment in verbal fluidity.

Conclusion: Children with ADHD displayed more problems on EF measures especially in fluidity and planning. There appears to be heterogeneity in EF impairment between gender and age.
**DD-36. Clonidine extended release tablets for the treatment of ADHD in children and adolescents with inadequate response to stimulants**

*Calder AJ (Bradenton, FL), Tenorio E (Springfield, MO), Wang C (Florham Park, NJ), Muniz R (Florham Park, NJ)*

**Objective:** This double-blind, flexible-dose study assessed the efficacy and safety of clonidine hydrochloride extended-release tablets (CLON-XR) combined with stimulants in pediatric and adolescent patients with attention-deficit/hyperactivity disorder (ADHD).

**Methods:** Patients aged 6 to 17 years with hyperactive or inattentive/hyperactive ADHD who had inadequate response after ≥30 days on a stable stimulant regimen received CLON-XR (total dose of 0.1–0.4 mg/d; >0.1 mg/d, twice daily) or placebo combined with their stimulant regimen. The primary endpoint was mean change in ADHD Rating Scale–IV (ADHD-RS-IV) total score from baseline to week 5. Safety data were collected throughout the study.

**Results:** At week 5, patients who received CLON-XR plus stimulants (n=102) had significant improvement in ADHD-RS-IV total score (P<0.009) and in inattention (P=0.017) and hyperactivity/impulsivity (P=0.014) subscale scores. Rates of treatment-emergent adverse events (TEAEs) were similar between treatment groups (45% and 41% for CLON-XR plus stimulants and placebo plus stimulants, respectively). Somnolence and fatigue were two of the most common TEAEs. Small changes in cardiovascular parameters occurred in the CLON-XR plus stimulants group, but these changes were not clinically significant and did not necessitate discontinuation of treatment. Alterations in electrocardiographic measurements were minimal and did not warrant discontinuation in any patient. Sinus bradycardia occurred in 11% and 2% of patients in the CLON-XR plus stimulants and placebo plus stimulants groups, respectively.

**Conclusions:** These results suggest that flexible-dose CLON-XR 0.1 to 0.4 mg/d is an effective and safe adjunctive therapy to stimulants for pediatric and adolescent patients with ADHD and an inadequate response to stimulants.

**DD-37. Safety and efficacy of chronic administration of Clonidine extended release tablet monotherapy or combination therapy in pediatric patients with ADHD**

*Giblin JM (Little Rock, AR), Tenorio E (Springfield, MO), Wang C (Florham Park, NJ), Muniz R (Florham Park, NJ)*

**Objective:** To evaluate the safety and efficacy of clonidine extended-release tablets (CLON-XR) alone or in combination with other medications for the treatment of attention-deficit/hyperactivity disorder (ADHD) in pediatric patients for up to 1 year.

**Methods:** Patients aged 6 to 17 years with ADHD who previously completed a phase 3 efficacy trial of CLON-XR alone or in combination with other ADHD medications or who discontinued for reasons other than safety were enrolled. Patients received flexible dosing of CLON-XR (0.1–0.4 mg/d; twice daily for doses >0.1 mg/d) alone or with other ADHD medications.

**Results:** The safety population comprised 301 patients; 33% received CLON-XR monotherapy, and 67% received CLON-XR in combination with other therapies. Treatment-emergent adverse events (TEAEs) were reported in 84% and 81% of patients in the CLON-XR alone and CLON-XR combination groups, respectively. The most common TEAEs (incidence ≥10%) were somnolence (32%), headache (16%), URI (13%), upper abdominal pain (12%), and fatigue (12%). Seventeen patients (6%) discontinued because of a TEAE (12 who received CLON-XR alone and 5 who received combination therapy). No cardiac-related serious adverse events occurred. After 4 weeks, mean change from baseline in ADHD Rating Scale–IV total score was -13.7, and improvement was sustained throughout the 12-month study (mean at 12 months, -14.6).

**Conclusions:** Flexible dosing of CLON-XR 0.1 to 0.4 mg/d (twice daily for doses >0.1 mg/d) as monotherapy or in combination with other ADHD medications for up to 1 year was safe and well tolerated. Improvement in efficacy was maintained through month 12.

**DD-38. New maternally acting gene alleles identified for autism using a Genome Wide Association Study (GWAS)**

*Johnson WG, Bayske S, Sternroos ES (Piscataway, NJ)*

**Objectives:** To use genome-wide array data to identify maternally-acting gene alleles (MAGAs) that contribute to autism in affected offspring. Over 20 MAGAs, 3 of them in autism, have so far been identified mostly in neurodevelopmental disorders using a candidate gene approach. MAGAs are a genetic effect from the maternal perspective but an environmental effect from the perspective of her affected offspring.

**Methods:** Genotype and phenotype data were made available to us by The Autism Genetic Resource Exchange (AGRE). Genotyping was done by Dr. Hakon Hakonarson at the Children's Hospital of Philadelphia on the Illumina Hap550 GWAS platform for full or partial trios (affected individuals and parents). Each child was diagnosed with autism or autism spectrum disorder. Statistical analysis by the log linear method of Weinberg et al (1998), based on stratification by parental mating type, tested SNP-by-SNP for MAGAs contributing to the autism phenotype in affected offspring.

**Results:** After QC, there were 763 full and partial trios (2,289 individuals) and 451,963 SNPs. One SNP, rs12487874 (intronic in gene RTF1N1), showed genome-wide significance (p<4.3e-10). Other SNPs of interest were in or near AJAPI (p=7.3e-6), SPAG17 (5.6e-8), TFAP2A (6.5e-7), CHST9 (1.8e-6), and ADARB1/POFUT2 (8.3e-6). The loci near TFAP2A and ADARB1/POFUT2 seemed particularly promising as each had numerous nearby SNPs with somewhat weaker p-values in linkage disequilibrium.

**Conclusions:** This is the first genome-wide association study for MAGAs that may contribute to autism in affected offspring. Several promising loci were found. The results will need to be replicated in a second dataset.

**DD-39. Clonidine hydrochloride extended release tablet monotherapy for children and adolescents with Attention Deficit/Hyperactivity Disorder**

*Brami M (Houston, TX), Tenorio E (Springfield, MO), Wang C (Florham Park, NJ), Muniz R (Florham Park, NJ)*

**Objective:** This 8-week, placebo-controlled, fixed-dose study evaluated the efficacy and safety of clonidine hydrochloride extended-release tablets (CLON-XR) for the treatment of children and adolescents with ADHD.
Methods: Patients aged 6 to 17 years with ADHD received CLON-XR 0.2 or 0.4 mg/d as twice-daily doses or placebo for 8 weeks. Improvement in ADHD symptoms, specifically inattention and hyperactivity/impulsivity, from baseline to week 5 were evaluated by ADHD Rating Scale-IV (ADHD-RS-IV) total and subscale scores using a last observation carried forward method. Safety data were collected throughout the study.

Results: Significant improvement in ADHD-RS-IV total score at week 5 was observed in the CLON-XR 0.2-mg/d (n=78; P<0.0001) and CLON-XR 0.4-mg/d (n=80; P<0.0001) groups compared with placebo (n=78). Additionally, ADHD-RS-IV inattention (P<0.0011) and hyperactivity/impulsivity (P<0.0012) subscale scores improved significantly in both treatment groups compared with placebo. The most common treatment-emergent adverse events were mild-to-moderate somnolence and fatigue, which caused discontinuation in 3% to 6% of patients in the CLON-XR groups. Minor dose-related changes in heart rate and blood pressure were observed but did not warrant discontinuation for most patients. The incidence of prolonged QTc interval (ie, QTc >450 milliseconds) was similar in the placebo (14%) and CLON-XR (11%-14%) groups.

Conclusions: CLON-XR monotherapy significantly improved ADHD symptoms, including inattention and hyperactivity/impulsivity, in this pediatric population and was generally well tolerated. These results demonstrate the potential of CLON-XR as monotherapy for children and adolescents with ADHD.

DD-40. Positive and negative predictive values for quantitative EEG method for predicting Sturge Weber syndrome

Ewen JB, Lakshmanan BL, Lanier K, Kosoff EH, Zabel TA, Crone NE, Comi AM (Baltimore, MD)

Objective: Children with V1-distribution port-wine birthmark (PWB) have about a 20% chance of developing brain involvement consistent with Sturge-Weber syndrome (SWS). Many children with PWB receive an MRI in the first year of life to rule-out SWS despite risks of contrast and sedation. We have previously published a quantitative EEG (qEEG) method to differentiate infants with SWS from those with PWB without SWS; we validated this technique in 9 infants. Because the small cohort did not allow us to assess sensitivity, specificity, positive predictive value and negative predictive value, we sought to examine a larger cohort.

Methods: Using a previously published qEEG method of assessing amplitude asymmetries (Ewen et al, Clin Neurophysiol 2009), we examined 44 EEGs in 21 subjects (SWS: 15 EEGs in 10 subjects; PWB only: 29 EEGs in 11 subjects). We calculated sensitivity and specificity. Assuming a prevalence of SWS of 20% in infants with facial PWB, we calculated positive and negative predictive values (PPV/NPV).

Results: Sensitivity for this technique was 73%, and specificity was 72%. PPV was 41%, and NPV was 92%.

Conclusions: While many children with PWB receive an MRI in the first year of life with a pre-test probability of 20%, the robust NPV of this qEEG assessment suggests that it may not be necessary to do an MRI in patients with a negative qEEG result.

DD-41. The relationship between manual ability and ambulation in youth with cerebral palsy

Majnemer A, Shikako-Thomas K, Shevell MI, Lach L, Law M, Schmitz N and the QUALA group

Montreal, QC

Objective: To determine whether gross motor function relates to hand function in adolescents with cerebral palsy (CP).

Methods: Adolescents 12–19 years of age (n=125, 15.2±2.1 years, 59.8% male) were assessed by an occupational therapist using the Gross Motor Function Classification System (GMFCS) to categorize ambulation performance and the Manual Ability Classification System (MACS) to classify hand function.

Results: Most adolescents were ambulatory with or without aids (GMFCS level I:31.2%, II:28.0%, III:7.2%) however 42/125 required a wheelchair for mobility (level IV:12.0%, V:21.6%). Similarly, most adolescents handled objects independently although for some, modifications were needed (MACS level I:30.2%, II:25.4%, III:19.0%), with a subset experiencing limited hand function (level IV:8.7%, V:16.7%). Correlation between GMFCS and MACS was strong (r=.79, p<.001) for the whole group, however this relationship could be differentiated by the distribution of motor impairment. Specifically, correlations were robust in youth with quadriplegia (r=.89, p<.001), were moderate in individuals with diplegia (r=.58, p=.01) but were not significantly associated for adolescents with hemiplegia (r=.24, p=.23).

Conclusions: Hand function is strongly associated with ambulation in adolescents with spastic quadriplegia, but modestly correlated in those with spastic diplegia. This incongruent relationship would be masked if individuals were categorized as having ‘bilateral’ CP (i.e. quadriplegia or diplegia). Children with hemiplegia (unilateral CP) can exhibit mild gross and fine motor difficulties, however the severity of these disabilities appear distinct and unrelated. Manual ability may not be equivalent to mobility and therefore should be specifically evaluated given its importance to daily life functioning.

DD-42. No association between C677T MTHFR gene polymorphism and Autism Spectrum Disorders among children in Puerto Rico

Montalvo-Ortiz Jocelyn (San Juan, PR), Collazo Madeline (San Juan, PR), Echegaray Marcos (Cayey, PR), Olivares-Rentas Rafael (Ponce, PR), Deliz Laura (Ponce, PR), Vazquez-Corrales Marisel (San Juan, PR), Carlo Simon (Ponce, PR), Negroni Xamayta (Ponce, PR), Hernandez Yanira (Ponce, PR), Acevedo Summer (Ponce, PR)

Objectives: To determine the allelic and genotypic frequencies for the Methyltetrahydrofolate Reductase (MTHFR) C677T gene polymorphism and compared them between a group with Autism Spectrum Disorders (ASD) and non-autistic Puerto Rican subjects. To examine the hypothesis of association between the C677T MTHFR polymorphism and distinct ASD endophenotypes, based on symptom severity, within a cohort of Puerto Rican children with ASD.

Methods: A total of 50 patients (cases) aged 3–12-year-old diagnosed with ASD were recruited. Control subjects consisted of 50 unrelated children aged 3–12-year-old, who were screened for ASD using the Social Communication Questionnaire Spanish version. The OSU Autism Rating Scale –DSM-IV (OARS-4) was administered to each autistic child and test scores were used as a severity measure of autistic behavioral symptoms. Amplification of the MTHFR gene was carried out by PCR and the polymorphic variant, C677T, was identified by restriction fragment length polymorphism. Differences in genotype and/or allele frequencies between cases and controls were assessed by chi-square.
Genotype-phenotype associations among cases were tested by ANOVA.

**Results:** The genotypic distribution for the C677T MTHFR polymorphism among the control group is similar to that reported in other healthy populations. Genotypic frequency for the C677T polymorphism did not show significant differences between autistic and control groups. Also no association was found between the gene allele and the selected autistic behaviors.

**Conclusion:** The C677T MTHFR gene polymorphism does not appear to be a useful marker of autism or its severity among Puerto Rican children.

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Sivaraman I, Hagmann S, Neugebauer R, Kairam R (Bronx, NY)

**Objective:** To assess the use of risperidone in children with ASD in an inner-city hospital.

**Methods:** Retrospective chart review of children with ASD, treated with risperidone from 2002–2010. Treatment response was compared by age, gender, cognition profile, and autism severity.

**Results:** Eighty children were treated with risperidone. Charts of children with available documentation on outcome (n=49) (79% male, 71% Hispanics, 23% African Americans, median age [range] of 7 [2 to 15] years) were reviewed. Most autistic children were low-functioning (69%), and nonverbal (69%). Risperidone was most used (90%) for aggressive behavior, at a dose range of 0.25 to 4 mg, for a median duration of 30 (1–76) months. Overall, aggressive behavior, stereotypes, social interaction, and self-injurious behavior improved for 90%, 53%, 51%, and 43% respectively. Reduced aggression was noted in 94% and 79% (p=1) of children with low-functioning autism and pervasive developmental disorder respectively. Stereotypes were more likely to improve among children with normal cognition vs. mental retardation (60% vs. 27% [p=.052]), and among children age ≥ 5 years vs. < 5 years (67% vs. 25% [p<.01]). After a median duration of treatment (range) of 22 (2-68) months, 17 (35%) children discontinued risperidone, mostly because of insufficient improvement or adverse effects. Side effects were noted among 30 (62%) children, the most common were drowsiness (25%), weight gain (20%), and dystonias (8%).

**Conclusions:** Phenotype may affect clinical response to risperidone. Further research is needed to better delineate which children with ASD will benefit most from risperidone.

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**DD-44. Results of an 8-week, open-label trial of STX209 (arbaclofen) in Autism Spectrum Disorders:**

Social and communicative function

Erickson CA (Indianapolis, IN), Ginsberg LD (Houston, TX), Raithmell B (Cambridge, MA), Cherubini M (Cambridge, MA), Zarrevis P (Cambridge, MA), Wang PP (Cambridge, MA, King BH (Seattle, WA)

**Objective:** To examine the safety, tolerability, and efficacy of STX209 (arbaclofen) in the treatment of autism. STX209, the active isomer of baclofen, is hypothesized to modulate excitatory/inhibitory balance through direct GABA-B agonism and indirectly by decreasing synaptic release of glutamate. It has shown promise in an initial blinded trial in fragile X syndrome (FXS).

**Methods:** An 8-week, open-label trial was conducted in children age 6–17 years with ASD. A minimum ABC-Irritability score (ABC-I) of 16 was required. Up to 2 concurrent psychoactive medications, but not antipsychotics, were permitted. Flexible dose titration was employed.

**Results:** 32 children (29 male) were enrolled, with IQ scores of 56 ± 4 (mean ± SD). 25 of 32 subjects completed the study, with 2 discontinuing due to adverse events and 5 for other reasons. STX209 was well-tolerated. There was 1 serious adverse event (increased aggression), which occurred during down-titration of study medication.

In the ITT population, there was significant improvement on the primary endpoint, the ABC-I, from 24.7 ± 8.3 at baseline, to 17.3 ± 10.5 at Week 8 (p<0.001). Subjects also showed significant improvements on the ABC-Social Withdrawal scale (from 18.1 ± 8.2 to 12.6 ± 9.3, p=0.001), the CGI-I (p<0.05), the CGI-S, the ABC-Total score (both p<0.001), and on other measures of social and communicative function.

**Conclusions:** STX209 showed broad beneficial effects on core symptoms of ASD in this open-label study. Similar improvements in social function were found in the recently-completed trial in FXS. A double-blind, placebo-controlled trial in ASD is underway.

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**DD-45. Altered dorsal and ventral dentatorubrothalamic pathways in children with autism**

Jeong J-W, Chugani DC, Chugani HT (Detroit, MI)

**Objective:** To assess fractional anisotropy (FA) in motor and language/cognitive portions of the dentatorubrothalamic pathway in children with high functioning autism (HFA) and low functioning autism (LFA) compared to typically developing (TD) children using tract-based morphometry (TBM) analysis.

**Methods:** Q-ball imaging tractography was performed for the three groups of children: 14 HFA (53±25 months, 12 males), 14 LFA (63±44 months, 12 males), 14 TD (82±21 months, 7 males). Regions-of-interest were identified in four segments of the cerebellar dentate nucleus (dorsal-rostral, dorsal-caudal, ventral-rostral, ventral-caudal) and red nucleus bilaterally. The average-shape fiber in the TD group for each tract was selected as ‘prototype’ to define common 2mm arc-length coordinates. These coordinates were used to register the corresponding coordinates of each fiber. FA value at each coordinate was calculated in each subject, and group differences were examined by two-sample t-test.

**Results:** Significantly reduced FA was found in children with LFA and HFA compared to the TD group in tracts originating in dorsal-rostral (left: P_{LFA}<0.03; right: P_{LFA}<0.02, P_{HFA}<0.03), ventral-caudal (left: P_{LFA}<0.03, P_{HFA}<0.001; right: P_{LFA} and P_{HFA}<0.001), and ventral-rostral (right: P_{LFA} and P_{HFA}<0.001) dentate.

**Conclusions:** Projections of dorsal dentate nucleus are related to motor function whereas ventral/caudal projections are related to language and cognitive functions of the cerebellum. Decreased FA in both dorsal and ventral portions of the tract may be related to motor, language and cognitive features in autism. These findings are consistent with previous PET studies showing an important role of dentate nucleus pathways in autism.
DD-46. A homozygous mutation in the tight junction protein JAM3 causes hemorrhagic destruction of the brain, subependymal calcification and congenital cataracts

Mochida GH, Ganesh VS, Felie JM, Gleason D, Hill RS, Clapham KR, Rakjic D, Hills LB, Tan WH (Boston, MA), Akawi NA (Al-Ain, UAE), Al-Saffar M, Parthlow JN (Boston, MA), Tinschert S (Dresden, Germany), Barkovich AJ (San Francisco, CA), Ali BR, Al-Gazali L (Al-Ain, UAE), Walsh CA (Boston, MA)

Objective: We ascertained a large, consanguineous pedigree from the United Arab Emirates, with eight individuals affected by a syndrome characterized by pre- and perinatal hemorrhagic destruction of the brain, subependymal calcification and congenital cataracts. In this study we aimed to identify the genetic basis of this multisystem disorder with presumed autosomal recessive inheritance and a devastating neurological presentation.

Methods: We used a case study approach utilizing retrospective analysis of clinical data. Twenty (n=20) affected individuals were recruited and were classified as either cases (n=11) or controls (n=9) based on their SCS symptoms. All participants had 2 hours of continuous EEG recording with one hour of sleep. The recordings were interpreted as normal or abnormal based on interictal epileptiform abnormalities. Plasma from fasting venous blood (5 ml) was collected, and inflammatory cytokines including TNF-a, IFN-g, IL-1b, IL-4, IL-6, IL-10, CRP as well as the glutathione redox ratio (GSH/GSSG) were measured.

Results: Five out of eleven SCS children had abnormal EEGs; however, overall SCS case group had higher levels of inflammatory markers. Specifically, the mean plasma levels of IL6, CRP, and IL-1b were almost two-fold higher, and the IFN-g 10-fold higher in the case group. Concentrated elevated oxidative stress, the glutathione antioxidant capacity (GSH/GSSG) was reduced in the SCS cases. None of the measurements reached statistical significance using 2 tail T tests.

Conclusions: The autistic children with SCS showed higher levels of inflammatory cytokines and reduced glutathione redox ratios, suggestive of chronic oxidative stress; however, these were not consistently associated with abnormal EEG changes. This may indicate that suspected SCS in autistic children should include screening for plasma inflammatory cytokines as well as GSH/GSSG ratios.

DD-47. Syndrome of pontobulbar palsy and sensorineural deafness (Brown-Vialetto-Van Laere syndrome) in two sisters: detailed neurophysiological and neuropsychopathological analysis

Karachunski PI, Clark HB, Dalton JC (Minneapolis, MN)

Objective: We report two cases of Brown-Vialetto-VanLaere syndrome (BVVL) in sisters from a non-consanguineous family. Purpose of this study is to further characterize this rare neurodegenerative disorder caused by mutations in the C20orf54 gene using new data from neurophysiological and neuropathological investigations.

Methods: We used a case study approach utilizing retrospective analysis of clinical data.

Results: Both sisters were born with no complications and had no developmental concerns prior to onset of symptoms. Sister A presented at the age of 11 months with eyelid ptosis, neck weakness and respiratory failure. She progressed to quadriplegia and required full life support in 4 months from the onset and died at 25 months of age. Postmortem analysis revealed severe degenerative changes in the brainstem, cerebellum and spinal cord. Sister B presented at the age of 13 months with subacute onset of irritability and ataxia. Cerebrospinal fluid analysis revealed transitory elevation of protein. Neurophysiology revealed attenuated sensorimotor and sensory responses and sensorineural deafness. She progressed with respiratory failure, sensory ataxia and weakness. Her care was withdrawn six months after the onset. Postmortem analysis revealed degenerative changes in the brainstem and spinal cord. Homozygous pathogenic mutation c.639C>G in exon 3 of the C20orf54 gene was identified in sisters and heterozygous mutations in both parents.

Conclusions: This study provides new data which further refines clinical, neurophysiological and neuropathological phenotype of BVVL and its variability even within one family. These data reveal neurodegeneration involving multiple systems of the nervous system including motor, sensory, and autonomic.

DD-48. Plasma inflammatory and oxidative stress markers in autistic children with suspected subclinical seizures


Objective: Subclinical seizures (SCS) are commonly misdiagnosed in autistic children. We investigated EEG patterns, oxidative stress and inflammatory cytokines in autistic children with suspected SCS to determine whether these measurements may be predictive biomarkers for SCS.

Methods: Twenty (n=20) autistic children were recruited and were classified as either cases (n=11) or controls (n=9) based on their SCS symptoms. All participants had 2 hours of continuous EEG recording with one hour of sleep. The recordings were interpreted as normal or abnormal based on interictal epileptiform abnormalities. Plasma from fasting venous blood (5 ml) was collected, and inflammatory cytokines including TNF-a, IFN-g, IL-1b, IL-4, IL-6, IL-10, CRP as well as the glutathione redox ratio (GSH/GSSG) were measured.

Results: Five out of eleven SCS children had abnormal EEGs; however, overall SCS case group had higher levels of inflammatory markers. Specifically, the mean plasma levels of IL6, CRP, and IL-1b were almost two-fold higher, and the IFN-g 10-fold higher in the case group. Consistent with elevated oxidative stress, the glutathione antioxidant capacity (GSH/GSSG) was reduced in the SCS cases. None of the measurements reached statistical significance using 2 tail T tests.

Conclusions: The autistic children with SCS showed higher levels of inflammatory cytokines and reduced glutathione redox ratios, suggestive of chronic oxidative stress; however, these were not consistently associated with abnormal EEG changes. This may indicate that suspected SCS in autistic children should include screening for plasma inflammatory cytokines as well as GSH/GSSG ratios.

DD-49. Effects of poverty on the assessment of language skills

Burton VJ (Baltimore, MD), Watkins RV (Urbana, IL)

Objective: To explore factors, including maternal education, that influence performance on language measures.

Methods: Three groups of first graders, those with language impairment and typically developing peers from high-risk and low-risk environments, were evaluated on four measures: the EVT (expressive vocabulary test), the PPVT-III (receptive vocabulary test), a dynamic assessment of word learning and a nonword repetition task. Risk was determined by maternal education, free lunch status and percentage of students attending the same school who were receiving free lunch. MANOVA was used to investigate group difference and effect size was calculated. Regression analysis was also completed.

Results: Statistically significant group differences emerged between the participants in the high-risk, low-risk and language disabled group on both the receptive and expressive vocabulary measures as well as both the word learning and nonword repetition tasks. There was overlap between
performance on the receptive measure between the high-risk and the language disabled group. Maternal education predicted a large amount of the variance in the receptive (50%) and expressive (14%) vocabulary tests but did not predict performance on the dynamic word learning measure nor the nonword repetition task.

Conclusions: By first grade, vocabulary, as well as measures of ability and process, is affected by environmental influences. It has been previously suggested that less language stimulation in families of poverty yield different vocabularies in children from the high-risk backgrounds. Perhaps, knowing fewer words also means less opportunity to practice using the language skills measured by processing tasks of ability and aptitude.

DD-50. Early gross motor milestones correlate to later social-communication abilities in infants at risk for autism spectrum disorders (ASD)

Jeste SS, Hutman T (Los Angeles, CA)

Objective: Motor delays and deficits are common in individuals with autism spectrum disorders (ASD). However, few studies have characterized motor function in infants at high risk for ASD. Here, we characterize the achievement of early gross motor milestones and investigate the relationship between early motor function and later social and communication abilities in high-risk infants.

Methods: Data were gathered from an ongoing longitudinal study of infants at high risk for ASD (risk incurred by having an older sibling with ASD), 65 children were included in the final analysis. Motor function was quantified by the Mullen Scales of Early Learning (MSEL) Gross Motor raw score. Variables of interest for bivariate correlation analysis included MSEL subscores (fine motor, visual reception, receptive and expressive language) and Early Social Communication Scale (ESCS) subscores (referencing, response to referencing, and requesting).

Results: At age 6 months, there was a wide range in achievement of gross motor milestones (MSEL gross motor raw scores ranging from 6 to 12). Gross motor function at age 6 months was significantly correlated with 12-month measures of visual reception, receptive language, and requesting (p’s<0.05).

Conclusion: The achievement of motor milestones in the first year of life may be important for the development of non-verbal communication as well as receptive language, both domains that are impaired in children with ASD. These findings highlight the importance of monitoring motor function in early infancy and document the need for further investigation of links between early motor function and social-communication development in infancy.

DD-51. Impaired face processing in young children with Tuberous Sclerosis Complex: Consideration of a pathway to autism spectrum disorders.

Jeste SS (Los Angeles, CA), Hirsch S, Vogel-Farley V, Gregas M, Prabhhu SP, Sahin M, Nelson CA (Boston, MA)

Objective: There is a high incidence of autism spectrum disorders (ASD) in Tuberous Sclerosis Complex (TSC). The mechanism underling this association is unclear, with most research focused on clinical factors such as tuber location or epilepsy. Given the evidence of impaired face processing in ASD, we sought to investigate face processing in a cohort of infants and toddlers with TSC using innovative, high-density, event-related electroencephalography.

Methods: We studied 19 children with TSC under age 4 years. We used a novel (ERP) paradigm of familiar-unfamiliar faces. 6 children with TSC (32%) had ASD. Components of interest included the P1 (early visual processing), the N290 and P400 (face sensitive components). Analysis focused on left and right temporal-occipital regions.

Results: There was a main effect of group in the N290 latency, with the TSC group showing a slower N290 latency (p=0.05). There was also a region by group interaction, with the TSC group failing to show the expected hemispheric differences in face processing. The longest N290 latency was seen in (1) children with ASD/TSC and (2) children with temporal lobe tubers, regardless of ASD diagnosis.

Conclusions: This study is the first to show that early face processing may be impaired in TSC, with the slowest processing seen in children with ASD. This functional impairment may provide insight into a mechanism underlying a pathway to ASD in TSC. The role of temporal lobe tubers in face processing needs further exploration.

DD-52. Single dose pharmacokinetics of NWP06, a novel extended release methylphenidate oral suspension for the treatment of ADHD

Berry S, Belden H (Cupertino, CA), Children A (Las Vegas, NV)

Objective: CDC prevalence data suggest 1 in 10 US children are diagnosed with ADHD, making ADHD the most common childhood neurobehavioral disorder. An unmet need exists for an extended-release (ER) liquid formulation of methylphenidate (MPH) for children with difficulty swallowing tablets or capsules. This study compares single-dose pharmacokinetics of NWP06, a novel liquid ER formulation of MPH to immediate-release (IR) liquid MPH and examines any effects of food.

Methods: 30 healthy adult subjects enrolled in this open-label, randomized, three-treatment crossover study. Subjects received NWP06 under fasting and fed conditions and IR MPH oral solution under fasting conditions (7-day washout). Blood samples were collected prior to dose and periodically up to 36 hours post-dose.

Results: Ratios for extent of exposure (AUC) following administration of NWP06 and IR MPH met standard bioequivalence acceptance criteria. The ratio for rate of exposure was outside standard bioequivalence limits, with IR MPH having a 45% higher Cmax.

Conclusions: NWP06 IR MPH

<table>
<thead>
<tr>
<th>NWP06</th>
<th>IR MPH</th>
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<tbody>
<tr>
<td>AUC0-∞ (ng-hr/mL)</td>
<td>143.65</td>
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<tr>
<td>Cmax (ng/mL)</td>
<td>13.61</td>
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<tr>
<td>T1/2 (hrs)</td>
<td>5.65</td>
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<tr>
<td>Tmax (hrs)</td>
<td>5.00</td>
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Food increased bioavailability of NWP06. The rate and extent of exposure were ~25% higher after a high fat meal. Vital sign changes were as expected for MPH. No clinically significant laboratory or ECG changes were reported. Most common AE's reported were headache, dizziness, palpitations, and nervousness.

**Conclusions:** NWP06 is bioequivalent to IR MPH in extent of exposure (AUC), but NWP06 has a lower Cmax than IR MPH. NWP06 has a modest food effect. Both treatments were well tolerated.

**DD-53. Rapid and dramatic decreases of cerebral 5-methyltetrahydrofolate: a treatable form of progressive neurodegeneration**

Starnes M, Voigt E, Hyland K, Shoffner J (Atlanta, GA)

**Objective:** The cerebral folate deficiency (CFD) syndrome describes any neurological condition where low levels of CSF 5-methyltetrahydrofolate (5-MTHF) are found within the CNS and where systemic folate levels are normal. CFD can be primary (inherited defect), or secondary (as in mitochondrial disease or an autoimmune disorder).

Methods: Seven children were identified with progressive neurologic symptoms that included epilepsy, movement disorders, and neurobehavioral difficulties. Previously documented CSF 5-MTHF levels were normal in all (>50 nmol/L). Of the seven, six were scored as Probable or Highly Probable Mitochondrial Disease using the Nijmegen Diagnostic Criteria (Neurology 2002;59:1402).

Results: CSF 5-MTHF levels dropped by 42.7% in an average of 28 months, with a majority dropping into the abnormal range. The most dramatic of these was a 50% reduction in CSF 5-MTHF in 9 months. Findings suggest that CSF 5-MTHF levels are not static over time and repeat assessment of CSF 5-MTHF should be considered in patients with progressive neurologic abnormalities.

Conclusions: CFD is an important mechanism in the progression of symptoms typical in mitochondrial disease. This phenomenon, however, is not limited to patients with mitochondrial disease. Additional research is needed to determine the mechanism of the development of CFD over time.

**DD-54. Clinical and radiological evidence for EPI-743 neuroprotection in mitochondrial disease**

Blankenberg F (Stanford, CA), Perlman SL (Los Angeles, CA), Kinsman SL, Spencer KM (Charleston, SC), Barnes A, Khreifets V, Shadrer WD, Thoelen M, Miller G (Mountain View, CA), Ens M (Stanford, CA)

Objective: Mitochondrial disorders are relatively common inherited conditions characterized by severe, multi-organ system disease. The central nervous system is most frequently involved, given the central importance of oxidative metabolism in brain function. Despite advances in understanding the genetics and pathogenesis of mitochondrial disease, there has been little progress in developing effective therapy.

Methods: Four inherited mitochondrial disease patients (Kearns-Sayre syndrome, POLG, Friedreich ataxia and MELAS) were treated in an expanded access study with the novel redox-active drug EPI-743. Each patient was treated with enteral EPI-743 50 mg twice daily initially, with dose escalation to 100 mg three times daily over three weeks with continued treatment thereafter. Physical examination, functional imaging, and Newcastle Paediatric Mitochondrial Disease Ratings Scale (NPMDS) assessments were used to monitor the children.

Results: All four patients tolerated EPI-743 and recorded both objective and subjective signs of clinical improvement that coincided with increased levels of reduced glutathione in the brain as observed by serial 99mTc-hexamethylpropyleneamine oxime single photon emission computed tomography radionuclide imaging (HMPAO-SPECT). Patients had gradual increases in whole brain HMPAO uptake between 29 to 177% above baseline with central gray (caudate, putamen, thalamus) and cerebellar values increasing approximately 50 to 100% more than the cortex. One patient (POLG) had an initial response at 3 months (50–100% above baseline) that progressively fell to 23% to 32% at 9 months, which correlated with progressive proximal muscle weakness.

Conclusions: Preliminary data suggest EPI-743 may represent a new class of disease-modifying therapeutics for inherited mitochondrial and neurological diseases.

**DD-55. Predictors of motor dexterity in cognitively intact institutionally reared children**

Behen ME, Veenstra A, Gjolaj N, Adams A, Chugani HT (Detroit, MI)

Objective: To determine predictors of motor performance in globally cognitively intact children raised from birth in orphanages. Studies have suggested that duration in orphanage is a robust predictor of neurocognitive outcomes in such samples. We investigated whether duration predicts motor dexterity when controlling for other potentially important predictors of outcome including global IQ, adoptive family characteristics (e.g., parent education), and indices of physical deprivation (e.g., body mass index).

Participants and Methods: One hundred and nine cognitively intact children (mean FSIQ=101.84, SD=15.1) raised from birth in orphanages (mean age= 8.98 years; SD=2.47; 43 males; mean duration in orphanage=21.4 months, SD=14.1) underwent comprehensive neuropsychological evaluations including assessment of intellectual and motor functioning. All children were monolingual English speaking and from Eastern European, Russian and/or Asian orphanages prior to being adopted into the US.

Motor dexterity was assessed using the Grooved Pegboard Test (Trites 1977); intellectual functioning using the Wechsler series.

Results: Separate regression analyses for dominant and non-dominant hands were conducted with duration of orphanage experience, body mass index, adoptive parents' education, handedness, attachment security, and global IQ entered simultaneously. For the dominant hand, the overall model was significant (p=0.03); only full scale IQ (p=0.037) contributed significant variance to this model. The overall model was also significant for the non-dominant hand (p<0.001). Full scale IQ (p<0.001), body mass index (p=0.02) and attachment security (p=0.012) each contributed significant variance to this model.

Conclusions: Results indicate that duration in orphanage does not predict motor dexterity after controlling for global IQ, attachment security, adoptive family characteristics, and indices of physical deprivation.
POSTERS: Demyelinating Disease

DM-1. Incidence of Acquired Demyelinating Disease among hospitalized children in the United States
Abanilla K (Boston, MA), Gorman M (Boston, MA), Cristiani N (Middletown, CT), Mazumdar M (Boston, MA)

Objectives: 1) To describe the epidemiology of acquired demyelinating disease among hospitalized children in the United States; and 2) to evaluate the relationship between the incidence of pediatric acquired demyelinating disease and hospital latitude.

Patients and Methods: The Pediatric Health Information System (PHIS) database was used to obtain information from 41 tertiary care hospitals on inpatient hospital admissions of children aged 0-18 years from January 1999 to December 2004. ICD-9 codes were used to identify children with demyelinating diseases. Incidences were calculated based on the number of cases per 10,000 hospital admissions.

Results: The PHIS database identified 1165 children with acquired demyelinating disease. The most commonly diagnosed acquired demyelinating disease was optic neuritis. Females were predominantly affected by demyelinating disease; however, the male:female ratio was higher at younger ages and in patients with acute disseminated encephalomyelitis (ADEM). During the study period, the incidence of all pediatric acquired demyelinating diseases was 5.28 per 10,000 hospital admissions. No relationship was found between the incidence of pediatric acquired demyelinating disease and hospital latitude.

Conclusions: Among hospitals participating in the PHIS database, the incidence of pediatric acquired demyelinating disease was 5.28 per 10,000 admissions. There was a clear female preponderance in disease that was more evident at older ages. There does not appear to be a relationship between demyelinating disease and latitude.

DM-2. Parent-patient quality of life perception in children with Multiple Sclerosis
Schreiner T, Ross C, Armstrong-Wells J (Aurora, CO)

Background: Recognized as common co-morbidities in adult MS, few studies have examined psychosocial concerns in children with MS. Children live longer with disabilities which may impact their families. Therefore, we conducted a pilot study to determine psychosocial aspects related to quality of life perception in this specialized population and their families by administering a valid parent-patient questionnaire.

Methods: We conducted a pilot sample of 10 parent-child pairs within our prospective cohort of pediatric MS patients at The Children’s Hospital Colorado. Quality of life was assessed with the Child Health Questionnaire (CHQ: Landgraf and Ware, 1996), which was administered by research staff during routine clinical follow-up. Selected data points are presented in this brief abstract.

Results: Of the pairs, 20% were male; ages ranged between 10–17 years with a median of 15.5. Only 20% of patients worried about their health more than others, but 70% of parents worried more. Thirty percent of patients felt that their health sometimes limited family activities; the majority of parents (60%) felt limited. Overall, the majority of patients and families (60% and 70%, respectively) felt that their family “got along” well.

Conclusions: In this pilot study of children with MS, we have demonstrated that parents are disproportionately affected by their children’s diagnosis. The CHQ is a feasible screening tool that is easily administered during our clinic session. By recognizing these non-physical aspects, providers can offer the proper psychosocial support to families. Ongoing studies will compare our pediatric MS cohort to children with other neurologic disease.

DM-3. Susceptibility weighted imaging as an MR biomarker for Acute Inflammatory Demyelinating Diseases in Children
Mar S, Benzinger T, D’Angelo G, Kelly J (St. Louis, MO)

Objectives: Susceptibility weighted imaging (SWI) has been shown to be very sensitive to iron. Brain iron accumulation has been known to occur in adults with multiple sclerosis (MS). However, the application of SWI in pediatric demyelination has not been studied. We plan to (1) test the utility of SWI in differentiating acute disseminated encephalomyelitis (ADEM) and MS (2) correlate the prevalence of SWI findings with Extended Disability Status Score (EDSS), or age.

Methods: 11 children with acute demyelination were prospectively imaged using SWI. The final diagnosis of ADEM (n=5) or MS (n=6) was made using the international consensus definitions after the mean follow-up duration of 32 months. SWI T1 and FLAIR images were co-registered using a semi-automated technique. Each FLAIR lesion was assessed for its SWI characteristics.

Results: Total FLAIR lesions ranged from 5 to 146, and the percentage of these lesions on SWI ranged from zero to 68 percent. On SWI, the lesions appeared as amorphous hypointense lesions, linear hypointensities, or as a combination of these features. Fractional SWI differs significantly between MS/ADEM diagnosis (p=0.05) on A Wilcoxon-Mann-Whitney Test with a 2-sided exact p-value. The median (min, max) of fractional SWI for those with a MS diagnosis is 0.23 (0, 0.68) and for those with an ADEM diagnosis is 0.07 (0, 0.16). Age (Spearman correlation=0.75, p=0.015) is correlated to fractional SWI, but EDSS is not (p=0.34).

Conclusion: SWI offers additional information on diagnosis and the pathophysiology of demyelinating diseases. A larger study is warranted to further evaluate its prognostic utility.

DM-4. A long term follow up study of children with Central Nervous System Inflammatory Demyelination using the International Pediatric Multiple Sclerosis (IPMS) Criteria
Mar S, Ibbell S, Benzinger T, Noetzel M (St. Louis, MO)

Objective: (1) Test the practical application of IPMS definitions in children with inflammatory demyelination episodes of CNS (2) Identify the possible over/under diagnosis of multiple sclerosis.

Background: The IPMS has proposed consensus definitions for pediatric MS and related disorders which raises the concern about misdiagnoses.

Design/Methods: Data was collected 1995 to 2004 retrospectively; 2005 to 2010 prospectively) from 123 children with acute first demyelination.

Results: 47 (38%) patients met criteria for ADEM, 67 (55%) for clinically isolated syndrome (CIS), and 4 (3%) for neuromyelitis optica and 5 (4%) did not fit into specific criteria. 53 (43%) patients presented with CIS monofocal group, among which 20 (16%) had optic neuritis, 20(16%) transverse myelitis, 3(2%) brain stem dysfunction, and 10(8%) hemispheric dysfunction. 14 (11%) patients presented with multifocal CIS. The rate of conversion to MS from CIS was 39 %. Monofocal CIS have lower rate of
DM-6. Lower urinary tract symptoms in children with demyelinating disease

Morgan-Followell B (Columbus, OH), Wilson TS, Ness J (Birmingham, AL)


Methods: The Incontinence Survey Index-Pediatric (ISI-P; Nelson et al, 2007) was completed by patients evaluated at the Center for Pediatric –Onset Demyelinating Disease at the Children’s Hospital of Alabama. Inclusion criteria were demyelinating event occurring at ≤18 years of age and age ≥11 years at the time of survey completion.

Results: Nineteen patients completed the survey (17 females, 2 males; mean duration of disease 2.9 years). Average age was 16.3 years. Nine patients had MS, 4 neuromyelitis optica, 3 transverse myelitis, 1 clinically-isolated syndrome, 1 undetermined demyelinating disorder, and 1 multi-phasic ADEM. Mean expanded disability status scale score (EDSS) was 1.6. The mean bowel/bladder system score of the EDSS was 0.6 (0 = normal).

Eleven of nineteen patients reported urinary symptoms on ISI-P compared to only 7/19 with review of systems and EDSS. Reported symptoms on the ISI-P included urge incontinence (n=5), stress incontinence (n=8), unaware urinary incontinence (n=5), and nighttime symptoms (n=4). Symptom severity was mild (median score=0.57).

Four reported tissue or pad use. Pad use, when reported, was moderate (median score=3). Five patients reported bother/impairment as a result of urinary symptoms.

Conclusions: Lower urinary tract symptoms are under-recognized in children with demyelinating disease. Subjective urinary symptoms may be under-reported by patients on the review of systems and the EDSS. A validated survey of lower urinary tract symptoms may be more effective in detecting patients with urological dysfunction.

DM-7. N-acetylcysteine as adjunctive therapy in hematopoietic stem cell transplantation in childhood cerebral adrenoleukodystrophy

Holmøy MJ, Coles L, Mishra U, Basso L, Orchard PJ, Cloyd JC (Minneapolis, MN)

Objective: Childhood cerebral adrenoleukodystrophy (CCALD) is effectively treated by hematopoietic stem cell transplantation (HSCT) when diagnosed early; however, it is ineffective in late-stage disease. Therapy with N-acetylcysteine (NAC), an antioxidant that reduces free radicals and facilitates glutathione biosynthesis, in combination with HSCT improves long-term survival of boys with late-stage CCALD. The objective of this study was to characterize the NAC clinical pharmacology in CCALD patients, so that the dose and duration of NAC therapy can be optimized.

Methods: This was an open-label study of hospitalized, CCALD patients undergoing HSCT. NAC was administered IV at 70mg/kg over one hour, four times daily. Blood samples were collected prior to and 7 and 21 days after HSCT at: pre-dose, 1.5,2,3,4, and 6 hours post-dose. Plasma and red blood cells (RBC) were separated and analyzed for total NAC, cysteine (CYS) and glutathione (GSH) concentrations using a validated HPLC-MS method.

Results: Maximum plasma NAC concentrations were 100–120 ug/mL with elimination half-lives of 1.3 to 1.6 hours. NAC also entered RBCs with maximum concentrations approximately 20% that of plasma. Despite measurable NAC concentrations in plasma and RBCs, there was no change or a transient decrease in plasma CYS and GSH concentrations. CYS concentrations were also unchanged in RBCs, while GSH concentrations increased, with significantly greater GSH exposure at 21 versus 7 days post transplantation.

Conclusions: NAC may exert its effects by increasing intracellular GSH concentrations. Future studies will evaluate the effect of NAC on brain GSH levels, and further elucidate the mechanism for this increase.

DM-8. Cognitive functioning and school performance in pediatric demyelinating diseases: A comparison between multiple sclerosis (MS) and transverse myelitis (TM) groups

Harper L, Spurgin AA, Greenberg B, Graves D (Dallas, TX)

Objective: Up to 10% of multiple sclerosis (MS) and 20% of transverse myelitis (TM) cases manifest before adulthood. Little is known about cognitive and school outcomes in these populations. The present objective was to compare cognitive functioning between TM and MS groups and explore their relation to school performance and clinical variables.

Method: Eighteen MS and 22 TM subjects, ages 5 to 18, completed a neuropsychological screening battery. It was hypothesized that MS subjects would show greater neuropsychological difficulties which would relate to poorer school performance.

Conversion to MS (30%) comparing to those with multifocal CIS, of which 71% developed MS (p=0.001). Among the ADEM, 7 (15%) had relapsing ADEM and 3 (6%) had multiple sclerosis. None of the relapsing ADEM cases had disease progression on long term follow-up. Patients with MS had mean EDSS score of 1.3 (0 to 8.5). The mean follow-up was 84 months (2- 282 m). All MS had at least one MRI or clinical relapses (mean 5.4) more than 6 months after initial onset. 84(70%) children had minimal of 2 yrs follow-up.

Conclusions: IPMS criteria can be applied in children with demyelination with minimal risk of misdiagnosis.
Results: Independent samples t-tests revealed significantly greater difficulties for the MS versus the TM group in verbal memory, attention, visual-motor integration, and visual perception. Multiple regression analyses determined clinical factors (disease duration, ambulation, age at onset, exacerbation rate) predicted variance in processing speed ($\text{p} = 0.12$) and complex attention ($\text{p} = 0.034$) for MS and variance in visual-motor integration ($\text{p} = 0.002$) and visual perception ($\text{p} = 0.04$) for TM. Chi-square analysis revealed no significant differences in school performance between MS and TM groups. MANOVA revealed significantly poorer performance on measures of cognitive functioning ($\text{p} = 0.021$) for subjects who were below average or failing in school.

Conclusions: Results are consistent with existing literature suggesting pediatric MS is associated with cognitive difficulties. Surprisingly, MS and TM groups showed similar rates of school problems, which related to cognitive functioning. Results advance understanding of the connection between neuropsychological deficits and academic outcomes in these populations. These novel findings warrant further exploration of cognitive and academic outcomes in pediatric demyelinating diseases to inform appropriate intervention.

Development of an algorithm to sensitively and specifically identify leukodystrophy patients was difficult because of the non-specific use of the 330.0 code. However, a combination of codes allowed us to design an algorithm that can be used to query national databases with acceptable sensitivity and specificity.

Conclusions: In-patient hospitalization is the greatest source of health care resource utilization in leukodystrophy patients. Strategies to improve care will need to determine the reasons for in-patient hospitalization. Our development of an algorithm to identify leukodystrophy patients in national databases will permit generalization of our findings to nationally representative samples.

DM-9. Determination of leukodystrophy costs and national impact

Nelson CR, Korgenski EK, Mundorff MB, Sheng X, Srivastava R, Bonkowski JL (Salt Lake City, UT)

Objectives: Inherited diseases of the white matter occur in ~1/7500 children, with substantial morbidity and mortality. Care for children with leukodystrophies is complicated by lack of data regarding national disease burden and health care utilization. We sought to determine the primary health care issues faced by children with leukodystrophies, and to determine their national impact.

Methods: We retrospectively analyzed MR images of 23 patients with AGS versus disorders that may have similar MR images [Alexander disease (n=9), Megalencephalic Leukodystrophy with subCortical cysts (MLC) (n=5), Vanishing White Matter disease (n=9), Calcifying Retinal Microangiopathy with Cerebral Cysts (CRMCC) (n=4), and congenital cytomegalovirus (CMV) infection (n=5)]. Chi squared test were used to test MRI characteristics against disease status. A stepwise logistic regression model was used (p-value for removal from model = 0.2). Latent class analysis identified fit of criteria with AGS diagnosis.

Results: Specific MR features statistically associated with AGS included calcifications visible on MR, cerebral atrophy, brainstem atrophy, white matter loss/ventricular dilatation, swollen frontal or temporal gyri and diffuse white matter abnormalities ($p<0.01$). Logistic regression identified a best fit model including the criteria of early cerebral atrophy, swollen temporal pole, calcifications visible on T2 or T1 images and temporal horn dilatation (sensitivity 90.9%, specificity 96.9%). A diagnostic algorithm is proposed.
Conclusion: We propose that specific MRI features can facilitate the early diagnosis of AGS.

Acknowledgements: Myelin Disorders Bioregistry Project

DM-11. Childhood Manifestation of Late Onset Tay Sachs
Musolino PL, Yerramilli-Rao P, Eichler F (Boston, MA)

Objective: To study first symptoms of adult neurodegeneration in patients with Late Onset Tay Sachs (LOTS) during childhood.

Methods: We developed questionnaires to investigate the early presentation of patients with LOTS and distributed them through the database of the National Tay Sachs and Allied Disease Foundation (NTSAD).

Results: We received 55 completed surveys from 9 patients with the juvenile and 46 patients with the adult form of the disease. Age at onset was 2.2 – 1.1 years for juvenile and 12.5 – 9.6 years for adult LOTS. The age at diagnosis was 4.5 – 2.3 years and 26.5 – 10.5 years for juvenile and adult patients respectively. The most common symptoms were difficulty running or participating in sports with peers (64%), speech abnormalities (56%) and inability to climb stairs (53%). The median interval between symptom onset until wheelchair-bound was 3.5 years in juvenile and 21 years in adult LOTS.

Conclusions: We conclude that childhood manifestation is common even in the adult form of LOTS. In general, the earlier the onset of symptoms the more rapidly the disease progresses.
POSTERS: Epilepsy

E-1. Public perception of Tourette Syndrome on YouTube
Lim Fat Mj, Sell E, Barrowman N, Doja A (Ottawa, ON)

Objective: Self-esteem and peer relationship difficulties are seen in children and adolescents with Tourette Syndrome (TS). The portrayal of TS on YouTube could reflect and influence public perception of TS. Our goal was to assess public perception and stigma surrounding TS through viewers’ response to videos on YouTube.

Methods: The top 20 videos on YouTube for search terms “Tourette’s”, “Tourette’s Syndrome”, “Tourette Syndrome” and “tics” were selected. Two investigators independently assessed the portrayal of TS in selected videos as positive, negative or neutral. The total number of views and viewer demographics were noted. Top 10 comments for each video were graded as “sympathetic”, “neutral” or “derogatory” towards TS. The relationship between viewer perception, nature of comments and popularity were then evaluated.

Results: 14 970 videos were obtained and 41 were retained. These had an average of 590 113 views (1 369 – 13 747 069) and 1761 comments (0 – 35 241). 22% of the videos portrayed TS negatively, 20% were neutral and 59% positive. Negative portrayals were significantly associated with more views (Spearman’s correlation rho = −0.46, p=0.003) and more comments (Spearman’s correlation rho = −0.47, p=0.002). A younger audience (< 25 years) did not favour any videos in terms of portrayal of TS (χ² test for trend, p=0.13). 27% of videos depicted coprolalia.

Conclusion: While some excellent examples of TS are available on YouTube, the presence and popularity of videos negatively portraying TS may reflect and reinforce existing stigma in society.

E-2. Clinical characteristics of the pediatric epilepsy with no interictal epileptiform discharges in initial EEG
Sang-Ook N (Yangsan, Gyeongnam, South Korea)
Yun-Jin L (Yangsan, Gyeongnam, South Korea),
Young-Mi K (Pusan, South Korea),
Kyu-Min Y (Yangsan, Gyeongnam, South Korea)

Purpose: To evaluate the clinical characteristics of pediatric epilepsy with no interictal epileptiform discharges (IED) in initial scalp EEG.

Methods: We retrospectively reviewed 201 children with epilepsy between 2 months and 18 years old who had EEG and brain MRI before antiepileptic medication. All of the 5 (100.0%) cases of kidney stones occurred in children less than 7 years old, however this comparison did not achieve statistical significance, p=0.078.

Recommendations:
1. Avoidance of TPM with other carbonic anhydrase inhibitors or other modalities predisposing to stones e.g. ketogenic diet.
2. Liberal fluids, monitoring serum bicarbonate and use of sodium bicarbonate or citrate.
3. Avoidance of acidosis.
4. Imaging by at least US.

E-3. Prevalence of asymptomatic nephrolithiasis in children with TPM therapy
Mahmoud AA (Riyadh, KSA), Rizk TG (Riyadh, KSH),
Dannawwi S (Beirut, Lebanon), al Tannir M (Riyadh, KSA)

Introduction: Topiramate (TPM) is a neuromodulatory agent that inhibits the activity of specific carbonic anhydrase enzymes in the kidney; with subsequent metabolic acidosis, and elevated urine pH, leading to an increased risk of kidney stone formation.

Objective: To assess the prevalence of asymptomatic nephrolithiasis in a group of children on TPM therapy for at least one year in order to investigate the effectiveness of recommending routine abdominal ultrasound during TPM use.

Results: The follow up ultrasound of the urinary system during the use of Topiramate showed that 5 children (5.2%) had developed kidney stones. All of the 5 (100.0%) cases of kidney stones occurred in children less than 7 years old, however this comparison did not achieve statistical significance, p = 0.078.

Recommendations:
1. Avoidance of TPM with other carbonic anhydrase inhibitors or other modalities predisposing to stones e.g. ketogenic diet.
2. Liberal fluids, monitoring serum bicarbonate and use of sodium bicarbonate or citrate.
3. Avoidance of acidosis.
4. Imaging by at least US.

E-4. HLA-B*1502 and Antiepileptic Drug-induced Stevens-Johnson Syndrome in Han Chinese in China
Dan S, Lian XH, xiu SK, Lin FW, Hui Y, Sheng JH, Fei GW, Sheng ZL (Wuhan, China)

Introduction: Stevens-Johnson Syndrome and toxic epidermal necrolysis (TEN) induced by antiepileptic drugs (AEDs) in order to prevent SJS–TEN by using HLA-B*1502 screening to prospectively identify subjects at genetic risk for the condition.

Methods: Subjects studied were 5 patients suffered from SJS or SJS/TEN. They were 4 boys and 1 girls from 2 year to 11 years (6.87±3.60). The controls included 32 subjects with age-, sex- and drug-tolerant patients with epilepsy. All these patients were treated with carbamazepine(CBZ), oxcarbazepine (OCZ) and phenobarbital (PB). We genotyped HLA-B*1502 gene in 5 patients with SJS/TEN induced by AEDs, including CBZ, OCZ, and PB, and 32 AED-tolerant controls.
Results: The five patients with SJS or SJS/TEN, among which of three were induced by CBZ and the other two by OCN and PB, respectively, were HLA-B*1502 positive. Among the control groups, HLA-B*1502 was present in 6.25% (2/32) of AED-tolerant patients. A strong association with HLA-B*1502 was found in patients with AED-induced SJS or SJS/TEN (p < 0.0001, OR = 150, 95% CI 8.99–1,969.997). HLA-B*1502 allele has 100% sensitivity (95% CI 46.29–100%) and 93.75% specificity (95% CI: 77.78–98.91%) for testing AED-induced SJS/TEN.

Discussion: We confirmed that a strong association between HLA-B*1502 gene and AED-induced SJS/TEN in Chinese Children in Mainland China.

Graph:

E-5. Levetiracetam: Safety and efficacy in neonatal seizures
Ramanthani G (Freiburg, Germany), Ikonomidou C (Madison, WI), Walter B (Dresden, Germany), Rating D (Heidelberg, Germany), Dinger J (Dresden, Germany)

Purpose: Neonatal seizures are common, especially in premature infants. Phenobarbital (PB) currently represents the antiepileptic drug (AED) of choice, despite being related to increased neuronal apoptosis in animal models and cognitive impairment in human subjects. Levetiracetam (LEV) may have a more favorable profile since it does not cause neuronal apoptosis in infant rodents.

Methods: In a prospective feasibility study, LEV was applied as first line treatment in 38 newborns with EEG-confirmed seizures, after ruling out hypoglycemia, hypocalcaemia, hypomagnesaemia and pyridoxin deficiency. Initial intravenous doses of 10 mg/kg LEV were gradually increased to 30 mg/kg over 3 days with a further titration to 45–60 mg/kg at the end of the week. Acute intervention with up to 2 intravenous doses of PB 20 mg/kg was tolerated during LEV titration. LEV was switched to oral as soon as the infants’ condition allowed. Based on clinical observation, EEG tracings (aEEG/routine EEGs), and lab data, drug safety and anticonvulsant efficacy were assessed over 12 months.

Results: In 19 newborns a single PB dose of 20 mg/kg was administered, while in 3 newborns received 2 PB doses. 30 infants were seizure free under LEV at the end of the first week and 27 remained seizure free at four weeks, while EEGs markedly improved in 24 patients at 4 weeks. In 19 cases, LEV was discontinued after 2–4 weeks, while 7 infants received LEV up to 3 months. No severe adverse effects were observed.

Conclusions: These results illustrate the safety of LEV treatment in neonatal seizures, including seizures in premature infants, and suggest anticonvulsant efficacy of LEV. Double blind prospective controlled studies and long-term evaluation of cognitive outcome are called for.

E-6. Diffuse hypometabolism pattern on FDG-PET in children with intractable epilepsy signify poor long-term outcome
Shandal V, Veenstra AL, Behen ME, Sundaram SK, Chugani HT (Detroit, MI)

Objective: In children with intractable epilepsy, positron emission tomography of glucose metabolism (FDG-PET) may provide seizure focus localization; however, patients with global or diffuse cortical hypometabolism are not suitable candidates for resective epilepsy surgery. We determined the long-term outcome of such children.

Methods: Seventeen children with intractable epilepsy showing bilateral, diffuse cortical hypometabolism on FDG-PET were followed from 1 year 4 months to 11 years 4 months (mean: 5 years 7 months ± 2 years 1 month) after their PET scans. One child had died. Mean age of the remaining 16 children (male/female = 9/7) during PET and at follow-up was 9 ± 5.85 years and 15 ± 4.88 years, respectively. Follow-up data and Vineland adaptive behavior scores were obtained through telephone interview.

Results: One child succumbed to Sanfillipo’s disease at 20 years. On follow-up, only 2 children were seizure-free. 50% had walking difficulties, 56.25% were not toilet-trained, all had speech difficulties, 43.75% had behavioral problems, 37.5% had poor eye contact, 75% had socialization difficulties and 87.5% attended special schools. Three children were found to have genetic causes including a 4 MB deletion of mitochondrial genome, MECP2 duplication and Lafora disease. All children, except one, were delayed significantly when tested through Vineland.

Conclusions: A diffuse pattern of hypometabolism on FDG-PET scans in children with intractable epilepsy may signify metabolic/neurogenetic causes responsible for their epilepsy. The developmental, behavioral and seizure-free long-term outcome in this patient population is usually poor. Of the 17 children, 13 did not have a specific diagnosis.

E-7. Ketogenic diet improves refractory status epilepticus
Hee-joon Y, Sook Hyun N, Cha Gon L, Jeehun L, Munhyang L (Seoul, South Korea)

Objective: The role of ketogenic diet (KD) in prolonged status epilepticus (SE) not been well described. This study aimed to report successful use of the ketogenic diet in patients with multidrug resistant SE after encephalitis.

Methods: We retrospectively reviewed the medical records of 5 patients with SE whom we tried ketogenic diet from October 2006 to August 2010.

Results: The study group comprised four children and one adult. All patients presented with SE associated with viral encephalitis. Patients were on mean five antiepileptic drugs, which were not effective for complete control. The time from onset of epilepsy to introduction of KD ranged from 0.5 month to 14 months. On initiation the KD, we administered the 4:1 ratio of lipid to non-lipid with 70%–80% liquid and calori of daily requirement using commercial ketogenic liquid. The median time to seizure improvement more than 50% was 8 days (1–19 days). At 1 month after starting KD, one of them became seizure-free and two others experienced more than 90% seizure reduction. The rest two of them improved more than 70% seizures and generalized seizures disappeared. In 4 children,
they had been on ventilator care and KD made them possible to be weaned the ventilator with reducing dose of AEDs. The duration of diet ranged from 1 month to 16 months. The complications were aspiration pneumonia, gastroesophageal reflux (n=2) and constipation (n=4).

Conclusions: The KD can be a valuable therapeutic option for the patients with pharmacoresistant SE.

E-8. Adverse effects of topiramate on the language problem solving abilities in children with epilepsy
Kim SJ, Choi YM (Jeonju, Korea)

Objective: The aim of this study was to investigate the effects of topiramate on problem solving ability in newly diagnosed pediatric patients with epilepsy.

Methods: Newly diagnosed 38 epileptic patients were assessed standard language tests and problem solving abilities. First test data were collected right before the topiramate monotherapy started and the treatment remained as monotherapy until the second tests were performed. Topiramate therapy dose was 1mg/kg/day for the first one or two weeks; increased to follow by slow increase of dose every 2 weeks until a maintenance dose of 5mg/kg/day or 200mg/day was reached. Language tests were included language problem solving ability test (TOPS), Peabody Picture Vocabulary Test, Velopharyngeal articulation screening test.

Results: All language parameters of TOPS were significantly reduced after initiation of topiramate (Determine Causes: 13.2±4.8 to 11.2±4.3, Problem Solving: 14.8±6.0 to 12.8±5.0, Predicting: 9.8±3.6 to 8.8±4.6, P<0.05). Patients with topiramate showed limited shorten the mean length of utterance during answers in words (Determine Causes: 51 to 33, Problem Solving: 78 to 52, Predicting: 59 to 43, P<0.05), answers were ambiguous during the test, and they also showed that the difficulty to select the appropriate word, took more time to answers, and used the wrong grammar. However, receptive language ability and precise articulation of patients were not changes after taking topiramate.

Conclusions: Our data suggests that topiramate could be negative effects on the abilities of problem solving abilities. We strongly recommend that language tests should be performed during the treatment with topiramate in children.

Kim SJ, Kim KS (Jeonju, Korea)

Objective: The purpose of this study was to assess the current therapeutic status of attention deficit-hyperactivity disorder (ADHD) treatment in children with epilepsy.

Methods: A cross-sectional survey of 178 patients aged 4–20 years from ten pediatric neurology departments in eight cities in South Korea from January 2005 to July 2010 was used to assess clinical characteristics of ADHD patients with epilepsy and risk factors associated with ADHD.

Results: A total of 178 pediatric epileptic patients were recruited for this study. One hundred and seven patients (61 subjects, M:F = 4:1, mean age: 12.2 ± 3.3 yrs old) records were evaluated excluding 4 patients due to incomplete data. One hundred twenty-five out of 174 patients (71.8%) had partial seizure disorder, 45 patients had generalized epilepsy. Eighty out of 112 patients showed ADHD combined type in DSM IV. The mean prevalence rate of ADHD treatment among the epileptic patients was 1.9%. Over 45% patients showed complete or persistent symptoms without difficulties in school life with CNS stimulants. Adverse reactions were reported in 19.8% of patients who received ADHD medica-

E-10. Atypical language patterns in pediatric epilepsy population
Zimmarno LA, Duke ES, Berl MM (Washington, DC), Khan O, Sato A, Theodore WH (Bethesda, MD), Guillard WD (Washington, DC)

Objective: To characterize patterns of language dominance in children with focal epilepsy assessed by fMRI

Methods: We studied 116 pediatric epilepsy patients [65 males; age 12.7 yrs, range (4–18.5); 48 right handed]. 68 children had left hemisphere seizure focus; 48 had right focus determined by clinical features, EEG/video-EEG, and MRI (29 normal, 17 MTS, 48 lesion (tumor, dysplasia), 4 inflammatory, 3 dual pathology, 3 other). Patients performed an auditory description decision task using 3T BOLD EPI fMRI. Laterality indices (LI) for regions of interest (ROI) [inferior frontal gyrus (IFG) and Wernicke's area (WA)] were calculated. Patients were categorized as left, right, symmetrically bilateral or crossed language dominant based on the LI of the ROIs. Demographic and seizure profiles were described for each pattern of language activation.

Results: 32 patients (27.6%) had atypical language dominance. Of these, 46.9% (15) patients had right language dominance, 3.1% (2) had symmetrical bilateral dominance, and 46.9% (15) had crossed dominance. Six patterns of atypical language activation emerged: A crossed dominant pattern of RIFG with LWA was most frequent (31.3%). Other patterns included bilateral (B) IFG/RWA (18.8%), RIFG/BWA (6.3%), RIFG/RWA (21.9%), and LIFG/RWA (15.6%). There was no difference in frequency of atypical language based on age, gender, or hemisphere focus.

Conclusions: We found that atypical language may take several forms, suggesting that there is considerable malleability within the distributed language network. The unexpected frequency of atypical language dominance in right hemisphere focus patients may represent a referral bias.

E-11. First time unprovoked seizure: family education by residents in the Emergency Department
Pinto ALR, Olson HE, Levin A, Rollins C, Schomer M, Elitt C, Spencer K, Mashi KP (Boston, MA)

Objective: To assess anticipatory guidance provided by child neurology residents to patients and families presenting with first time unprovoked seizure to the emergency department.

Methods: 17 child neurology residents (PGY 3–5) at Children’s Hospital Boston were surveyed on a 20 item questionnaire regarding the frequency and content of their anticipatory guidance provided to patients/families evaluated in the emergency room for first time, unprovoked seizure.

Results: All 17 residents responded. Ninety-four percent of the respondents reported that they always included anticipatory guidance during consultation on patient with first time unprovoked seizure. Verbal information was provided on what to do during a seizure (100% always or usually), when to call for emergency help (88% always or usually, 12% sometimes), and activity restrictions (100% always or
usually). Less than 50% of the residents typically provided written information on these topics and only 6% typically provided written or on-line references for families.

**Conclusions:** While the majority of the residents provide verbal information to families and patients seen in emergency department for first unprovoked seizure, less than 50% of the residents provide written information. In order to standardize anticipatory guidance provided by residents for first time unprovoked seizure, written material developed for resident use for counseling patients is needed.

**E-12. Predictors of status epilepticus in children**
Vendrame M, Gregas M, Gedik M, uysal S, Gooy V, Rotenberg A, Kothare SV, Loddenkemper T (Boston, MA)

**Objective:** To describe clinical features of patients at risk for status epilepticus (SE) and to identify SE predictors in hospitalized children admitted with seizures.

**Methods:** We retrospectively reviewed medical records for all admissions for seizures at our institution in 2008 and compared clinical features of patients with history of SE to those without history of SE. Statistical analysis was conducted with non-parametric measures (Wilcoxon test). When appropriate, chi-square tests and odds ratio were calculated.

**Results:** 1291 patients (54% male) were identified. Median patient age was 28 months (IQR 6–72). Overall, 553 children (42.8%) had one seizure type, and 738 (57.1%) experienced multiple seizure types; 553 (42.8%) had developmental delay, 280 (21.7%) had abnormal EEGs, and 568 (44%) had abnormal MRI. We found 770 children (62%) on <2 antiepileptic drugs (AEDs), while 491 (38%) were on 2 or more AEDs. Overall, 669 (53%) had multiple admissions.

We identified 458 (35.5%) children with history of SE and 833 (64.5%) without history of SE. Comparison between the two groups revealed that SE patients more likely had (1) multiple seizure types (OR=2.77, p<0.001); (2) developmental delay (OR=1.62, p<0.001); (3) prior EEG abnormalities (OR=1.52, p=0.004), (4) MRI abnormalities (OR=1.56, p<0.001); (5) multiple hospital admissions (OR=2.01, p<0.001); (6) higher numbers of AEDs (OR=1.72, p<0.001).

**Conclusions:** These identified differences may contribute to predicting SE risk in hospitalized pediatric epilepsy patients. Prospective studies are necessary to identify biomarkers for SE risk in children with epilepsy.

**E-13. Oxcarbazepine and ethosuximide desensitization in children with intractable epilepsy**
Lee BL, Lee M, Lee J (Seoul, Korea)

**Objective:** We review our experience with oxcarbazepine and ethosuximide desensitization in six children with medically intractable epilepsy.

**Methods:** Medical records of six consecutive children (mean age 11.8 ± 3.6 years, from July 2009 to November 2010) desensitized by incremental challenge to oxcarbazepine or ethosuximide were retrospectively reviewed. All children were intractable epilepsy patients with refractory seizures to more than five antiepileptic drugs. All six children had hypersensitivity reaction to oxcarbazepine and one child had also allergic reaction to ethosuximide. Although alternative antiepileptic drugs were tried on our patients, their seizures were refractory to several drugs. Desensitization to oxcarbazepine was performed in five children with partial seizures and ethosuximide was attempted in one child with atypical absence seizures. Desensitization was started at 0.1mg daily and the doses were increased slowly over 2 to 4 months as scheduled.

**Results:** The desensitization protocol was well tolerated in all children without serious allergic reaction. Two children developed mild itching and erythema during desensitization, but the symptoms disappeared after the next dose increasing was withheld. Except for one child with no seizure reduction, seizure frequency was reduced in five children; seizure-free in two, >90% reduction in two, and >50% reduction in one.

**Conclusion:** In our study, the desensitization protocol has been well tolerated and safe. Desensitization could enable to re-administrate effective antiepileptic drugs in our patients who had been previously experienced hypersensitivity reaction to oxcarbazepine or ethosuximide. However, careful consideration is needed due to the risk of severe drug reactions, such as Stevens-Johnson syndrome.

**E-14. Evaluation of the Bien diagnostic criteria for Rasmussen Encephalitis**
Olson HE, Loddenkemper T, Anjum M, Gooy T, Gorman MP (Boston, MA)

**Objective:**
1) To determine the correlation between 2005 Bien diagnostic criteria for Rasmussen Encephalitis (RE) and biopsy-proven cases,
2) To describe patients with biopsies consistent with RE who do not meet full clinical criteria.

**Methods:** Children's Hospital Boston medical records database was searched using the term "Rasmussen" between 1994 and 2010 to identify patients with suspected RE. We abstracted data from charts using a pre-determined process and classified whether patients met 2005 Bien diagnostic criteria.

**Results:** Fifty-seven eligible patients were identified. Another etiology was identified in 13, no clinical criteria were met in 9, and partial clinical criteria were met in 20. Fifteen met full clinical criteria (4 by the A, 5 by the B, and 6 by both criteria). Of these, the diagnosis depended on consistent biopsy in three cases. Biopsies were performed and consistent with RE in 12 cases, not performed in 1 case, and inconsistent with RE in 2 cases (showed gliosis without inflammation). Of patients meeting partial clinical criteria, 4/20 (20%) had biopsies consistent with RE and no other explanation for their encephalitis, 2/20 (10%) had biopsies showing gliosis without inflammation, and biopsy was not performed in 14/20.

**Conclusions:** The 2005 Bien clinical criteria for RE correlated with consistent biopsies in most cases, but were falsely positive in two patients. 20% of patients who met partial clinical criteria had biopsies consistent with RE suggesting a wider spectrum of RE than is captured by strict application of the Bien criteria.

**E-15. Cranial computed tomography (CT) in the evaluation of neonatal seizures - a description of the current practices at a regional perinatal center**
Holmman JK (New Hyde Park, NY), Lesser M (Manhasset, NY), Smith RE (New Hyde Park, NY)

**Objective:** We observed the use of cranial CT as first imaging study for neonatal seizures. It is known that exposure to radiation increases a child's risk for cancer. This study identifies neuroimaging referral patterns in neonates presenting with seizures.

**Methods:** Neonates >= 34 weeks gestation diagnosed with seizures/ apnea 1990–2009 at our regional perinatal center, were identified via electronic database. Pre-existing neurological conditions were excluded. Demographic factors, clinical variables and neuroimaging results were collected.
E-16. Efficacy of Vigabatrin in controlling clinical seizures for patients with infantile spasms (IS): clinical experience from the Children’s Hospital of Michigan (CHM)

Khodabaksh K, Chugani HT (Detroit, MI)

Objective: In a retrospective analysis, we investigated clinical experience with vigabatrin for IS.

Methods: CHM is a major referring center for IS patients who require surgical evaluation. We employed records of 263 patients treated 1999–2009. Many patients have been receiving vigabatrin, while others have received alternative AEDs. We performed a retrospective review of data for our IS patients via electronic health records (EHRs), as well as follow-up telephone calls with patients’ parents/caregivers, to assess the efficacy of vigabatrin in controlling patients’ clinical seizures. We assigned subjective ratings of 1) poor or no control of seizures with vigabatrin, 2) moderate to good control of seizures with vigabatrin, and 3) excellent control of seizures with vigabatrin, for each patient, as a way of assessing vigabatrin’s effect in treating real-world patients.

Results: As of June 2009, of 263 patients, 130 (49.4%) had been receiving vigabatrin. Of these 130, 71 (54.6%) had achieved excellent seizure control, (21.5%) had achieved moderate to good control, and 31 (23.8%) had poor or no seizure control with vigabatrin. The percentage of vigabatrin patients achieving excellent control versus those achieving poor or no control was highly statistically significant (p<0.0001, chi-square test). We have an additional cohort of 63 patients with tuberous sclerosis, most of whom are receiving vigabatrin, that we are assessing.

Conclusions: To our knowledge, this is one of the largest single-center cohorts of IS patients treated with vigabatrin. Our results indicate vigabatrin is highly effective in clinically controlling seizures in a real-world cohort of IS patients.

E-17. Presurgical SISCOM evaluation in children with multifocal MRI abnormalities

Wong-Küsel LC, Witte RJ, Kootenas AL, Wirrell EC (Rochester, MN)

Objective: To determine whether subtraction ictal SPECT co-registered to MRI (SISCOM) provides additional localizing information and if resection of SISCOM hyperperfusion abnormality predicts surgical outcome in children with multifocal MRI abnormalities.

Methods: A retrospective review was performed in all children with intractable epilepsy and multifocal MRI abnormalities (not due to tuberous sclerosis complex), who underwent SISCOM prior to epilepsy surgery at the Mayo Clinic Rochester between 1996 and 2008. Favorable surgical outcome was defined by rare or seizure freedom (Engel’s class I and II).

Results: Thirty children were identified, including two patients undergoing a second resective surgery (male 63%, median age at surgery 10.7 years). Focal SISCOM hyperfusion was present in 23 patients, rendering further localization in 11 of 15 patients who had no dominant ictal onset on scalp EEG. Twelve patients underwent intracranial EEG monitoring. The median duration of post-surgical follow-up was 4.9 years, with overall favorable outcome in 14 of 28 patients (50%). Favorable outcome was seen in 6 (40%) patients with dominant ictal EEG focus, 10 (45%) patients with single SISCOM abnormality, and 11 (58%) patients with lateralized hemispheric MRI abnormalities (non-significant). Post-operative MRIs were available in ten patients, and favorable outcomes were present in 4/8 (50%) patients with completely or partially resected versus 0/2 with non-resected SISCOM abnormality.

Conclusions: SISCOM may provide further localizing information for planning resective epilepsy surgery in children with multifocal MRI abnormality. Furthermore, resection of SISCOM abnormality appears predictive of favorable surgical outcome.

E-18. Registry characterizes visual loss associated with Vigabatrin therapy

Pellock JM (Richmond, VA), Faught E (Atlanta, GA), Seregot RC (Philadelphia, PA), Shields WD (Los Angeles, CA), Burkhardt GA (Reston, VA), Krauss GL (Baltimore, MD), Foroozan R (Houston, TX), Weinberg MA (Deerfield, IL), Wesche DL (Deerfield, IL)

Objectives: To manage risk of visual loss associated with vigabatrin, the FDA and Lundbeck Inc. require a comprehensive Risk Evaluation and Mitigation Strategy (REMS), including an ongoing patient registry, to assess incidence, prevalence, time to onset, progression, and severity of vision loss.

Methods: Registry participation is mandatory for prescribers and patients. Prescribers’ specialities/locations, demographics, and clinical characteristics are collected. Vision assessments are required throughout therapy — at baseline (≤4 weeks after initiation), at least every 3 months during therapy, and 3–6 months after discontinuation. Visual assessments are summarized via the REMS for the FDA. Mandatory benefit/risk evaluations are conducted by treating physicians within 2–4 weeks for patients <3 years of age, and within 3 months for patients ≥3 years. Analyses were completed every 6 months during Year 1 (2009–10), and are now being conducted annually for 6 years.

Results: As of Feb. 1, 2011, 2,473 patients had enrolled — 1,500 with IS, 846 with rCPS, and 120 with other diagnoses. At enrollment, 751 (30.4%) had previously received or were currently receiving vigabatrin. Kaplan-Meier analyses of time in registry for all patients indicate that 1,383 (97%) with IS had remained in the registry beyond 1 month, and 594 (83%) with rCPS had remained beyond 3 months. Of Sabril-naïve patients, 892 (95%) with IS had
remained beyond 1 month, and 277 (73%) with rCPS had remained beyond 3 months.

Conclusions: The registry provides important information focused on results of visual assessments, including visual-loss risk factors, which may help guide treatment decisions.

E-19. Diffusion tensor imaging abnormalities in frontal cortex in drug resistant pediatric partial epilepsy


Objectives: To investigate the hypothesis that, in children with drug-resistant partial epilepsy (DR-PE) and otherwise normal MRI of the frontal lobes, Diffusion Tensor Imaging (DTI) reveals abnormalities in the fractional anisotropy (FA) of frontal cortical regions.

Methods: Twelve children (7 boys) with DR-PE (6 frontal, 6 temporal; duration 2.53 ± 1.88 years) between the ages of 4 and 17 years and 12 age- and gender-matched healthy controls underwent DTI and conventional MRI at 3T. DTI data was transformed to the ICBM-152 atlas and the Type II White Matter Parcellation Map (H. Jiang, S. Mori; Johns Hopkins University, Baltimore, MD) was applied, allowing quantification of FA values in predefined segmented structures within a common coordinate system. Mean FA values of frontal lobe regions of interest were compared using the Wilcoxon Signed-Rank Test with Holm-Bonferroni correction.

Results: Patients demonstrated decreased FA bilaterally in the lateral fronto-orbital gyrus (0.192 ± 0.025 vs. 0.248 ± 0.027; p=0.000076), middle fronto-orbital gyrus (0.200 ± 0.045 vs. 0.282 ± 0.0034; p=0.00011) and the superior frontal gyrus (0.209 ± 0.017 vs. 0.228 ± 0.016; p=0.0013). No significant differences in FA values were observed in the middle frontal, inferior frontal, precentral, gyrus recti and cingulum gyri (p>0.01).

Conclusions: This study presents evidence that there are abnormalities in frontal cortical regions in children with DR-PE that are not detected by conventional MRI. Although the full significance of these findings remains to be determined, they suggest the presence of previously unsuspected abnormalities in the frontal lobe in such patients.

E-20. Electrographic seizures in critically ill children are associated with mortality and worse short-term outcomes

Abend NS, Topjian AA, Gutierrez-Colina AM, Dlugos DJ (Philadelphia, PA)

Objective: Non-convulsive seizures (NCS) and status epilepticus (NCSE) are common in critically ill children with acute encephalopathy, but their impact on outcome is unknown. We aimed to determine whether NCS and NCSE were associated with higher mortality and worse short-term outcome.

Methods: Critically ill children with acute encephalopathy underwent EEG monitoring in the pediatric intensive care unit in a tertiary care children’s hospital. EEGs were scored as (1) no seizures, (2) seizures, or (3) status epilepticus. Clinical information obtained included age, acute encephalopathy etiology, mortality, and whether there was a change in Glasgow Outcome Scale (GOS) from admission to ICU discharge. Chi-square analysis and multi-variable logistic regression were used to evaluate the associations between NCS and NCSE and mortality and short-term outcome.

Results: 200 children underwent eEEG. NCS occurred in 84 (42%) of which 43 (22%) had NCSE. 83 (41%) had a decrease in GOS including death in 36. GOS decrease was significantly more common in children with than without NCS (54% vs 33%, p=0.003) and with than without NCSE (74% vs. 32%, p<0.001). Mortality was significantly higher in patients with than without NCSE (30% vs. 15%, p=0.018) but there was no difference in mortality with or without NCS (21% vs. 16%, p=0.28). These associations persisted after controlling for age and acute etiology.

Conclusions: NCS and NCSE are associated with worse outcomes in critically ill children with acute encephalopathy. Further investigation is needed to determine whether this association is causal, and whether management of electrographic seizures improves neurodevelopmental outcome.

E-21. EEG monitoring in critically ill children: indications and monitoring strategies

Gutierrez-Colina AM, Dlugos DJ, Topjian AA, Abend NS (Philadelphia, PA)

Objective: Continuous electroencephalographic monitoring (cEEG) often detects non-convulsive seizures (NCS) in critically ill children, but the intense resource utilization it requires leads to feasibility concerns.

Methods: We performed a prospective observational study in which each patient in a tertiary care 45-bed pediatric intensive care unit was screened daily for 21 days for specific potential cEEG indications. The percent of children who would require cEEG each day based on specific indications was determined. Using this data, we then calculated the number of cEEG days that would be required each month based on three cEEG strategies that differed in indications and monitoring duration.

Results: A brief-broad strategy involved monitoring all children with altered mental status for their first day with altered mental status and required 32 days of cEEG per month. A prolonged-targeted strategy involved monitoring all children with altered mental status and a known acute encephalopathy for all days on which they had altered mental status, and required 102 days of cEEG per month. A brief-targeted approach involved monitoring all children with altered mental status and a known acute encephalopathy for the first day on which they had altered mental status, and required 32 days of cEEG per month. Based on published seizure occurrence data, these three strategies would require 14, 7, and 2 days of cEEG for every one patient with seizures detected, respectively.

Conclusions: This data suggests a framework for optimal cEEG utilization. A brief-targeted strategy provides the highest yield of NCS detection per day of EEG performed.

E-22. Prevalence of seizures and associated comorbidities in neonates treated by a neurocritical care service

Teng J, Chang T, Tsuchida TN, Scalfi J, Hecht JH (Washington, DC)

Objective: To examine causes and comorbidities associated with neonatal seizures in a tertiary care NICU.

Methods: We performed a cross-sectional study of neurologic consults between 2004–2010 for seizures identified by a neonatal neurocritical care service (NNCS) in a Level IIIIC NICU. We examined demographic data, comorbidities, resource utilization, anticonvulsants used, etiologies and outcomes.
Results: Between 2004–2010, the NNCS consulted on 17.1% of all NICU admissions. Seizures occurred in 222 (27.7%). Of infants with seizures, 56% were male, 49% born via vaginal delivery, and 69% were term. The average length of stay was 28.6 days. The most common categories of non-neurologic comorbidities were respiratory issues (22%), metabolic disturbances (14%), congenital malformations (12%), and infection (11%). The most common neurologic diagnoses were neonatal encephalopathy (39%), hemorrhage (19%, of which 50% were IVH), stroke (18%), CNS infection (8%), CNS malformations (8%), hydrocephalus (7%), and chronic insults (2%). Seizures alone were present in 6.8%, refractory seizures in 32%, and status epilepticus in 7.2%. Almost all received EEG monitoring (94%) and neuroimaging (99% - 73% MRI, 64% HCT, 37% HUS). Anticonvulsants used were phenobarbital (85%), phenytoin/fosphenytoin (28%), levetiracetam (7%), topiramate (5%), or midazolam (5%). Cerebral herniation occurred in 3% and mortality in 14.4%.

Conclusions: In our experience, seizures are a common reason for neurologic consultation in the intensive care nursery. Understanding the comorbid conditions, resource utilization, and treatments of neonates with seizures will help guide future development of neonatal neurologic services.

E-23. Clinical efficacy of Vigabatrin in infantile spasms
Patel P, Miller-Horn J, Mangunas L, Pulipati B, Mittal A, Andriola M (Stony Brook, NY)

Objective: Vigabatrin (VGB), has now been approved by the FDA for infantile spasms (IS) with strict ophthalmologic monitoring for children between 1-48 months of age secondary to permanent loss of peripheral vision. We conducted a retrospective analysis of children treated initially with VGB versus those who received VGB as an adjunct and treated with other anti-epileptics (AED), ACTH, or a ketogenic diet. Our goal was to evaluate children treated with VGB and assess its value as a first line agent for IS.

Methods: A retrospective chart was completed on children with IS treated with VGB from January 2001 to March 2011. Variables included gender, age, length of treatment, neurologic conditions, dosage, MRI imaging, adverse effects, and treatment response. AED prior, after, and during VGB use were recorded. Seizure frequency was recorded over at least a 6 month period.

Results: We identified 11 patients diagnosed with IS who were treated with VGB (7 females and 4 males) between the ages of 1–15 yrs. Eighty-one percent were treated with ACTH/AED and 18% with a ketogenic diet prior to VGB. Thirty-six percent were controlled on VGB monotherapy and 36% were managed on AED/ACTH plus VGB. Overall, 72% of patients had a decrease in frequency of spasms.

Conclusion: Our studies show that VGB significantly reduces the frequency of infantile spasms. VGB was well tolerated with no evidence of peripheral vision loss on ophthalmologic surveillance. This data adds to the increasing evidence that VGB is effective as a first-line agent for IS.

E-24. The role of EEG in complex febrile seizures: a retrospective study
Vazquez A, Fenton G (Albuquerque, NM)

Objective: The aim of this study is to investigate the presence of EEG abnormalities in patients with complex febrile seizures (CFS) and its relationship with clinical variables.

Methodology: This is retrospective study that consist of medical chart review of pediatric patients with CFS seen in the University of New Mexico Hospital (UNMH) from 1/1/2007 to 2/28/2011. The relationship between clinical variables like: first time febrile seizure, recurrent febrile seizure, timing of the EEG since CFS, family history of febrile seizures (FS) or epilepsy, neurological exam abnormalities was statistically analyzed.

Results: Fifty two patients were included in the study. Of these, 53% had normal EEG’s (nEEG) and 46% had abnormal EEG’s (aEEG). Those patients with aEEG, 54% had background abnormalities, 25% epileptiform activity and 21% with both. Those with background abnormalities, 33% had focal slowing and 42% generalized slowing. Multivariate analysis showed that clinical variables like: first time febrile seizure and recurrent febrile seizure had a p<0.02, family history of epilepsy p<0.73, family history of FS had a p<0.026. Only one patient had an EEG done after 5 days of the FS.

Conclusions: Background abnormalities, was the most common EEG abnormality found in our study group with CFS. Generalized slowing was found to be the most common EEG background abnormality. Of the clinical variables studied; history of febrile seizures was found to be related to the like hood of finding abnormalities in the EEG.

E-25. The effect of treatment of obstructive sleep apnea on seizure outcome in children
Segal E (Bronx, NY), Vendrame M, Gregas M, Loddenkemper T, Kothare S (Boston, MA)

Objective: To assess the effect of tonsillectomy adenoidectomy (TA) on seizure frequency.

Methods: Retrospective review of patients with epilepsy treated with TA from January 2008 to October 2010 was performed for age, gender, type of epilepsy, and seizure frequency.

Results: Of 4600 patients who had TA during the study period, 269 patients had history of seizures, 57 had epilepsy with pre/post TA seizure frequency and PSG data available, and 27 (median age 5y) had no adjustment to their AEDs around TA. Three months post-TA, 19(71%) demonstrated improvement; with 10(37%) patients becoming seizure-free, 12(44%) had >50% seizure reduction, and 6(22%) with an amelioration of seizure frequency. Two had an unchanged seizure frequency (7%) and 6(22%) had a worsening of seizure frequency. Median seizure frequency prior to TA was 8.5(IQR:2-90), post-TA was 3(IQR:0-75) with a 53% median seizure reduction. Multivariate analysis demonstrated a trend towards seizure freedom with each percentile increase in BMI and early age of TA. The 6-subjects with seizure exacerbation after TA had progressive epilepsy. Of the patients with an amelioration (or unchanged) seizure frequency (n=21; median age 5.75y), median seizure frequency pre-TA was 8.5(IQR:2-67.5), post-TA 0.5(IQR:0-13, p<0.01), and a 87% median seizure reduction. Multivariate analysis in this cohort confirmed similar trends.

Conclusion: TA can significantly decrease seizure frequency, especially those with elevated BMI scores, and younger age at time of surgery.

E-26. Outcome of epileptic spasms under age 3 years: single center US experience
Loddenkemper T, Vendrame M (Boston, MA), Guilhoto L (Sao Paolo, Brazil), Agarwal A, Gregas M, Bourgeois BF, Kothare SV (Boston, MA)

Objective: To describe outcome of epileptic spasms (ES) in patients <3 years over a 7-year period.
Methods: Retrospective review was performed to assess age at onset of symptoms, etiology of spasms, antiepileptic drugs (AEDs) used, short-term (<6months) and long-term (≥6months) outcomes.

Results: We included 173 children (104 boys, median-age of onset 6.8months) with known (62%) and unknown (38%) etiology. Hypsarrhythmia at onset was observed in 104(60%). AEDs included ACTH(n=103), VGB(n=82), phenobarbital(n=34), and others(n=121).

ACTH and VGB had similar efficacy on short-term spasm-control, in both groups with known(33%&40% respectively), and unknown etiology(50%&44% respectively; n.s.). Higher rates of failure were seen with use of other AEDs (71% for both-groups;p<0.05). In children with initial developmental delay/DD, there were no differences in spasms control between ACTH, VGB or other AEDs, independent of the etiology of spasms.

ACTH treatment provided a better long-term outcome in comparison to VGB and other AEDs, both in terms of development and seizure control (p=0.02 and p<0.01 respectively).

On long-term follow-up (median: 27 months), 83% had DD, and 54% had persistent seizures. Higher risk of persistent seizures was associated with typical hypsarrhythmia at onset(p<0.01), generalized abnormalities on MRI, and DD with hypotonia prior to onset of ES(p<0.01).

Conclusions: ACTH was found to be more effective in long-term control of seizures and developmental outcome. Results need to be interpreted in the setting of data acquisition and therefore confounding by indication cannot be ruled out. Patients with DD and hypotonia prior to ES (symptomatic sub-type) did poorly, independent of ACTH, VGB or other AEDs used.

E-27. Predictors of early symptomatic seizures in children with cerebral sino-venous thrombosis
Teh CM, Go T, Arkanal R, deVeerh G, MacGregor D, Moharir M (Toronto, ON)

Objective: Seizures are common in childhood cerebral sino-venous thrombosis (CSVT). Seizures at presentation are reported to predict poor outcome. This study aims to describe the characteristics and determine the predictors of early symptomatic seizures (ES) in childhood CSVT.

Methods: Children (29-days to 18-years) with CSVT from January 1992–December 2009 were identified from Paediatric Ischaemic Stroke Registry at The Hospital for Sick Children, Toronto. Clinical, radiological and electroencephalogram (EEG) data was analyzed. ES were defined as seizures occurring within 2-weeks of CSVT diagnosis.

Results: One-hundred sixty-one children were identified with CSVT. One-hundred and seven children were included (males: 62(58%)). Mean age was 6.75 years. ES occurred in 33(31%) children. Seizure data was available in 28. Seizure types were generalized (14(50%)), complex partial (14(50%)) and partial with secondary generalization (2(7%)). Subclinical/electrographic seizures occurred in 3(11%). Status epilepticus was present in 5(18%). EEGs were performed in 21. Seven (33%) were normal. Fourteen (67%) had abnormal background and 4(19%) had epileptiform discharges. Superior sagittal sinus thrombosis, cortical vein thrombosis (CVT), intra-parenchymal hemorrhage and venous infarction predicted ES on univariate analysis. On multivariate analysis, venous infarction continued to predict ES (OR:4.095%CI:2.0–12.2, p<0.004) while CVT showed a trend (OR:3.595%CI:0.9–13.7, p=0.07).

Conclusions: About one-third of children with CSVT present with ES. Venous infarction and cortical vein thrombosis increase the risk of ES. A subset of children with increased risk of ES in CSVT can be potentially identified. The role of EEG monitoring and prophylactic anti-convulsants in these patients during the acute period merits future studies.

E-28. Recurrent copy number variations in developmental epilepsies including infantile spasms
Paciorkowski AR (Seattle, WA), Rosenfeld J (Spokane, WA), Thio LL (St Louis, MO), Marini C (Florence, Italy), Christian S (Seattle, WA), Guerrini R (Florence, Italy), Shaffer LG (Spokane, WA), Dobyns WB (Seattle, WA)

Objective: To report on the increasing number of recurrent de novo copy number variants (CNVs) associated with developmental epilepsies -- including infantile spasms.

Methods: We present data on epilepsy and neurodevelopmental outcome for 15 children with deletions of 1p36 and 7q11, duplications of 14q12 and of the maternal allele of 15q11q13. Gene content was analyzed for mechanisms of pathogenesis.

Results: The presenting epilepsy phenotypes in this cohort included early infantile epileptic encephalopathy, infantile spasms, and Lennox-Gastaut syndrome. Not all patients developed intractable epilepsy. Autistic features were common among the children in this cohort. Analysis of gene content suggested dosage of critical genes such as KLHL17, GABRD (1p36), STX1A (7q11), FOXG1 (14q12) and several other GABA receptor subunits (15q11q13) may play a role in pathogenesis.

Conclusions: Several recurrent de novo CNVs are associated with developmental epilepsies, including infantile spasms. Chromosomal microarray should therefore be a first-line diagnostic test for these disorders. The epilepsy phenotypes underline the biologic kinship of early infantile epileptic encephalopathy, infantile spasms, and Lennox-Gastaut syndrome. Autistic features in these patients may not be explained by the presence of intractable epilepsy. Abnormalities of GABAergic interneuron development and pathways of synaptic development and function may be common features of developmental epilepsies in this cohort. Taken together, these recurrent CNVs provide an important tool toward understanding the pathogenesis of these severe forms of epilepsy.

E-29. Impact of epilepsy on activity involvement: implications for social acceptance and friendship
Hammouka LD, Bair LD, Yeates KO, Vannatta K (Columbus, OH)

Objective: To compare participation in activities in the home, school, and community for children with epilepsy and classmate controls and explore if participation is associated with friendships at school.

Methods: Data are obtained at school and the homes of children with established epilepsy, age 9–11, and controls classmates matched for gender, race, and age. Children and their classmates nominate their three best friends, producing a list of names for each child. Children and classmate controls and explore if participation is associated with friendships at school.

Results: The presenting epilepsy phenotypes in this cohort included early infantile epileptic encephalopathy, infantile spasms, and Lennox-Gastaut syndrome. Autistic features in these patients may not be explained by the presence of intractable epilepsy. Abnormalities of GABAergic interneuron development and pathways of synaptic development and function may be common features of developmental epilepsies in this cohort. Taken together, these recurrent CNVs provide an important tool toward understanding the pathogenesis of these severe forms of epilepsy.
children with epilepsy and 11 control classmates. We expect 30 and 20 children in the final epilepsy and control groups respectively.

**Results:** Total participation scores were lower for children with epilepsy than controls ($p<0.02$) including both school ($p=0.02$) and home and community living activities ($p=0.02$). In children with epilepsy, lower total participation was associated with fewer friendship nominations ($p=0.007$) and reciprocal friendships ($p=0.02$).

**Conclusions:** Restriction in developmentally typical activities for children with epilepsy may limit exposure to other children and the opportunity to develop social skills and friendships. Additional work is needed to further consider the bidirectional influence of activity participation and social adjustment for these at risk children.

**E-30. Variations in hospitalizations and total costs in children admitted with seizures between 2003 and 2006.**

_Brandridge SM, Horn PS (Cincinnati, OH)_

**Objective:** Economic factors play an increasingly important role in the management of medical conditions. This study evaluates the economic impact of pediatric seizures in the United States using a large national data set. The aim of this study was to characterize hospitalizations including total costs and length of stay and assess variations in children discharged with seizure between 2003 and 2006.

**Methods:** Analysis of the Kids’ Inpatient Database (KID2003 and KID2006), maintained by the Healthcare Cost and Utilization Project, was performed to determine hospitalization outcomes including length-of-stay and total costs of seizure in children ages 1 month to 20 years. Discharges with the International Classification of Disease, Ninth Revision, clinical modification code for seizure were selected.

**Results:** After statistical weighting there were 37,330 pediatric seizure discharges in KID2003 and KID2006. Mean hospital charges and cost were $10,106 and $4,105 for 2003 and $12,546 and $4,553 for 2006. The mean length of stay was significantly higher ($p < 0.0001$) in the urban teaching hospitals compared to urban non-teaching or rural hospitals (2.6 vs. 1.9 and 2.0) for 2003; results were similar for 2006. It is noteworthy there was no significant difference in total costs between the different payor groups including Medicare, Medicaid, and private insurance.

**Conclusions:** This analysis provides a reflection of healthcare utilization in pediatric seizure management. Within this study no payor group was significantly cost efficient. In a stressful economic climate, all health care entities must focus on appropriate cost management of pediatric seizure.

**E-31. Children with epilepsy: how do their classmates and teachers perceive them?**

_Bair LD, Hamiuka LD, Yeates KO, Vannatta K (Columbus, OH)_

**Objective:** Research suggests children with epilepsy are at risk for social difficulties, yet information about positive and negative patterns of peer interaction are lacking. This study compares peer and teacher perceptions of the social behaviors of children with epilepsy relative to comparison classmates.

**Method:** Data collection is ongoing for 35 children, age 9–11 years, with established epilepsy. Data are collected at school in the child’s primary academic, mainstream classroom. Teachers and classmates with parental consent (>80%) complete the Extended Class Play (ECP), a descriptive-matching instrument that yields 5 behavioral subscales: Popularity-sociability, Prosocial, Aggressive, Shy-withdrawn, and Rejection-victimization. Teacher and peer nominations are completed, tallied, and standardized ($M = 0$, $SD = 1$) for children the same gender as the child with epilepsy within each class. One comparison classmate, matched for gender, race and age, is identified for each child with epilepsy. Preliminary analyses have been completed for a subsample of 30 classrooms and effect sizes (Cohen’s $d$) are presented.

**Results:** Children with epilepsy are described by peers as displaying more Shy-withdrawn behavior ($d=0.50$) and Rejection-victimization ($d=0.43$); as well as less Aggressive behavior ($d=0.40$) and Popularity-sociability ($d=0.35$) than comparison classmates. Teachers also report more Shy-withdrawn behavior ($d=0.53$), more Rejection-victimization ($d=0.76$), and less Popularity-sociability ($d=0.41$) for the epilepsy group.

**Conclusions:** Children with epilepsy are at risk for social withdrawal and rejection-victimization by their peer group, yet may not display aggressive or disruptive behavior at school. Significance tests and considerations for further research and interventions will be presented and discussed.

**E-32. Impact of a neonatal neurocritical care service: treating neonatal encephalopathy and seizures**

_McIntyre E, Teng J, Tsuichida TN, Scafidi J, Lateef T, Masaro A, Short BL, Hoffman H, Chang T (Washington, DC)_

**Objective:** To examine the impact of a neonatal neurocritical care service (NNCS) in the treatment of neonatal encephalopathy (NE) and seizures in a tertiary NICU.

**Methods:** A cross-sectional study was conducted pre (2000–2003) and post (2007–2010) conception of a NNCS for newborns admitted to our NICU with the diagnosis of NE or seizures. Resource use including anticonvulsant medication, EEG, neuroimaging, ventilator support, enteral feeding, procedures, length of stay (LOS), and total hospital charge were collected from patient billing records. Univariate analysis on resource use was conducted. Multivariable regression was used to create a prediction model for total hospital charge.

**Results:** There was a four-fold increase in NE (51 vs. 210, $p<.0001$) and an almost two-fold increase in seizure (121 vs 212, $p<.0001$) referrals to our NICU between these time periods. In the post period, infants were admitted at a younger age ($p<.01$), had more comorbidities (NE: $p=0.09$, seizures: $p=0.002$), required longer ventilator support ($p<.01$), and were more likely to receive an EEG ($p<.0001$) and a MRI ($p<.0001$). LOS and mortality did not differ for either diagnosis between the time periods. After adjusting the total charges to 2010 dollars and controlling for LOS, comorbidities, ventilator use, procedures, and mortality, there was a 15.2% and 15.7% median hospital charge increase in the post period, respectively for NE & seizure.

**Conclusion:** A NNCS has changed the referral pattern and management of NE & seizure in a tertiary NICU without changing the LOS or mortality despite the increased patient complexity.

**E-33. Pairwise Granger Causality Findings in patients with partial epilepsy**

_Andrade EO, Cadotte A, Liu Z, Talabhi S, Carney PR_ (Gainesville, FL)

**Objective:** Based on the developing association between ictal onset and a neuronal network, we prospectively studied
the directionality in ninety seizures of twenty-five consecutive patients with non-lesional pharmaco-resistant partial epilepsy (NLPE) utilizing Pairwise Granger Causality (PGC) to test the hypothesis of contra-lateral ictal spread (inter-hemispheric theory) versus no contra-lateral ictal spread (intra-hemispheric theory).

Methods: Bootstrapping was used to address the issue of testing statistical significance of using PGC to evaluate network interactions before the onset of the seizure and during the seizure. Bayesian information criteria (BIC) were used to select the model order. Time frequency distribution was plotted for each seizure and compared with controls.

Results: PGC was consistently significant within the hemisphere (intra-hemispherical) for seizure ictal onset over the left frontal (p = 0.0465) and left temporal (p = 0.0458), right frontal (p = 0.0558), and right temporal regions (p = 0.0257). Furthermore, there were no significant differences when looking at the possible inter-hemispheric PGC directionality measures tested for seizures emanating over the left frontal (p = 0.2882), left temporal (p = 0.1572), right frontal (p = 0.6772) and right temporal regions (p = 0.7795).

Conclusions: The findings indicate an intra-hemispheric ictal spread, however, it is still possible that the results are affected by limitations of the linear autoregressive PGC model and/or the ‘hidden element’ theory. The conclusions obtained will serve as a principle for the development of maps of neuronal traffic and define models capable of predicting directionality and its strength on seizure generation and prediction.

E-34. Look and you will find: A prospective look at early seizures in children with mild to moderate traumatic brain injury using continuous EEG monitoring

Lerner JT (Los Angeles, CA), Arrut DH (Grand Rapids, MI), McArthur DL, Leung M, Valino HD, Madikians A, Yudovin S, Matsuzomo JH (Los Angeles, CA), Brooks-Kayal AR (Denver, CO), Giza CC (Los Angeles, CA)

Objective: Traumatic brain injury (TBI) is the principal cause of morbidity and mortality in the pediatric population. A few adult studies have documented subclinical early post-traumatic seizures (EPTS) in the ICU. Incidence of and risk factors for pediatric subclinical EPTS have not been determined.

Methods: Consecutive moderate-severe TBI patients admitted to two pediatric ICUs were monitored prospectively with continuous video EEG monitoring (cEEG). Monitoring was initiated at PICU admission, continued for 12–48 hours and extended if necessary clinically. Additionally, demographic data, imaging results and global outcomes were collected.

Results: 67 patients (44 males and 23 females) between the ages of 1 month and 17 years were consented. Severity of injury included: 38 moderate and 29 severe. Mechanism of injury included fall (34%), followed by abusive head trauma (AHT) (30%) and motor vehicle (21%). 27 (40%) had EPTS, and 8% had subclinical-only seizures. Therefore, cEEG after pediatric moderate-severe TBI is necessary to capture subclinical-only EPTS, particularly under the age of 1 and in those with abusive head trauma.

Conclusions: 35.5% of pediatric moderate-severe TBI patients had EPTS, and 8% had subclinical-only seizures. Therefore, cEEG after pediatric moderate-severe TBI is necessary to capture subclinical-only EPTS, particularly under the age of 1 and in those with abusive head trauma.

E-35. The clinical and diagnostic utility of prolonged video EEG in diagnosing psychogenic and other non-epileptic events in children

Gutu ST, Grigg-Damberger M (Albuquerque, NM)

Objective: Evaluate non-epileptic events (NEE) including psychogenic events (PNE) in children undergoing prolonged inpatient video-EEG monitoring (v-EEG).

Methods: Retrospective analysis of pediatric v-EEG studies identifying those with NEE collecting data regarding age, gender, comorbidities including epilepsy, antiepileptic treatment (AEDs), time to confirm the diagnosis, and outcome.

Results: NEE were diagnosed in 22 (5.8%, 10 females, mean age 10.4 years) of 378 children who had prolonged inpatient v-EEG at our institution over a 33 month period. Mean v-EEG duration was 52.5 hours. NEE were psychogenic in 9 (41%, mean age 13.5 years, 8 females), six had psychiatric problems, and three had or were being sexually abused. Causes of NEE in the remaining 13 (59%, mean age 8.25 years, 11 males) included dystonia, abnormally migraines, reflux, motor stereotypies. Comorbidities were intellectual disabilities in 6 (27%, 5 Males), epilepsy in 3 (all males with intellectual abilities but none with PNE). A mean of 18.5 hours of v-EEG were needed to confirm first NEE. Seven (32%) had been unnecessarily treated with AEDs for a mean of 3 years (6 months to 12 years). We weaned AEDS when unnecessary, and referred those with PNE to Psychiatry.

Conclusions: NEE in younger children are more often not psychogenic. NEE in adolescent females are often psychogenic. V-EEG can confirm the diagnosis, avoiding inappropriate treatment. Sexual abuse is a high risk factor for PNE in adolescent girls.

POSTERS: Genetics

G-1. Preliminary study the role of epsilon-sarcoglycan in myoclonus dystonia syndrome with small interference RNA

Zhang Yangwei (Yangzhou, Jiangsu, China), Shang HuiFang (Chengdu, Sichuan, China)

Objective: Myoclonus dystonia syndrome (DYT11) is an early-onset dystonia disease with autosomal dominant inheritance. Recently, epsilon-sarcoglycan (SGCE) gene mutations have been reported to result in MDS. Although one study showed focal brain glucose hypermetabolism in MDS, the role of SGCE gene in the development of MDS is still unclear. This study was to investigate the function of SGCE gene in neurons and probable mechanism to MDS.

Methods: Construct small interference RNA expression vector designed to target SGCE mRNA and transfect into NIH3T3 cell line which is proved by detecting SGCE protein with western-blots. Then construct recombinant adenovirus small interference RNA vector to target SGCE gene (siRNA-SGCE) and infect neurons. Western-blots tested the
**POSTERS: History/Teaching of Child Neurology**

**HI-1. Current practices of the child neurologist in the management of sports concussion**

Brosek DK, Samples H, Goodkin HP (Charlottesville, VA)

**Objective:** The 2008 Consensus Statement on Concussion in Sport (Zurich) and the earlier Vienna and Prague versions recommended that the grading scales proposed in the 1997 AAN guidelines be abandoned and that gradual return-to-activity could occur as soon as all symptoms had resolved. Our objective was to assess current clinical practice for return-to-activity among child neurologists.

**Methods:** An IRB-approved survey targeting respondent demographics and clinical practice in concussion was distributed electronically. Of approximately 1100 active CNS members, 237 responded. Incomplete surveys and one trainee were excluded, resulting in a sample of 227.

**Results:** Although the majority had practiced over 25 years (25.1%), nearly an equal number were early career (22.0%). Respondents were split on whether their training had provided adequate training in concussion. Although a majority agreed/somewhat agreed (15.4%/50.2%) that there are adequate resources to maintain competency in concussion, a majority (68.7%) had not completed concussion CME. The majority (78.4%) identified the use of the 1997 guidelines as guiding return-to-activity decisions while a minority (21.1%) was guided by the more recent Zurich guidelines. Those familiar with Zurich were more likely to have completed CME, to see >20 sports concussions annually, and to return an athlete to activity as soon as all signs/symptoms resolved.

**Conclusions:** The finding that half the respondents felt that their training in this topic was inadequate and that those who completed CME had a greater familiarity with the more recently proposed consensus-based concussion guidelines supports the development of additional education in sports concussion at all levels of neurology training.

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**HI-2. Cost-benefit analysis of physician-placed appointment confirmation calls in a resident-based child neurology outpatient clinic.**

Keros SI, Solomon GE (New York, NY)

**Objective:** To perform a cost-benefit type analysis on the use of physician telephone calls to improve patient show rates in a resident-based pediatric neurology outpatient clinic.

**Methods:** Clinic days were randomized to a ‘call’ or ‘no-call’ group. For a ‘call’ day, the senior pediatric neurology resident called patients 7–10 days in advance of their visit to confirm the appointment. New patients were asked for the chief complaint, and asked to send any pertinent records in advance. Follow-up patients were asked for interval history. If necessary a voice mail was left requesting a return call to confirm the appointment. The total time spent performing the ‘call’ intervention was carefully kept on a stopwatch. Both groups received confirmation calls from administrative staff as usual; only the calling resident knew the group assignments.

**Results:** The median show-rates for the ‘no-call’ and ‘call’ groups were 62% (SD=12; range=49%) and 88% (SD=9; range=34%) respectively. The average time spent calling was 2.5 minutes per patient. Other benefits were seen, but which were harder to quantify, such as: Fewer patients needed to be rescheduled or overbooked due to missed appointments; more patients came with records, or sent records which were harder to quantify, such as: Fewer patients needed to be rescheduled or overbooked due to missed appointments; more patients came with records, or sent records which could be reviewed in advance which led to more efficient work-ups; families appreciated the personal connection with their physician.

**Conclusions:** Adding physician calls to a confirmation strategy significantly increases show rates and decreases variability with a reasonable expenditure of time. We feel this investment is recouped through other benefits such as increased clinic efficiency.
HI-3. Utilization of educational resources available through the Child Neurology Society (CNS)
Petana Knight EM (Cleveland, OH), Joshi SM (Ann Arbor, MI), Leber S (Ann Arbor, MI)

Objective: To explore utilization of the case studies of the CNS website as teaching and self-learning resources among child neurologists.

Methods: A survey about utilization of the CNS website case studies and their link to SimulConsult was distributed to 1150 subscribers of the Child-Neuro listserv, asking if the subjects used the CNS case studies and the link to SimulConsult to teach or for self-learning. Responses were correlated to academic position, practice setting, and years in practice since training.

Results: 67 physicians responded [58 (87%) faculty/attending/private practitioner, 9 (13%) resident/fellow]. Practice setting was: academic hospital associated with university in 53 (79%); private practice in 7 (10%); and free-standing children's hospital in 4 (6%). Six (9%) physicians were still in training. Time in practice was <10 years in 17 (29%), 11–20 years in 13 (22%), and >20 years in 29 (49%).

Faculty attending/private practitioners used the resource to teach residents/fellows (20, 77%) and medical students (11, 42%) vs. other physicians (8, 30%) or nurses 1 (4%). Residents/fellows used the resource to teach other resident/fellows 4 (80%) and medical students 1 (20%).

Conclusion: Use of case studies of the CNS website and SimulConsult for teaching at different educational levels is limited. The CNS case studies seem to be an attractive tool for self-learning for residents and fellows but SimulConsult as linked to the case studies is underutilized by the in-training group. Increased awareness about these resources could impact the education of Child Neurology trainees and keep practicing physicians up-to-date.

Response | CNS Case Teaching | SimulConsult Teaching | CNS Case Self-learning | SimulConsult Self-learning
--- | --- | --- | --- | ---
Yes Used by | 31/66 (47%) | 16/31 (53%) | 36/66 (54%) | 19/36 (53%)
Faculty/Attending/Private Practitioner | 26/57 | 15/16 (94%) | 28/57 | 16/19 (84%)
Resident/Fellow | 5/9 | 1/16 (6%) | 8/9 | 3/19 (16%)
Frequency | | | | |
Daily- weekly | 7 (23%) | 9 (25%) | |
Monthly | 10 (32%) | 9 (25%) | |
Quarterly or less | 14 (45%) | 18 (50%) | |
No | 35/66 (53%) | 30/66 (45%) | |
Reason | | | | |
Too busy | 12 (34%) | | 15 (50%) | |
Not aware of resource | 9 (26%) | | 11 (37%) | |
Teaching not primary responsibility | 9 (26%) | | | 11 (37%)
Did not know how to access/use the resource | 6 (17%) | 5 (17%) | |
Did not find it useful | 4 (11%) | 4 (13%) | |
Other | 3 (9%) | 1 (3%) | |
POSTERS: Headache/Migraine

HM-1. Chronic daily headache in adolescents: initial evaluation of an interdisciplinary pain rehabilitation program
Rotiner AD, Wojnowicz AA, Banee GA, Buchanan K, McDonald K, Zabukovec M, Henry D (Cleveland, OH)

Objective: The purpose of this research is to describe the effectiveness of interdisciplinary pain rehabilitation for adolescents with chronic daily headache. Chronic daily headache affects 2.4% of adolescent girls and 0.8% of adolescent boys. A subset of these patients experiences a downward spiral of increasing functional disability. For severely affected patients, an interdisciplinary rehabilitation approach provides an understandable and useful model of care.

Methods: Twenty-four adolescents (mean age = 14.87) with chronic daily headache and associated disability were treated in a three-week, combined inpatient and day hospital pain rehabilitation program.

Results: Mixed model regression analyses revealed significant improvements made during and after the program. At admission, surveyed patients rated their pain a '7.29' on a '0'–'10' scale. They averaged 2.14 missed school days, and their parents reported an average of 1.17 missed work days/week. At 2- and 3-year follow-up points, surveyed patients rated their pain a '4.5' and '2.25', respectively. Patients surveyed 2 years following the program averaged 0.71 missed school days/week, and their parents reported an average of 0.14 missed work days/week. Those surveyed 3 years after the program averaged 0.14 missed school days/week, and their parents reported no missed work days/week.

Conclusions: These results suggest that interdisciplinary pain rehabilitation is a promising approach to the management of chronic daily headache and associated disability. Enduring improvements on real-world indices of pain and functioning were found two and three years following program completion. Ongoing research will examine program effectiveness on a broader range of self-report, parent report, and objective measures.

HM-2. Relationship of calcitonin gene related peptide and pediatric headache in obesity
Young IR (Gwangju, South Korea)

Objective: Both of headache and obesity are prevalent and chronic conditions among children. It is one of the well-known pathophysiologies of migraine that calcitonin gene-related peptide (CGRP) is an important postsynaptic mediator of trigemino-vascular inflammation. Plasma CGRP levels increase in obese individuals and during the headache phase of migraine. The purpose of this study was to assess the relationship between headache and plasma CGRP level in obese children.

Methods: We prospectively studied plasma CGRP levels in 35 patients (20 overweight and obese subjects without headache; Group A, 13 overweight and obese subjects with headache; Group B) who visited Chosun University. Blood samples were collected from cubital veins. Plasma levels of CGRP were measured by radioimmunoassay.

Results: Mean age was 12.3±2.3 (range 6–15 years). The mean CGRP level was 19.1±2.5 pg/ml in Group B and 17.4±5.1 pg/ml in Group A. In the group under 19 pg/ml CGRP level, mean headache frequency per month, mean severity and mean disability were 17.0±18.4, 4.0±2.8 and 2.0±0.0, respectively. In the group with CGRP level of 19 and more pg/ml, they were 11.0±9.8, 5.6±1.0, and 23.1±8.2, respectively.

Conclusions: The mean CGRP level in overweight and obese children with headache was not significantly higher than in overweight and obese children without headache (P = 0.202). There was no significant correlation between CGRP level and frequency, severity of headache and disability due to headache (P > 0.05). Further studies are needed to access relationship of CGRP and pediatric headache in obesity.

HM-3. White matter changes and stroke in childhood migraine
Iboll S, Prensky R, Mar S (St Louis, MO)

Migraine is a recognized risk factor for both stroke and subclinical white matter (WM) lesions in adult. The prevalence of these in pediatric migraine is unknown. Up to 19% of ischemic strokes in adults could be due to migraine, but the diagnosis of migrainous stroke is still called into question in children.

Objective: Investigate whether migraine is a risk factor for WM changes or stroke in children.

Method: Clinical data was prospectively collected from 1016 children referred with chief complaint of headache to neurology clinic. MRI data was retrospectively reviewed.

Results: Among 1016 patients presenting with headaches, 899 had migraine of these 322 had migraine with aura (MWA) and 660 had migraine without aura (MWOA). Among MWA, incidental WM lesions were noted in 14 patients, punctuate <1mm-35%, medium 2–5 mm-59%, large >6 mm-6%, periventricular-35%, deep WM-30%, pericallosal-6%, other 29%. Among MWOA, incidental WM lesions were noted in 11 patients, punctuate-40%, medium-57%, large 29%, periventricular 46%, deep WM 23%, pericallosal 8%, other 23%. 44 had WM changes related to underlying diseases. 475 patients had clinical follow-up (mean 3.2yr), 52 had MRI follow-up (mean 3.8yr). None of incidental WM patients developed new lesions nor stroke during the follow-up period.

Conclusion: WM lesions are relatively common in pediatric migraineurs. There is significant difference (p<0.02) between the prevalence of incidental WM lesions in migranours with aura as opposed to no aura. All incidental white matter changes appear benign and non-progressive in children with migraines.

HM-4. The spectrum of diagnosis and management of headaches in a pediatric emergency department: a large retrospective study
Mar S, Iboll S, Prensky A (St Louis, MO)

Objective: To analyze the diagnoses and management of children presenting with headaches as the chief complaint.

Method: A retrospective chart review at the St. Louis Children’s Hospital ER between 2007 and 2010.

Results: We reviewed 1533 charts with the presenting diagnosis of headache according to ICD 9 codes. The mean age was 12.5 years, 918 female and 615 male. We identified 726 (47%) primary headaches, 712 migraine and 14 tension headaches, 550 (35%) secondary headaches, and 271(18%) non-classifiable. Viral illnesses accounted for 70% of secondary headaches. Head imaging was performed in 129 patients of which 26 (20%) were abnormal, but only 3(2%) had diagnostic value for acute secondary headache. Among secondary headaches, 419 patients (51%) were treated with oral minor analgesics, 11 needed IV pain medications. Among the primary headaches, 229 received oral medications (Ibuprofen alone or with Sumatriptan) and 186 received IV medications (Ketorolac, Prochlorperazine, etc.).
Ondansetron or IV fluid). The rest did not require pain medication. The reduction in pain scores was not significant among the different treatment groups.

**Conclusion:** The vast majority of ER visits with the chief complaint of headache were due to migraine headaches and minor illnesses, mostly requiring minor analgesics only. The cost of health care and the use of expensive resources of a hospital ER could be significantly reduced if these patients were treated in non-emergency settings. The brain imaging is low yield and should be used conservatively, particularly in those with primary headaches.

**HM-5. Arachnoid cysts in children and adolescents**

**Indulkar S, Rothner AD (Cleveland, OH)**

**Objective:** To review clinical features, treatment and prognosis of arachnoid cysts.

**Methods:** All patients with an arachnoid cyst between January 2005–2011 were reviewed. IRB approval was obtained. Patients >18 years, no neuroimaging, intracranial tumors, infection were excluded. Demographics, clinical features, neuroimaging, medical and surgical intervention, and outcome were collected.

**Results:** Study population included 200 children, male female ratio 1.8:1, mean age 8 years 7 months. CT (n=16), MRI (n=107) or both (n=77). Symptoms: headache (n=90,45%), seizures (n=35,17.5%), trauma (n=31,15.5%), dizziness (n=21,10.5%), developmental delay (n=18,9%) and macrocephaly (n=17,8.5%).

Headache patients (90): 23 migraine (25.5%), 67 (74.5%) daily headaches, tension type or unclassified, duration prior to presentation 13 months. Neurological abnormalities: papilledema (n=2), abducens nerve palsy (n=1), ataxia (n=1). 14 patients (7%) had increased intracranial pressure (ICP), headache, vomiting, cranial nerve palsy, papilledema; all underwent surgery.

Arachnoid cyst: Temporal fossa (n=90,45%, left/right), posterior fossa (n=77,38.5%), frontal (n=18,9%), other locations (n=26,13%). Bony remodeling seen in 15.5%, hydrocephalus 4.5%, progressive increase in size of cyst 3.5%, rupture 2%.

30 children underwent surgery, 16.7% had post-operative complications. Details will be presented. Preoperative headache was reduced in 23 patients (76%), 5 unchanged headache, 1 worse. Conservative treatment of headache resulted in similar outcome.

**Conclusion:** In children and adolescents presenting with headache and arachnoid cysts in the absence of increased ICP, a trial of conservative headache treatment should be undertaken. In the presence of hydrocephalus, increased ICP or neurological dysfunction, neurosurgical referral should be made. Recommendations regarding periodic follow-up, surgery, and sports activity will be discussed.

**HM-6. Headache 3 and 12 months after pediatric traumatic brain injury: differences related to age and gender**

**Blume HK (Seattle, WA), Vasilada MS (Seattle, WA), Durbin DR (Philadelphia, PA), Wang J, Jaffe KM, Koepsell TD, Temkin NR, Rivara FP (Seattle, WA)**

**Objective:** To determine the prevalence and risk of headache 3 and 12 months after pediatric traumatic brain injury (TBI) compared to orthopedic arm injury (OI).

**Methods:** This study was conducted using data from a prospective study of function following pediatric TBI, the Child Health After Injury Study. We analyzed the prevalence of headaches 3 and 12 months following mild TBI (mTBI) (n=402), moderate/severe TBI (n=60) or OI (n=122) in children ages 5–17 at the time of injury.

**Results:** The risk of any headache 3 months after injury was significantly higher after mTBI than after OI: overall (43% vs. 26%, RR: 1.7 (95%CI: 1.2–2.3)), in adolescents (13–17 years) (46% vs. 25%, RR: 1.8 (95%CI: 1.1–3.1)), and in girls (59% vs. 24%, RR: 2.4 (95%CI: 1.4–4.2)). The risk of any headache at 3 months was also higher after moderate/severe TBI than OI in younger children (5–12 years) (60% vs. 27%, RR: 2.0 (95%CI: 1.2–3.4)). The risk of serious headache (≥5/10 pain) 3 months after injury was significantly elevated after mTBI for girls, and after moderate/severe TBI for younger children compared to those with OI.

Twelve months after injury, TBI was not associated with significantly increased risk of headache compared to OI. However, more girls with mTBI reported serious headache than those with OI (27% vs. 10%, RR: 2.9 (95%CI: 0.9–5.6)).

**Conclusion:** While most children and adolescents recover after TBI, many continue to have chronic headaches. This is particularly striking for girls and adolescents following mTBI and for young children following moderate/severe TBI. The risk of posttraumatic headache is different in children, adolescents and adults and merits further study to improve our understanding and treatment of this common and disabling disorder.

**HM-7. The efficacy and safety of a combination product containing sumatriptan and naproxen sodium for the acute treatment of migraine in adolescents**

**Derosier FJ (RTP, NC), Pearlman E (Savannah, GA), Hershey A (Cincinnati, OH), Winner P (West Palm Beach, FL), Rothner AD (Cleveland, OH), Linder S (Dallas, TX), Goodman DK (RTP, NC), Jimenez TB (RTP, NC), Lewis D (Norfolk, VA)**

**Objective:** To evaluate the efficacy and safety of a range of doses of sumatriptan and naproxen sodium (suma/nap) combination product for the acute treatment of migraine in adolescents.

**Methods:** This study was a randomized, double-blind, placebo-controlled, parallel group study. Adolescent migraineurs (with or without aura; ICHD-II) ages 12–17 years were enrolled into a Run-In Phase to treat one moderate-to-severe attack with single-blind placebo. Subjects who reported pain 2 hours after dosing (placebo non-responders) were eligible to be randomized into the Double-Blind Treatment Phase to treat a migraine with: 1) placebo; 2) suma/nap 10/60 mg (low dose); 3) suma/nap 30/180 mg (middle dose); or 4) suma/nap 85/500 mg (high dose). The primary endpoint was the percentage of subjects who were pain-free at 2 hours after double-blind treatment. Multiplicity adjusted p-values less than 0.05 were considered to be statistically significant.

**Results:** 490 subjects took double-blind treatment. Statistically significantly more subjects were pain-free at 2 hours in the high (24%), middle (27%), and low (29%) dose groups compared to placebo (10%). There was no evidence of a difference between active dose groups. Statistical significance was also observed for the high dose vs. placebo for sustained pain-free 2–24 hours and photophobia- and phonophobia-free at 2 hours.

All doses were well tolerated, with a similar adverse event (AE) incidence (placebo, 8%; low, 13%; middle, 9%; high, 13%) and no unexpected AEs.

**Conclusions:** In adolescent migraineurs, sumatriptan/naproxen sodium was effective across three dose combinations compared with placebo and was well tolerated.

**Study supported by:** GlaxoSmithKline
HM-8. Referral and treatment patterns in chronic daily headache
Sivaswamy L, Patelik K (Detroit, MI)

Objective: Chronic daily headache (CDH) is most commonly encountered and treated by primary care providers. The objective of this study was to evaluate treatment and referral patterns of CDH by primary care physicians in a large metropolitan area.

Methods: Patient records with a final diagnosis of chronic daily headache, who were referred to the Pediatric Headache Clinic at a tertiary care hospital, were retrospectively analyzed (n=56, 40 females, mean age 13.1 yrs). ICHD-II criteria were applied to stratify them into chronic tension type (32%) and chronic migraine subgroups. Use of prophylactic agents, advice regarding over the counter analgesics, time lag prior to referral, work up, counseling regarding lifestyle changes and referral to specialties other than neurology were evaluated.

Results: 8/56 (8.4%) of children were advised prophylaxis, with natural remedies suggested in half the cases. The average time lapse to being seen by a neurologist was 18.3 months (range=4 months -62 months). 16/56 had brain imaging, however none required intervention. 30/56 families recalled being counseled regarding lifestyle issues and weight whereas only 10/56 (17.8%) were cautioned regarding overuse of analgesics. 8.9% were either referred or chose to see other pediatric subspecialists prior to seeing a neurologist.

Conclusions: Preliminary data seems to suggest that children with CDH experience significant delay in seeing a neurologist. There appears to be a low rate of use of prophylactic agents and insufficient information being given to families regarding overuse of analgesics while discussion of lifestyle changes occurs in over half the study population.

HM-9. Intravenous magnesium as abortive treatment for headaches in children
Gertsch EA (Aurora, CO), Loharuka S (Berkley, CA), Wolter-Warnerdam KG, Tong S, Kedia S (Aurora, CO)

Objective: To examine effectiveness and tolerability of intravenous (IV) magnesium for abortive headache treatment in children.

Methods: An IRB approved retrospective chart review at The Children’s Hospital of Aurora, Colorado of individuals age 5-18 years old who received IV magnesium in the emergency room (ER) or hospital for migraine, tension-type headache (TTH), or status migrainosis. Responders were those with moderate to significant improvement in qualitative or numeric pain scores. Patients with complex medical conditions, secondary etiology for headache, or multiple encounters were excluded.

Results: Twenty children with an average age of 15.7 years (SD 1.7), predominately female (80%), received IV magnesium, 13 (65%) receiving magnesium in the ER and seven (35%) as an inpatient. Five (25%) had migraine, four (20%) had TTH, and 11 (55%) had status migrainosis. Responders had an (IPG), which responded to an external programming computer, placed in the gluteal region.

Conclusions: In our pediatric cohort, IV magnesium was tolerated in children but not effective in reducing headache. Magnesium deficiency may have a role in the pathophysiology of both TTH and migraines. However, use of magnesium as abortive therapy remains unclear. Prospective randomized controlled studies will help to further establish the effectiveness, tolerability, and role of magnesium for abortive treatment of pediatric headaches.

POSTERS: Infectious Disease

1.1. Unusual presentation of Rocky Mountain Spotted Fever (RMSF).
Mudigoudar B, Arya K, Jalandoni K, McSwen T (Brooklyn, NY)

Objective: RMSF is a life threatening infection caused by Rickettsia rickettsii. Its early recognition is crucial but difficult. Severe rhabdomyolysis in patients with RMSF is rare and there are no such cases reported in those without rash. We report an unusual case of RMSF without rash causing severe rhabdomyolysis.

Methods: A case report.

Results: A 16 year old boy, native of Brooklyn, NY was hospitalized with 4 days of high fever and 2 days of gastrointestinal symptoms. Later he developed severe pain in both lower extremities and difficulty walking. There was no history of tick bite, recent travel or sick contact. On examination he had severe tenderness in both thighs but no rash. Motor examination in lower extremities was limited due to pain but rest of his neurological examination was normal. Laboratory investigations revealed thrombocytopenia, hyponatremia, elevated liver enzymes and C Reactive Protein. Serum levels of muscle enzymes were extremely elevated (CPK up to 19,195) and urinalysis showed myoglobinuria. Initial work up was negative for several infections (Influenza A & B, RSV, CMV, EBV, Hepatitis Panel, HIV Elisa, Ehrlichiosis, Babesiosis, Comprehensive Viral, Blood, Stool and Urine Cultures). Titers for RMSF were positive (IgG > 1:1024 and IgM 1:1024 and IgM > 1:1024).
I-2. Basal ganglia inflammation in children with post-infectious neuropsychiatric manifestations: a positron emission tomography study using $^{11}$C-PK-11195

Chugani HT, Kumar A, Chakraborty P, Muzik O (Detroit, MI)

Objective: Swedo and colleagues (1998) described 50 children with obsessive-compulsive disorder and motor tics associated with group-A β-hemolytic streptococcal infections and coined the acronym 'PANDAS' (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections). However, this disorder remains controversial. We applied PET scanning with $^{11}$C-PK-11195 (PK) to detect potential neuroinflammation in children with clinically-diagnosed PANDAS-like conditions.

Methods: Twelve children (mean age: 11±2.2 years; 10 males) with PANDAS-like disorders, and 11 normal adults (mean age: 27±7.7 years; 5 males) underwent dynamic PK-PET imaging and binding potential (BP) was calculated in different brain regions. Tourette syndrome patients were excluded.

Results: BP was increased in the caudate nuclei (N=5), lentiform nuclei (N=5) and thalami (N=4) of PANDAS-like subjects, compared to normals (TABLE). Two children underwent repeat PK-PET following IVIG treatment. One showed normalization of PK binding in right caudate and left thalamus, accompanied by clinical improvement; the other showed normalization of PK binding in right lentiform nucleus, but interval increase in right caudate, with some clinical improvement.

**Table:** BP values in children with PANDAS-like conditions and increased PK binding

<table>
<thead>
<tr>
<th>Condition</th>
<th>n</th>
<th>Binding Potential (range)</th>
<th>Normal range (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudate nucleus</td>
<td></td>
<td>Left: 2 0.169–0.178</td>
<td>0.09–0.16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right: 3 0.168–0.228</td>
<td>0.09–0.16</td>
</tr>
<tr>
<td>Lentiform nucleus</td>
<td></td>
<td>Left: 2 0.262–0.291</td>
<td>0.20–0.26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right: 3 0.224–0.228</td>
<td>0.15–0.21</td>
</tr>
<tr>
<td>Thalamus</td>
<td></td>
<td>Left: 2 0.41–0.42</td>
<td>0.33–0.40</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right: 2 0.41–0.42</td>
<td>0.32–0.40</td>
</tr>
</tbody>
</table>

Conclusions: Our findings suggest increased activated microglial cells in basal ganglia and thalamus of some children with PANDAS-like conditions, suggesting underlying neuroinflammation. Further evaluation in a larger drug-naive sample is required to gain more insight into this condition.

I-3. Anti-N-methyl-D-aspartate (NMDA) Receptor Limbic Encephalitis presenting as refractory seizure followed by Hashimoto’s thyroiditis and systemic lupus erythematosus: case report and review

Binalsheikh IM, Wang SG (Boston, MA)

Objective: To report a case of anti-NMDA limbic encephalitis that evolved into Hashimoto’s thyroiditis and systemic lupus erythematosus (SLE) to emphasize the importance of autoimmune mechanism in pediatric limbic encephalitis.

Methods: chart review.

Results: A healthy 14 year old girl was admitted with confusion and seizure. She had a 5 days history of viral prodrome followed by headache and photophobia. On day of admission, she had confusion and developed seizure. Upon arrival to the hospital, she was confused, febrile with nuchal rigidity. Lumbar puncture showed pleocytosis with subsequent negative culture. EEG showed bilateral temporal seizure. MRI brain showed a symmetrical hippocampal T2 hyper intense signal. During her stay, she required both Levetiracetam and Phenytoin to achieve seizure control. Over the following months, she started to complain of weight gain, hair loss, depression, impaired memory and Déjà vu feeling. Serial thyroid function testing eventually revealed hypothyroidism with positive anti-thyroid peroxidase and anti-thyroglobulin antibodies. Repeated MRI showed persistent hippocampal T2 hyper intense signal with volume loss. She had persistent neutropenia and high ESR, with positive ANA and dsANA, along with proteinuria. Anti-NMDA antibody was positive in both serum and CSF. She experienced subjective improvement with thyroxin therapy. Despite fulfilling the criteria for SLE, family declined steroids or other immune modulating therapy.

Conclusions: Limbic encephalitis is a potential treatable condition. Anti-NMDA antibodies most likely contribute to the pathophysiology of SLE psychosis. The identification of anti-NMDA antibodies in cases of pediatric limbic encephalitis may represent autoimmune diseases especially SLE.

I-4. Benign Acute Childhood Myositis: a comparative study between young and old children in Korea

Youngmi K, Hyewon K, Taeyeong K (Busan, Korea), Yoonjin L, Saeun P, Sangook N (Yangsan, Korea)

Objective: The aim of this study was to describe the difference of the clinical and laboratory findings of benign acute childhood myositis (BACM) between young-aged children (group 1; 1≤age<6) and old-aged children (group 2; age≥6).

Methods: We conducted a retrospective review of 57 BACM cases diagnosed in Pusan National University Hospital between July 2009 and June 2010. We compared clinical and diagnostic characteristics between two groups.

Results: 42 (73.7%) were boys with 2.8:1 male predominance. Mean age was 2.6 years in group 1 and 10.1 years in group 2. Preceding symptoms were fever, cough, headache, rhinorrhea, and sore throat. The mean interval between onset of viral illness and onset of BACM was 3.8 days in group 1 and 3.1 in group 2. The mean duration of BACM was 4.1 days in group 1 and 9.0 in group 2. Chief complaints were a refusal to walk in group 1 and myalgia in group 2. The calf muscles were involved in 71.4%. Serum creatine kinase was increased in all cases (219-23012 U/L). Viral studies were positive in 34 patients (60%) with positive for parainfluenza (14.0%), influenza A (H1N1) (12.3%), influenza B (12.3%), rhinovirus (7.0%), metapneumovirus (7.0%), enterovirus (5.3%), adenovirus (3.5%), mumps virus (1.8%) and RSV (1.8%). All the patients had a good outcome and fully recovered.

Conclusions: BACM has excellent prognosis and mainly due to a viral etiology. Pediatric neurologists must be aware the characteristics of BACM to prevent unnecessary investigations and to differentiate BACM from serious neuromuscular conditions.
POSTERS: Neuroimaging

NI-1. Neuromagnetic abnormalities in somatosensory system in children with cerebral palsy: a MEG study

Objective: The objective of this study is to investigate somatosensory dysfunction in children with spastic cerebral palsy (CP) using magnetoencephalography (MEG).

Methods: Six children with CP and six age- and gender-matched healthy children were studied using a 275-channel MEG system while their left and right index fingers were stimulated in a randomized order.

Results: In comparison to the healthy children, the latency of the first response of somatosensory evoked magnetic fields (SEFs) in the children with CP was significantly delayed (left figure stimulation: 34.9±12.1 milliseconds vs 21.3±2.0 milliseconds, p<0.05; right figure stimulation: 26.6±3.4 vs 20.9±1.7, p<0.05, Paired Student’s t-test). The volume of neuromagnetic activation elicited by left finger stimulation of the patients with cerebral palsy was significantly smaller than that of the controls (232.8±130 vs 1068.7±768.4, p<0.05, Paired Student’s t-test). Children with CP had significantly higher odds of having ipsilateral activation in the somatosensory cortex following right (100%, 6/6) and left finger stimulation (67%, 4/6), compared to healthy children following right (17%, 1/6) and left (33%, 2/6) stimulation ($X^2 = 3.769$, p=0.05, Chi-Square test).

Conclusion: The results suggest that children with CP have a measurable delay of SEFs and high odds of ipsilateral cortical activation, which implies impairment of white matter pathways and functional lateralization of the developing brain. This is the first MEG study to demonstrate abnormal activation of somatosensory cortices representing the finger in children with CP.

NI-2. Detection of microstructural abnormalities using comparative diffusion tensor imaging techniques in children with Neurofibromatosis Type 1
Roser T, Tabar E, Tavare J (Los Angeles, CA), Panigrahy A (Pittsburgh, PA)

Histopathologic studies and neuroimaging modalities have demonstrated increased water content in the myelin of children with neurofibromatosis type 1 (NF1).

Objective: To evaluate brain microstructural properties by measuring the apparent diffusion coefficient (ADC) and fractional anisotropy (FA) with region of interest (ROI) manual placement and tract-based spatial statistics (TBSS) DTI techniques in children with and without NF1.

Methods: Retrospective analysis of conventional T2/FLAIR and DTI brain MRIs in 10 children with NF1 ages 22 months to 15 years was performed. ADC and FA were measured in 11 standardized ROI. TBSS was performed on the same population. Comparison was then made to age-matched controls using both techniques.

Results: No significant differences were found in FA between the NF1 and control populations using either technique. ROI measurements showed a predominance of statistically significant changes in the axial diffusivity of children with NF1 involving the putamen (p=0.0052), internal capsule posterior limb (p=0.0007), parietal white matter (p=0.0024), parietal-occipital gray matter (p=0.0001) and anterior white matter (p=0.0011). Radial diffusivity was also affected but less so. TBSS measurements showed statistically significant changes (p<0.01) in axial diffusivity involving the internal capsule, centrum semiovale as well as subcortical and frontal white matter.

Conclusion: ROI and TBSS DTI techniques yielded similar results. Axial diffusivity was more affected than radial diffusivity involving white and gray matter. These findings suggest that in NF1 microstructural brain changes may be due more to an axonal than a demyelinating process which may have important implications for understanding the intracranial abnormalities seen in NF1.

NI-3. Comparison of language lateralization patterns between healthy and left hemisphere stroke children: A functional MRI study

Objective: Language functions lateralization in the left hemisphere begins on the 3rd month. Pediatric stroke is a devastating cerebrovascular event and may cause reorganization of the developmental language network.

The aim of the study is to identify lateralization patterns of language function in children with stroke and healthy controls.

Methods: 12 children with left hemisphere stroke: 7 perinatal and 5 childhood onset (mean age 11.4) and 12 healthy voluntary controls (mean age 10.7) were investigated using functional MRI and neurocognitive assessments by NEPSY. Two tasks (verb generation and sentence comprehension) were employed to activate expressive and receptive language areas. Image analysis was performed using SPM8. The resulting t-maps for each subject were analyzed within Brodmann areas 44+45 and 22, defined by MIRico templates. The weighted laterality indices (wLI) were calculated by combined bootstrap/histogram analysis.

Results: By the age of 10 years the language functions in healthy children in most cases: 10/12 were lateralized into the left hemisphere (wLI>0.2). Children with stroke showed left side activation in 7 right and right side or bilateral activation (wLI ≤0.2, 0.2) in 5 cases. The significantly (p<0.05) lower scores in receptive (mean 6.1) and expressive language (7.0) were revealed in left -hemisphere language areas activation compared to right hemisphere or bilateral activation (9.0 and 9.5 respectively). Correlation was found between the higher score for expressive language and wLI within BA 44+45 ($r = 0.607$, p= 0.046) in right hemisphere.

Conclusion: (Re)organized lateralization in stroke children correlates with higher scores in language tests due to brain plasticity.

NI-4. Postsurgical white matter changes in the contralateral hemisphere in children following occipital lobe resections
Munian GR, Shandal V, Sood S, Chugani HT (Detroit, MI)

Objective: Following unilateral cortical injury, the contralateral hemisphere undergoes compensatory adaptive changes. However, functional recovery of contralateral hemifield visual loss following unilateral occipital resections is modest. We studied contralateral white matter (WM) changes using diffusion MRI and Tract-Based Spatial Statistics (TBSS) in order to better understand visual plasticity in children undergoing occipital lobectomy.

Methods: We analyzed postsurgical diffusion MRIs in 26 children (age: 7.9±4.5 years) who underwent epilepsy surgery including the occipital lobe (13 left-sided; hemispherectomy: 7, subtotal hemispherectomy: 7, temporo-parieto-occipital: 8, parieto-occipital: 4) and compared them to those of 17 healthy controls (age: 8.3±2.5 years). TBSS analysis was used to identify regions with significant differences in
mean fractional anisotropy (FA), age-related FA changes between groups, and regions showing significant correlation with duration between surgery and postsurgical MRI.

**Results:** We found many WM regions showing decreased FA in the post-surgical group. In structures relevant to the visual system, regions containing superior thalamic radiation in the intact hemisphere of patients showed significantly higher rate of age-related FA increase compared to controls. In addition, FA values in the intact parieto-occipital WM showed a significant negative correlation with postsurgical duration.

**Conclusions:** Higher-than-normal rate of FA increase in the superior thalamic radiation and a strong correlation with postsurgical duration of FA values in the intact parieto-occipital WM suggest complex postsurgical WM changes in the contralateral hemisphere. These changes may be related to the greater reliance of the intact hemisphere in visual function of these individuals and to the modest hemifield recovery.

**NI-5. Cerebrovascular reactivity investigation during MRI of children at risk for stroke**

*Logan WF (Toronto, ON)*

**Objective:** To determine the yield of cerebrovascular reactivity (CVR) imaging studies during the MRI investigation of children at risk for stroke.

**Methods:** Since 2000, 88 CVR examinations were performed in 59 patients with cerebral vasculopathy during MRI investigation of their cerebrovascular disease. These were obtained as part of their MRI evaluation. The CVR were obtained using BOLD MRI techniques combined with altered respiration by breath holding in awake and cooperative patients or by altering the ventilation rate in anesthetized patients in order to alter the PCO2. The conditions studied included Neurofibromatosis type I, Down syndrome, hemoglobinopathies, PHACE syndrome, Turner syndrome, vasculitis and moyamoya disease. Several patients had previous revascularization procedures.

**Results:** Most patients had had a previous stroke. Eight had a normal CVR study including all of the PHACE patients. The study was unsuccessful in seven patients due to excessive movement, poor compliance or technical factors. 73 had an abnormal CVR with poor reactivity in at least one brain region with or without evidence of vascular steal. Most of these patients had moyamoya syndrome or disease. The findings were often informative for subsequent revascularization treatment.

**Conclusions:** CVR evaluation of patients with cerebrovasculopathy reveals a high yield of abnormality, particularly in moyamoya syndrome and disease. CVR can be incorporated into the standard MRI evaluation of these patients and can provide more detailed information about regions at risk for stroke.

**NI-6. Cortical striatal functional connectivity in children with histories of early social deprivation**

*Veenstra AL, Behen ME, Wilson BJ, Kuman A, Jeong JW, Chugani HT (Detroit, MI)*

**Objective:** This study investigated cortical-striatal connectivity in children with histories of early social deprivation (ED).

**Methods:** Twelve internationally adopted children, orphaned at birth, (mean age=123±22months; 5 males) and 9 typically developing non-adopted children (mean age=110±16months; 7 males) participated. Exclusion criteria included FSIQ<70, pre/perinatal difficulties, alcohol exposure, and medical problems. Probabilistic tractography was performed to investigate the connectivity pattern from the caudate nuclei to ipsilateral cortex and frontal-pole target regions. We also investigated the ratio of striatal connectivity to frontal-pole to ipsilateral cortex.

**Results:** Fiber connectivity patterns between caudate and cortex regions revealed two orphan subgroups: a diffuse connectivity group (N=7) and a severely decreased left-hemispheric connectivity group (N=5). Separate 3x2 mixed-design ANOVAs for connectivity and cortical/frontal-pole ratio revealed significant interactions. Post-hoc analyses revealed connectivity differences for the Diffuse (Higher: p=0.04) and Low-Connectivity (Lower: p=0.07) groups for the right, but not left hemisphere, compared to controls. Additionally, the probability score ratio in the left hemisphere was lower in both orphan groups compared to controls (Diffuse:p=0.04; Low-connectivity:p=0.02) in both the cortex and frontal-pole. In the right hemisphere, the probability score ratio was only significantly lower for the Diffuse group (p=0.01).

**Conclusions:** Results indicate an anomalous pattern of functional connectivity in cortical-striatal projections in children with ED. These findings suggest that ED can have different impacts on the cortical-striatal structural connectivity. The results support previous findings indicating that early deprivation leads to incomplete pruning, which impacts the connectivity between the head of caudate and the cortex.

**NI-7. Neurometabolic abnormalities and epileptogenesis in Sturge-Weber syndrome**

*Juhász C, Alkonyi B, Hu J, Xuan Y, Chugani HT (Detroit, MI)*

**Objective:** Abnormal brain energy metabolism and related decrease of glutamate-glutamine cycling (resulting in increased extracellular glutamate levels) contribute to epileptogenesis. We used proton magnetic resonance spectroscopy ($^1$H-MRS) combined with glucose metabolism PET to test the hypothesis that cortical glucose metabolic abnormalities are associated with abnormal levels of glutamate/glutamine (Glx) in children with Sturge-Weber syndrome (SWS)-associated seizures.

**Methods:** Three children (7-months, 10-months, 2.5-years old) with unilateral SWS underwent glucose metabolism and CVR evaluation of patients with cerebrovasculopathy. These patients underwent glucose metabolism PET followed by 3T MRI scanning including $^1$H-MRS, with voxels placed over cortex showing abnormal glucose metabolism. Glx/Cre ratios (Glx/Cr) were calculated and their ipsilateral/contralateral (I/C) asymmetries were used to quantify Glx abnormalities.

**Results:** Two infants showed increased (interictal) cortical glucose metabolism: a 7-month-old infant with frequent seizures showed markedly elevated Glx/Cr in parietal cortex (I/C ratio: 2.1), and a 10-month-old infant prior to seizure onset showed a mildly elevated Glx/Cr (I/C ratio: 1.14) in the hypermetabolic frontal cortex. In this latter patient, I/C Glx/Cr ratios increased dramatically (to 4.5) after onset of her first seizure (at age 2.4 years), while the frontal cortex became hypometabolic. The third child, a 2.5-year-old girl with occasional seizures, showed moderately elevated Glx/Cr (1.2) in the severely hypometabolic occipital cortex.

**Conclusions:** Increased Glx, measured by $^1$H-MRS, in metabolically abnormal cortex, may indicate excessive glutamate release contributing to seizures, and could be an early biomarker of epileptogenesis and subsequent excitotoxic cortical damage in children with SWS. These data may be useful for strategies aimed at targeting brain regions at risk for damage from SWS.

**NI-8. Perivascular enhancement on brain MRI in children.**

*Mineyko A, Kirton A, Ng D, Wei X-C (Calgary, AB)*

**Background:** Large vessel vasculitis is an important etiology of childhood stroke. While early research suggests wall enhancement may be a marker of CNS vasculitis, normal perivascular...
enhancement has not been systematically described. We aimed to establish perivascular enhancement norms in children.

Methods: Patients were identified through our institutional neuroimaging database (2007–2010). Inclusion criteria were: (1) age <18 years; (2) thin-section (<3 mm) axial and coronal post-contrast T1-weighted images with fat saturation; (3) normal parenchymal imaging; and (4) absence of vascular disease, intracranial infection, head/neck radiation, or malignancy. Perivascular enhancement at 11 predefined locations was scored by two blinded experts as 0 (none), 1 (mild), or 2 (marked). Mean enhancement scores (range 0–2) were compared across factors including age, sex, and region.

Results: Forty-four children (50% male; mean age 7 (range 0.3–16) years) were included. Enhancement scores were highest in cavernous (2.00) and petrous (1.08) internal carotid artery (ICA), and proximal middle cerebral artery (M1, 1.13). Scores were lowest in supraclinoid ICA (0.03), vertebral artery (0.19), and proximal posterior cerebral artery (P1, 0.27). Arteries surrounded by CSF consistently showed none or minimal enhancement while the remainder had highly symmetrical, thin-linear enhancement. Enhancement was more common in the anterior circulation than the posterior (mean difference 0.56; 95% CI 0.47–0.65; p < 0.0001). There was no correlation with age or sex. Inter-rater agreement was excellent.

Conclusion: Perivascular enhancement of intracranial arteries in children is common with specific patterns. Our findings will hopefully facilitate the diagnosis of pediatric cerebral arteriopathy.

POSTERS: Neuromuscular Disease

NM-1. Spectrum and utility of nerve biopsy in 239 children: study from a tertiary care university hospital in south India

Bindu PS, Pratap K, Mahadevan A, Yasha TC, Taly AB (Bangalore, India)

Objectives: To ascertain the profile and role of sural nerve biopsy in children.

Methods: This retrospective study, spanned over 10 years (1999–2008) included nerve biopsies from 239 children (M: F- 1.5:1, Age range- 9mo– 18 yrs). The clinical and electrophysiological data from these patients were correlated with neuropathologic observations.

Results: Pediatric nerve biopsies comprised 18% of all nerve biopsies during the study period. The common indications for biopsy were; hereditary neuropathies (37.65%), other genetically determined disorders (43.09%), and inflammatory neuropathies (10.87%). Findings on nerve biopsies were “diagnostic” in 40.58%, “non-diagnostic” in 42.67%, and “normal” in 16.73%. Among the 199 biopsy proven neuropathies, the various diagnostic categories were as follows: Hereditary neuropathies-134, metachromatic leukodystrophy- 39, giant axonal neuropathy-9, CIDP-8, vasculitis-6, Hansen’s disease-4 and angiomaticosis of the nerve-1. Predominant pathology was axonal in 43.21% and demyelination in 41.20%. Clinico-pathological concordance was noted in 144 (60.25%) & Electrophysiologically-pathological concordance in 81.49% (185/ 227). Nerve biopsy was essential for diagnosis in 97 (40.58%), helpful in 109 (46.02%) but was of no value in 33 (13.80%). While the largest category of patients included hereditary neuropathies in all age groups, highest prevalence of acquired disorders, especially inflammation (29.41%) was seen in the adolescence (n= 68).

Conclusion: This study on a large cohort of children is a critical appraisal of the value and limitations of nerve biopsy in resource poor setting, where biochemical and genetic studies are not freely available.

NM-2. A Phase-3 multicenter, open-label study assessing the safety of glycopyrrolate oral solution for the management of pathologic drooling in pediatric patients with cerebral palsy or other neurologic conditions

Davidson J, Wang C, Neiman R, Cavanaugh P (Florham Park, NJ)

Objective: To assess the safety of glycopyrrolate oral solution (1 mg/5 mL) in pediatric patients with chronic, moderate-to-severe drooling associated with cerebral palsy or other neurologic conditions.

Methods: In this multicenter, open-label, 24-week study, males and females aged 3–18 years and weighing at least 27 lb received glycopyrrolate oral solution, at starting doses of 0.02 mg/kg TID and titrated in increments of 0.02 mg/kg every 5–7 days for an optimal maintenance dose or a maximum dose of 0.1 mg/kg, but not exceeding 3 mg TID. Safety was assessed by description and tabulation of all adverse events (AEs).

Results: Of the 137 intent-to-treat participants, 10 (7.3%) received a maximum dose of 0.1 mg/kg TID; 122 (89%) had at least one treatment-emergent AE (TEAE), with 47% deemed related to glycopyrrolate oral solution. The most commonly reported TEAEs were constipation (20.4%), vomiting (17.5%), diarrhea (17.5%), pyrexia (14.6%), dry mouth (10.9%), flushing (10.9%), and nasal congestion (10.9%). Nineteen patients discontinued due to an AE, but no type of event was associated with discontinuation. Two patients had clinically significant toxicity grade shifts, one each in platelet count and calcium concentration. No deaths were reported while patients were on study drug; the deaths of 3 patients, considered treatment-related by the investigators.

Conclusions: Glycopyrrolate oral solution was well tolerated by pediatric patients aged 3–18 years for the management of chronic, moderate-to-severe drooling associated with neurological conditions.

NM-3. Kinematics of essential tremor and enhanced physiologic tremor in children

Pandika V (Rochester, NY), Srivivasan J (Melbourne, Australia), Mink JW (Rochester, NY)

Objective: The kinematics of childhood onset tremor has not been well studied. Previous studies in adults have shown that Enhanced Physiologic Tremor (EPT) demonstrates a decrease in frequency with load, due to its inertial and elastic property dependent mechanical-reflex component, but Essential Tremor (ET) does not. We investigated the kinematics of tremor in children to determine whether similar finding hold in children.

Methods: We recruited 12 children with tremor: 9 with the clinical diagnosis of ET and 3 with the clinical diagnosis of EPT (mean current age-13.8 years; male; female ratio 1:1). Recordings were made with a triaxial accelerometer taped to the index finger of the most affected upper extremity. Subjects were seated with arms maintained in one of four conditions: 1) at rest on the lap, 2) outstretched posture at shoulder height with elbows extended and forearms pronated, 3) outstretched posture while holding a 135-gram

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weight load in the palm of the tested hand, and 4) near posture with elbows flexed, forearms pronated, and fingers at the level of the nose.

Results: In all children, the mean frequency difference (frequency without load - frequency with load) was <1 Hz, which is more consistent with ET than EPT. Additionally, all our subjects in the outstretched position demonstrated a narrow frequency range of 4–8 Hz, which is characteristic of ET. Among all our cases, there was a significant correlation between condition and amplitude, with increased amplitude in the outstretched position versus rest.

Conclusions: The clinical diagnoses of EPT and ET in children may be challenging and kinematics studies may provide diagnostic utility.

NM-4. Improvements in muscle function and accidental falling in Ataluren-treated patients with nonsense mutation dystrophinopathy (Duchenne/Becker Muscular Dystrophy - nmDBMD)

Rusman BS (Portland, OR), Mathews KD (Iowa City, IA), Sampson JB (Salt Lake City, UT), Renfroe JB (Gulf Breeze, FL), Morry MA, Elffing GL, Barth JA, Pelz SW (South Plainfield, NJ)

Objective: Dystrophinopathy patients progressively lose muscle function and become susceptible to accidental falling, the most common cause of limb fractures in this population. Ataluren is an investigational drug designed to overcome the effects of nonsense mutations, which are responsible for ~13% of dystrophinopathy cases. In a pivotal trial in nmDBMD, low-dose ataluren demonstrated a clinically meaningful difference (29.7 m) in change in 6-minute walk distance (6MWD) versus placebo (p = 0.0584; post-hoc analysis). Secondary endpoints included timed function tests and patient/parent-reported accidental falling.

Methods: Males ≥5 yr of age with nmDBMD were stratified by age, corticosteroid use, and baseline 6MWD; randomized 1:1:1 to placebo; low-dose ataluren (10,10,20 mg/kg); or high-dose ataluren (20,20,40 mg/kg) orally TID; and evaluated every 6 wks for 48 wks.

Results: The study enrolled 174 subjects (median [range] age = 8 [5–20] yr, corticosteroid use = 123/174 [71%], median [range] baseline 6MWD = 360 [75–554] m). Differences in mean changes from baseline to Week 48 for low dose versus placebo were -2.40s stair ascend, -1.62s stair descend, -1.35s 10-m walk/run, and -0.01s stand from supine. Over 48 weeks, accidental falling declined in the low-dose arm versus placebo (relative ratio = 0.37; post-hoc analysis). High-dose-treated subjects with approximate peak plasma concentrations similar to low-dose-treated subjects generally had outcomes similar to low-dose-treated subjects.

Conclusions: Subjects treated with ataluren 10,10,20 mg/kg experienced trends toward improvements in timed function tests and had fewer accidental falls versus placebo. These findings support the primary endpoint (6MWD) results showing a positive treatment effect for low-dose ataluren in this population.

NM-5. Congenital Muscular Dystrophy (CMD) frequencies in the US: an overview

Eskuri JM (Iowa City, IA), Stephan CM (Iowa City, IA), Iannaccone ST (Dallas, TX), Andersen M (Dallas, TX), Greene M (Dallas, TX), Darras BT (Boston, MA), Connolly AM (St Louis, MO), Anand P (St Louis, MO), Acsadi G (Hartford, CT), Bennett L (Detroit, MI), Burnette WB (Nashville TN), Mathews KD (Iowa City, IA)

Objective: Little is known about the frequencies of CMD subtypes. We describe the frequencies of CMDs in a subset of child neurology clinics in the US.

Methods: Child neurologists with expertise in neuromuscular disease were invited to participate. Patients included are actively followed and have a clinical diagnosis of CMD. Key clinical data including diagnosis, diagnostic testing, functional ability, and phenotype were abstracted from the medical record, de-identified, and collated centrally. Data collection was approved by each institution’s human subjects review board.

Results: Six institutions participated. Ninety-three abstracts were reviewed; four were eliminated for failure to meet inclusion requirements. The distribution of the remaining 89 cases: Collagen VI-deficient CMD—28 (31%); MDC1A (merosin-deficient)—27 (30%); unknown—21 (24%); dystroglycanopathies—11 (12%); LMNA—2 (2%). In the total study population, diagnosis was genetically confirmed in 50 (56%). Of those assigned to a subtype, 73% were genetically confirmed (79% of Collagen VI-deficient CMD, 59% of MDC1A, 91% of dystroglycanopathy, and 100% of LMNA subjects).

Conclusions: In this series, Collagen VI-deficient CMDs and MDC1A are the most prevalent CMD subtypes. The next largest group of CMDs in this series had no specific diagnosis. Financial constraints and/or personal preferences may limit the diagnostic testing. In other cases, testing has not identified a diagnosis, consistent with previous indications that additional causes of CMD will be found (Rocha and Hofman, 2010). The CMD frequencies will provide a basis for planning future clinical studies, including clinical trials.

NM-6. Glucocorticoids may act through natural killer cells in Mdx Mice

Goldwasser P (St. Louis, MO), Gutting K (St. Louis, MO), Maglia LJ (Nashville, TN), Unanue ER (St Louis, MO), Calderon B (St Louis, MO), Connolly AM (St Louis, MO)

Objective: To determine whether Natural Killer (NK) cells play a role in the therapeutic effect of prednisolone on mdx mice. Twice weekly oral prednisolone improves muscle strength, running speed, and lifespan in mdx mice, through an unknown mechanism of action. Given its anti-inflammatory effects, and the abundance of inflammatory cells in dystrophic muscle, we previously showed prednisolone’s positive effect is independent of T-cells, B-cells (Ig) and the complement cascade (C3−/−). These previous studies could not eliminate the possibility that the beneficial effect of prednisolone may be through the remaining innate immune components or a direct effect on muscle itself.

Methods: Male mdx mice where depleted of NK cells with biweekly IP injection of PK136 antibody starting at 3 weeks of age. Mice were given oral prednisolone (at 5 mg/kg, 2x/week) starting at 4 weeks of age. Forelimb grip strength (FGS), hanging wire time and voluntary wheel running speed were used as physiologic outcome measures. Muscle histology and serum CK are supportive outcome measures. We assessed prednisolone’s therapeutic effect on strength in the presence and absence of NK cells.

Results: Oral prednisolone increases strength in mdx mice. Removal of NK cells produces an identical effect on FGS (in magnitude and time course) as prednisolone treatment alone. After NK cell removal there is no additional effect of strength from prednisolone.
Conclusions: NK cells have a deleterious effect on mdx mouse strength. Prednisolone may be therapeutic due to inhibition of NK cell activity. Prednisolone could act on NK cells or the muscle target.

NM-7. Robotic assisted therapy in pediatrics - active vs. passive participation
Mast J, Ladenheim B (Valhalla, NY), Krebs HI (Cambridge, MA)

Objective: Robot-assisted therapy can increase mobility and functional outcome in adults following stroke. Here we report the outcomes of robot-aided therapy in children with spastic hemiparesis from brain injury after therapy and six months later.

Methods: 22 patients, age 5 to 18, with upper extremity mobility impairment due to brain injury, whose injury occurred at least 6 months prior were randomly assigned to active (ActiveP) or passive (PassiveP) participation groups. Each had sixteen 45 minute sessions. ActivePs played a simple video game, using a handle to move the cursor on the screen, with robot assistance as needed. PassivePs watched an unrelated video, while the robot always moved the handle. Motor function was evaluated before, after, and 6 months after therapy. Portions of the Pediatric Evaluation of Disability Inventory (PEDI), Fugl-Meyer Motor Assessment Scale (F-M), Modified Ashworth Spasticity Scale (MA) and Shriners Hospital for Children Upper Extremity Evaluation (SHUEE) were primary measures.

Results: Increased motor function was seen after treatment for both ActivePs and PassivePs for most measures; ActivePs showed greater improvement. Shoulder/Elbow F-M scale and dynamic positional analysis SHUEE measure scores improved for ActivePs. PEDI and SHUEE immediate post-therapy gains were not significant; however, additional gains made during the 6-month post-therapy period resulted in a significant improvement for both groups.

Conclusions: Robot-assisted therapy is effective for children. Active participation is an important factor. Gains were not only preserved but some increased months after therapy ended. Therapies that produce sustained improvement can influence development and decrease lifetime morbidities associated with spasticity.
POSTERS: Neonatal Neurology

NN-1. Thrombin and plasmin generation in children following perinatal arterial ischemic stroke
Armstrong-Wells JL (Aurora, CO), Simpson ML (Chicago, IL), Villalobos-Menuey L, Bernard TJ, Goldenberg NA, Manco-Johnson M (Aurora, CO)

Objective: Perinatal arterial ischemic stroke (PAS) is a leading cause of disability. Although the mechanism(s) remains unclear, presumably disruptions of coagulation inherent to the perinatal period exist. Given the low rate of recurrence in PAS, we sought to determine if clotting profiles by thrombin and plasmin generation were normal beyond the newborn period in those children with prior PAS.

Methods: We studied all children in our prospective cohort presenting with PAS between 08/01/2000 and 11/31/2009 at The Children’s Hospital, Colorado. Twenty-seven cases of PAS were identified and confirmed by imaging and chart review. Of the 27 cases, 18 (67%) had blood samples available for thrombin and plasmin generation in comparison to 91 pediatric normals (1–18 years old). Thrombin and plasmin were assayed by continuous fluorometric detection following activation by calcium, 5 pM tissue factor and 450 ng/mL tissue plasminogen activator and reported by enzyme kinetics: lag time to initial generation (lag), maximal velocity (Vmax) and maximal amplitude (MA).

Results: Of these 18 patients, 15 had blood samples beyond 1 year old. The majority (n=13/15; 87%) of our cases had normal enzyme kinetics compared to our healthy reference population. Two children had low plasmin Vmax but otherwise normal lag and MA.

Conclusions: In our small cohort of newborns with PAS, most children had normal thrombin and plasmin generation beyond the newborn period, suggesting that disorders of coagulation contributing to PAS do not persist. This supports the low recurrence rate of PAS. Ongoing studies will compare neonatal with follow-up coagulation enzyme kinetics.

NN-2. Follow-up neuroimaging in perinatal arterial ischemic stroke
Hoover W, Bernard TJ, Goldenberg NA, Manco-Johnson M, Armstrong-Wells JL (Aurora, CO)

Objective: Perinatal arterial ischemic stroke (PAS) is a leading cause of disability. We sought to determine if there is indication for follow-up neuroimaging (MRI) in PAS given the low rate of progression or recurrence in this population.

Methods: We studied all newborns within our prospective cohort study (Colorado Pediatric Stroke Program) with PAS from 08/01/2000 - 04/30/2009. Radiologically confirmed PAS cases were identified in our cohort database and confirmed with chart review by a pediatric stroke neurologist.

Results: Of the 27 cases of PAS in our cohort, 63% were male. Stroke was identified within 72 hours of birth in 59% (n=16). Most cases presented with seizure (23; 85%). Over one-half of newborns had initial CT imaging (n=15; 56%); MRI was obtained within 72 hours of presentation for most (n=16; 59%). Strokes were commonly left-sided (n=16; 59%). Two cases had bilateral involvement. All 27 cases involved the anterior circulation. The majority involved the MCA distribution (n=23; 85%). Imaging follow-up ranged from 5.69 months - 15.78 years (median 11.64 months). One-third of newborns (n=9) received follow-up MRI at 1 year; only one was for clinical indication (infantile spasms). There were no new MRI findings among those cases receiving follow-up neuroimaging. There was no stroke symptom progression or recurrence in our cohort.

Conclusions: In our cohort, there was neither radiological or clinical progression—nor stroke recurrence—in newborns who received routine follow-up MRI. Our findings suggest that there is no indication for subsequent MRI in asymptomatic children with prior perinatal arterial ischemic stroke.

NN-3. Multimodality neuromonitoring during hypothermia and rewarming for neonatal hypoxic ischemic encephalopathy
Shellhaas RA, Swenson AW, Barks JDE (Ann Arbor, MI)

Objective: Neonatal hypoxic ischemic encephalopathy (HIE) is commonly treated with therapeutic hypothermia. Multimodality neuromonitoring, with amplitude-integrated EEG (aEEG) and rSO2 measured by near infrared spectroscopy (NIRS) could help identify infants at highest risk for unfavorable outcomes. We aimed to determine which parameters are the most instructive for neonates with HIE.

Methods: Between 1/2009 and 2/2011, infants with HIE were monitored with bilateral cerebral and unilateral somatosensory-evoked EEG (aEEG) and rSO2 measured by near infrared spectroscopy (NIRS). Ongoing studies will identify infants at highest risk for unfavorable outcomes. We aimed to determine which parameters are the most instructive for neonates with HIE.

Results: 21 infants, mean gestational age 38.8±SD 1.6 weeks, median 10-minute Apgar score 4 (range 0–8), and mean initial pH 6.9±SD 0.19, were enrolled. High (abnormal) Thompson score immediately after rewarming correlated with a narrow aEEG band (Pearson correlation, r=-0.55, p=0.027), decreased aEEG variability (r=-0.44, p=0.09), and increased cerebral rSO2 variability (r=0.48, p=0.028) during the 6-hour rewarming period. The absolute rSO2 value was not correlated to Thompson score (r=-0.014, p=NS).

Conclusions: This is the first study to combine aEEG and NIRS monitoring during hypothermia and rewarming for neonatal HIE. aEEG patterns, as expected, correlated with Thompson scores after rewarming. Absolute cerebral rSO2 value may be less relevant than its variability during rewarming. Long-term follow-up will allow further identification of the most informative aEEG and NIRS parameters, or combinations thereof, for these vulnerable patients.

NN-4. Intraventricular hemorrhage (IVH) in the term infant is rare compared with preterm infants, and associated risk factors have not been studied extensively
Hayes B, Soul J (Boston, MA)

Objective: To identify the perinatal/neonatal risk factors associated with the development of IVH in term/near term infants.

Methods: The databases of a large children's hospital were used to identify infants with a diagnosis of grade 2–4 IVH, born at greater than 34 weeks gestation for the period 1995–2010.

Results: Of 123 infants identified, pregnancy complications were found in 31 (25.2%) and one or more associated co-morbidities were found in 79 (64.2%). Only 10 (8.2%) had an associated risk factor. Neonatal co-morbidities included congenital heart defect (26); ECMO therapy (20); pulmonary hypertension (18); cerebral sinus venous thrombosis (6); diaphragmatic hernia (7); sepsis (4). Consequences
of IVH included progressive ventricular dilation in 75 (61%), and neonatal seizures in 52 (42.3%). Evidence of brain injury other than IVH/hydrocephalus by neuroimaging was present in 82 (66.6%). Treatment for progressive ventricular dilation with serial lumbar punctures and/or surgical drainage procedures was administered in 5/64 (7.8%) infants with grade 2 IVH, 15/47 (31.9%) with grade 3 and surgical drainage procedures was administered in 5/64 (7.8%) infants with grade 2 IVH, 15/47 (31.9%) with grade 3 and 5/12 (41.7%) with grade 4 IVH.

Conclusions: Similar to the preterm infant, IVH in the term/near term infant is commonly multifactorial. Although the associated congenital or neonatally acquired co-morbidities are different from those in preterm infants, the mechanism of altered cerebral hemodynamics is similar. Rates of brain injury and posthemorrhagic ventricular dilation are high and thus warrant careful neonatal monitoring and neurologic follow-up.

NN-5. Predominant hippocampal injury (HI) identified on magnetic resonance imaging (MRI) in term infants (TI) with hypoxic-ischemic encephalopathy (HIE) treated with selective head cooling (SHC): a novel observation

Kasdorf E, Rainaldi M, Engel M, Perlman JM (New York, NY)

Objective: HI is invariably identified in conjunction with basal ganglia (BG) necrosis upon autopsy in TI with moderate/severe HIE and has also been observed at follow-up MRI in infants with severe BG injury. We have treated TI at risk for evolving HIE with SHC and have identified predominant hippocampal without BG changes on diffusion weighted MRI in a subset of infants. Objective is to determine perinatal characteristics leading to hippocampal versus BG injury.

Methods: Retrospective chart review of obstetric/perinatal risk factors, patient characteristics, MRI findings in TI undergoing SHC.

Results: 69 infants have been treated with SHC. MRI abnormalities included BG (n=20, 29%) (Group 1) and hippocampus (n=6, 8.6%) (Group 2). No differences between groups 1 vs 2 with regard to GA, BW, sex, cord pH (6.84 vs 6.77) or base deficit (BD). Pertinent characteristics are listed below.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPR</td>
<td>12/20</td>
<td>1/6</td>
<td>0.06</td>
</tr>
<tr>
<td>10 minute</td>
<td>12/19</td>
<td>1/6</td>
<td>0.07</td>
</tr>
<tr>
<td>Apgar ≤ 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial Postnatal pH</td>
<td>6.86 ± 0.19</td>
<td>7.15 ± 0.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Initial Postnatal BD</td>
<td>−21 ± 6</td>
<td>−13.2 ± 3.4</td>
<td>0.005</td>
</tr>
<tr>
<td>Sarnat Stage 3 at enrollment</td>
<td>16/20</td>
<td>1/6</td>
<td>0.009</td>
</tr>
<tr>
<td>Clinical seizures at enrollment</td>
<td>13/20</td>
<td>5/6</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusions: Infants with hippocampal or BG injury both exhibited fetal acidemia (cord pH < 7.00). The subsequent pathways leading to injury may in part be related to predominantly hypoxia with HI or prolonged cerebral hypoperfusion (CPR, persistent postnatal acidosis) with BG injury. Alternatively these findings may indicate neuroprotection of BG with SHC in those infants with HI.

NN-6. Risk factors and outcomes of fetal intracranial hemorrhage

Taru T, Candie L, Barnes K, Barnewolt C, Estroff J, Soul J, Grant E, Khwaja O (Boston, MA)

Objective: Fetal brain injury is increasingly recognized as a major etiology of childhood neurodevelopmental disabilities including cerebral palsy (CP) and non-CP neurodevelopmental impairment. We aim to describe the etiology, imaging characteristics and immediate and long term neurodevelopmental outcomes of fetal intracranial hemorrhage.

Methods: We examined all cases of radiologically-confirmed fetal intracranial hemorrhage seen at our fetal center in the time period 2005–2010. We collected pregnancy and obstetric history as well as outcome data. We assessed the longitudinal neurological and developmental outcomes of live births using the Bayley Scales of Infant Development, the Receptive and Expressive Language Scales 3 and Vineyard Adaptive Behavior Scores.

Results: We identified 38 cases of intracranial hemorrhage of which 21 were primary intraventricular hemorrhage. Associated factors were fetal cardiac disease, fetal-maternal alloimmune thrombocytopenia, maternal physical trauma and uteroplacental dysfunction. Risk factors for poor outcome were large parenchymal hemorrhage, posterior fossa hemorrhage and progressive ventricular dilatation. Fetuses with germinal matrix hemorrhage and/or small parenchymal hemorrhages had universally normal cognitive and motor outcomes as assessed between 18–36 months.

Conclusions: Fetal intracranial hemorrhage is a lesion associated with a range of neurodevelopmental outcomes. The most common form is intraventricular hemorrhage. It is a risk factor for fetal demise and poor neurological outcomes and is associated with specific maternal and fetoplacental factors. Trauma is a common association. Small hemorrhages are not associated with poor early neurodevelopmental outcome.

NN-7. Ipsilesional cortical volumes are diminished in fetal periventricular venous infarction

Li DD, Hodge J, Wei XC, Kirton A (Calgary, AB)

Objective: Perinatal stroke causes most term-born hemispheric cerebral palsy and many suffer additional sequelae. Periventricular venous infarction (PVI) is a common fetal stroke where isolated subcortical white matter injury has been suggested to cause only motor deficits. However, cognitive, language, and behavioural deficits do occur. We hypothesized that ipsilesional cortical gray matter volumes are reduced in PVI.

Methods: Children (12 mos–18 years) with MRI-confirmed PVI were identified through the Alberta Perinatal Stroke Project. Employing anatomical MRI, we developed a method to quantify grey (GM) and white matter (WM) volumes from lesioned and unlesioned (control) hemispheres (Osirix software). Three validation steps were performed. Differences in cortical GM and WM volumes were compared between hemispheres and pre-selected regions: "above" the lesion (middle), and anterior and posterior to this (paired t-test). Outcomes were dichotomized for "higher deficits" (cognitive, behavioural, language) according to the Pediatric Stroke Outcome Measure (PSOM) and compared to GM volumes (t-test).

Results: Twenty-two children (81% male, median 7.5 (range 1–18) years) were included. Methods demonstrated high intra- and inter-rater reliabilities (0.988, 0.943) and minimal observer bias. Ipsilesional GM volume was
significantly reduced ($p=0.003$), specifically in the middle ($p=0.004$) and posterior ($p=0.02$) regions. Middle ipsilateral WM volumes were reduced ($p<0.001$). For 19 subjects with PSOM, four had higher deficits but no difference in GM volumes could be appreciated.

**Conclusions:** Ipsilateral GM volume is diminished in PVI. Speculative mechanisms include retrograde neuronal degeneration and disrupted neuronal migration. Neuro-psychological testing of larger samples is required. Understanding PVI pathophysiology will advance treatment strategies.

**NN-8. Outcome of hypoglycemia in neonatal encephalopathy**

Haeuslein EA, Tam EWY, Bonifacio SL, Barkovich AJ, Ferriero DM (San Francisco, CA)

**Objective:** To examine the relationship between early neonatal hypoglycemia, MRI, and neurodevelopmental outcome in term infants at risk for neonatal brain injury.

**Methods:** Term infants born at our institution between 1994 and 2007 with glucose measures within 24 hours of life were analyzed in a prospective cohort study of early MRI in newborns at risk for neonatal brain injury from hypoxia-ischemia. Hypoglycemia ($<40.0$ mg/dL) was correlated with neurologic examination using the validated neuromotor score and cognitive outcome using the Bayley Scales of Infant Development (BSID-II) at 12 months of age. To account for the degree of hypoxia-ischemia, linear and logistic regression analyses were performed adjusting for uterine artery pH at birth.

**Results:** Out of a cohort of 70 infants, 12 (17%) had hypoglycemia within the first 24 hours. 17 (29%) without and 6 (50%) with hypoglycemia had basal ganglia injury on MRI. 27 (42%) without and 8 (67%) with hypoglycemia had watershed injury. Outcome at one year was available in 55 (79%) infants. Hypoglycemia is associated with a 2.6 fold increased odds of a 1 point worsening in neuromotor score at one year ($p=0.007$). Hypoglycemia is associated with 15 point decrease in the mental developmental index of the BSID-II at one year ($p=0.01$).

**Conclusion:** Adjusting for the degree of hypoxia-ischemia at birth, the occurrence of hypoglycemia within 24 hours of birth in term infants is associated with an additional risk of abnormal motor and cognitive outcomes at 12 months.

**NN-9. Alterations in GABA-mediated connectivity in prematurely-born young adults**

Benjamin JR, Lacadie C, Qu M, Myers EH (New Haven, CT), Vohr BR (Providence, RI), Schneider KC, Katz KH, Constable RT, Ment LR (New Haven, CT)

**Objective:** Gamma aminobutyric acid (GABA) interneurons initiate connectivity in the developing brain. Pterm (PT) infants are at risk for developmental disorders, and emerging data suggest that PT birth may decrease GABA interneurons. We hypothesized that PT subjects have decreased regional GABA concentrations compared with term controls at young adulthood, and that these differences are associated with alterations in resting state functional connectivity (fcMRI).

**Methods:** 13 PT subjects (600–1250g) and 13 term controls underwent GABA-edited magnetic resonance spectroscopy and fcMRI at 20 years using a 3T Siemens Trio. Right frontal Brodmann’s area 10 (BA10) and left temporal (BA22) GABA concentrations (corrected for H2O, “GABA/H2O” = 0.83) were calculated. Connectivity changes identified (11 PT, 13 term) and correlated with cognitive outcomes. Nonparametric Wilcoxon rank sum tests, Student’s t test and GLM analyses were performed.

**Results:** There were no significant differences in gender, hand preference, maternal education or age at study. PT subjects had lower R BA10 GABA/H2O compared to term controls ($p = 0.014$) but no significant difference in L BA22 GABA/H2O ($p = 0.83$). fcMRI demonstrated increased connectivity from R BA10 to R BA39 in PT compared to terms ($p = 0.04$). Preterms demonstrated connectivity correlations with the Delis Kaplan Executive Function total achievement score ($r = 0.47$).

**Conclusions:** Prematurely-born subjects showed decreased GABA concentrations in the right frontal region compared to term controls at young adulthood, and lower GABA concentrations correlated with alterations in connectivity and cognitive outcomes. Regional variations in GABA may impact neural connectivity and neurodevelopmental outcome in preterm infants.

**NN-10. Toll-like receptors expression is determined by stages of brain development**

Shi H, Hickey E, Van Arsdell G, Arkalan R (Toronto, ON)

**Introduction:** We have shown that giving a low dose of lipopolysaccharide (LPS) to P7 rat pups will result in 90% reduction in ischemia-induced brain damage. This dramatic LPS neuroprotection was observed in P7 rat pups which correspond in terms of brain development to human term newborns. Preterms demonstrated preconditioning against cerebral ischemia as early as 50% in P3 and P5 pups which correspond to human premature infant. LPS is a known Toll-like receptor 4 (TLR-4) ligand. We investigated whether lack of LPS-mediated preconditioning in very young rats could be explained by different pattern of TLRs expression in the maturing rat brain.

**Methods:** Brains from P3, P5 and P7 rats were removed, fixed in 10% formalin, embedded in paraffin and cut in 5μm coronal sections. TLR-2, TLR-3, TLR-4 and TLR-9 expression was assessed by immunohistochemistry.

**Results:** TLR-4 was highly expressed in brains of P7 rat pups but not in P3 or P5 rat pups. The number of TLR-4 positive cells was significantly lower in P3 and P5 rat brains compared to P7 pups ($p < 0.05$). TLR-2 was significantly more expressed in P3 and P5 compared to P7 ($p < 0.05$). TLR-3 was predominately expressed in P5 ($p < 0.05$). There was no significant difference in TLR-9 expression among the three age groups.

**Conclusion:** Lack of TLR-4 in the younger rats may explain why LPS was not protective in this age group. The expression of other TLRs family members was developmentally determined. We hypothesize that TLRs other than TLR-4 may mediate preconditioning against cerebral ischemic injury in the developing brain.

**NN-11. Epilepsy is associated with adverse outcome in children at risk for perinatal hypoxic ischemic injury**

Glass HC, Rogers EE, Bonifacio SL (San Francisco, CA), Hong KJ (Seattle, WA), Tam EW, Jeremy RJ, Barkovich AJ (San Francisco, CA), Miller SP (Vancouver, BC), Sullivan JE, Ferriero DM (San Francisco, CA)

**Objective:** To determine whether epilepsy is associated with adverse neurodevelopmental outcome, independent of the severity of brain injury on MRI.

**Methods:** Newborns at risk for hypoxic-ischemic brain injury were enrolled, imaged, and followed long-term using
standardized evaluations by a trained psychologist. Parents were administered a telephonic seizure questionnaire. Cognitive disability was defined as <70 on a cognitive subscale; motor disability as <70 on a motor subscale or ≥3 on the neuromotor score (NMS). Borderline disability was considered for scores 70–84 or a 2 on the NMS.

**Results:** Of 113 children evaluated at a median of 33 months (range 1–14 years), 12 were diagnosed with epilepsy (all prior to latest evaluation). All children with epilepsy had neonatal seizures and MRI injury as neonates. Ten were taking anti-epileptic medication; two had daily seizures. Epilepsy was associated with adverse outcome (Table). In a logistic regression model accounting for encephalopathy, neonatal seizures, and degree of injury as assessed by watershed and basal ganglia/thalamic scores, epilepsy was associated with abnormal cognitive outcome (OR 23.0, P=0.02).

**Conclusions:** Epilepsy is a risk factor for adverse outcome in children at risk for hypoxic-ischemic brain injury. This is consistent with similar results among children with perinatal stroke (Ballantyne, 2008), and may be related to impaired plasticity by seizures, medication side effect, or differences in care.

<table>
<thead>
<tr>
<th>Motor</th>
<th>Epilepsy</th>
<th>No Epilepsy</th>
<th>P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1(8%)</td>
<td>85(87%)</td>
<td>&lt;0.0005</td>
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<tr>
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<td>9(9%)</td>
<td></td>
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<tr>
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<td>10(83%)</td>
<td>4(4%)</td>
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<th>P-Value*</th>
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<td>6(6%)</td>
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**Fisher’s exact test**

**Data missing for one subject.**

**NN-12. Early neonatal MRI is associated with neurodevelopment at 12 months in children treated with therapeutic hypothermia**

Glass HC, Bonifacio SL, Rogers EE, Wickremasinghe AC, Tam EW, Jeremy RJ, Rowitch D, Ferriero DM, Barkovich AJ (San Francisco, CA)

**Objective:** To determine the relationship between neonatal MRI and developmental outcome at 12 months in newborns treated with therapeutic hypothermia.

**Methods:** 43 newborns cooled for neonatal encephalopathy, imaged at median 5 days of life (range 2–11), and followed to death or evaluation at 12 months were included. A trained psychologist administered Bayley Scales of Infant Development III (BSID). Disability was defined as <70 on any BSID subscale.

**Results:** Death (8) or disability (1) was present in 21% (Table). Degree of illness at the time of birth was not associated with outcome. However, all deceased/disabled children had severe brain injury, except one who died of multi-organ failure. Among the survivors, severe MR injury was associated with lower scores in all three BSID subscales (p<0.001, Figure 1). Children with mild/moderate injury had lower scores than those with normal MRI, though the difference was not significant.

**Conclusions:** Severe MR injury remains predictive of 12-month outcome in the setting of hypothermia, whereas features of the resuscitation are not. Longer follow up will be necessary to investigate associations between milder injuries and neurodevelopmental impairment.

**NN-13. Combined hyperthermia and hyperoxia following hypoxia-ischemia (HI) increases brain injury (BI) in the term neonatal rat: preliminary findings**

Rainaldi MA, Vannucci SJ, Perlman JM (New York, NY)

**Objective:** Hypoxic-ischemic BI has been shown experimentally to be minimized by hypothermia or exacerbated by hyperoxia during the reperfusion period. The impact of concurrent hyperthermia and hyperoxia on the extent of BI is unclear. The study objective was to determine the effect of combined hyperthermia and hyperoxia on BI immediately following HI in the term-equivalent rat pup.

**Methods:** Postnatal day (P) 10–11 Wistar rat pups underwent unilateral common carotid artery ligation plus hypoxia (8% O2 / balance N2) for 60 minutes. Following HI, rat pups were exposed to normoxic normothermia (21% O2/36.5°C, n = 13) or hyperoxic hyperthermia (95% O2/38.5°C, n = 14) for 2 hrs. After 72 hrs, animals were sacrificed, brains removed and frozen in isopentane (−30°C). 18 μm coronal cryosections were stained with H&E. Infarct area (%) of the ipsilateral hemisphere was calculated using ImageJ, NIH software. Data were analyzed using Student’s t-tests and Fisher’s exact test.

**Results:** Mean infarct area of the ipsilateral hemisphere of hyperoxic hyperthermic recovered rats was significantly greater compared to normoxic normothermic recovered rats; 68.6 ± 9.6% vs 49.5 ± 21.2% (p = 0.009). Additionally, 2/14 hyperoxic hyperthermic vs 0/13 normoxic normothermic rats died during the recovery period (p = 0.26).
Conclusions: Exposure to combined hyperthermia and hypoxia immediately following HI in the neonatal rat significantly increases infarct size compared to recovery in a normoxic normothermic environment. The mechanisms contributing to increased injury are unclear but important to delineate. Inadvertent hyperthermia and hypoxia following hypoxia-ischemia may aggravate BI in term newborns.

NN-14. Hypothermia therapy results in improved microstructure and metabolism in the deep gray nuclei

Objective: To evaluate the effect of hypothermia on brain microstructure and metabolism using Diffusion Tensor-MRI (DT-MRI) and Proton MR Spectroscopy (MRS) in term neonates at risk for brain injury.

Methods: 41 neonates with moderate-severe encephalopathy (29 hypothermia treated, 12 non-treated) and 12 healthy neonates (Control) underwent DT-MRI/MRS at < 2 weeks. Conventional images were assigned a predominant pattern of injury: Normal, Watershed (WS), Basal ganglia/Thalamus (BG/T). ADC and Lactate:N-Acetylaspartate (NAA) of basal ganglia(BG) and thalami were calculated. Left and right values were averaged. Mann-Whitney U-test was used for comparison between groups.

Results: ADC and Lactate:NAA differed in treated vs non-treated neonates in all regions (data not shown). In those with BG/T pattern, differences were seen in Lactate:NAA, and not in ADC. In those with WS pattern, differences were seen in ADC and not in Lactate:NAA. Treated neonates with normal imaging had higher ADC than controls. Outcome was assessed by Gross Motor Function Classification System (GMFCS). Poor outcome was when GMFCS = 4 or 5 or death. Diffusion Toolkit was used for tract reconstruction with 35 threshold. We selected entire cortical, subcortical, and thalamic areas.

Conclusions: Hypothermia is associated with decreased lactate and higher ADC suggesting improved metabolism and potential microstructure alterations with treatment. When there is no visible injury, treated neonates have lactate levels similar to control. DT-MRI and MRS may be useful biomarkers of treatment response. Association with long-term follow-up will confirm this.

NN-15. Emergence and evolution of neurological deficits over time following acute neonatal arterial ischemic stroke
Aziz AS, deVeber G, MacGregor D, Askalan R, Yau I, Moharir M (Toronto, ON)

Objectives: Neonatal Arterial Ischemic Stroke (NAIS) causes significant long-term morbidity. Information on evolution of neurological deficits after acute NAIS is lacking. We aimed to study the emergence and evolution of deficits over time following acute NAIS.

Methods: Retrospective analysis of neonates with acute AIS from 1999–2009 was conducted. Outcome was assessed by the validated Pediatric Stroke Outcome Measure (PSOM), administered prospectively during follow-up. PSOM scores between 3–6months, 6–12months, 1–3years, 3–5years and after 5 years were analyzed. Neonates with minimum 3 assessments, each during different time-interval, were included. Within individual PSOM sphere, any neurodeficit was considered abnormal.

Results: Fifty-two (27 males) of 87 neonates were selected. The table depicts our salient findings on interim analysis.

Sensorimotor and language deficits emerge in early infancy and between 1–3years respectively; these remain persistent in many thereafter. Cognitive/behavior problems surface in pre-schoolers and worsen during school age.

Conclusions: A distinctive pattern of emergence and evolution of neurological deficits following NAIS is evident. This information can be helpful for timely initiation and maintenance of rehabilitative measures. Further studies on neurobiological basis and predictors of recovery patterns from NAIS are warranted.

NN-16. Diffusion tractography in term neonates with hypoxic-ischemic encephalopathy: Projection fiber system and corpus callosum involvement as predictors of neurodevelopmental outcome
Fons C, MacLean A, Ginsburg D, Soul J, Pienaar R, Khwaja OS, Grant PE (Boston, MA)

Objective: To determine if projection fiber system (PFS) and corpus callosum (CC) are injured in term neonates with hypoxic-ischemic encephalopathy (HIE), and if their involvement predicts motor outcome.

Methods: Term newborns with clinical diagnosis of HIE and 3T MRI including DTI performed < 1 week of life, between 2008–2010, were selected. Newborns without clinical diagnosis of HIE and normal MRI’s served as normative controls. Outcome was assessed by Gross Motor Function Classification System (GMFCS). Poor outcome was when GMFCS = 4 or 5 or death. Diffusion Toolkit was used for tract reconstruction with 35 threshold. We selected entire CC, genu (GCC), splenium (SCC) and PFS passing through the posterior limb of internal capsule (PLIC) with a ROI approach using TrackVis. Tractography metrics and neuromotor outcome were compared. Statistical analysis was performed using unpaired T-test.

Results: 29 newborns with HIE and 8 controls were studied. Mean gestational age was 38.86 and 38.13 weeks and mean age at MRI was 3 and 5 days. Outcome in HIE patients was good (17) and poor (12). Mean age at last follow-up was 12.48 months. Only mean ADC in PFS-PLIC was lower in HIE compared to controls (Left: p = 0.009; Right: p = 0.022). Compared to HIE with good outcome, those with poor outcome had lower ADC in PFS-PLIC (Left: p = 0.01; Right: p = 0.002), CC (p = 0.013) and SCC (p = 0.016) but not in GCC.

Conclusions: Tract based ADC measures in newborns with HIE showed selective involvement of PFS-PLIC.
Additional involvement of CC and SCC was associated with poorer neuromotor outcome.

NN-17. Systemic injection of human CD34+ enriched cord blood cells modulates post-stroke neural and glial response in a sex-dependent manner in CD1 mice
Kadam SD (Baltimore, MD), Chen H (Baltimore, MD), Markowitz GJ (Durham, NC), Loechel B (Washington, DC), Johnston MV (Baltimore, MD), Kanani N (Washington, DC), Comi AM (Baltimore, MD)

Objective: To determine the impact of CD34+ enriched human cord blood cells (HCBC) on post-stroke sub-acute recovery, neurogenesis, microglial and astroglial response after ischemic injury in an immature mouse model of stroke.

Methods: P12 CD1 mice received right common carotid ligation and acute seizures were scored. 48 hours after ligation mice were injected i.p. with $1 \times 10^7$ freshly isolated CD34+ enriched HCBC. Developmental behavioral milestones were evaluated pre-and post-treatment from age P9 to P21. 5-bromo-2′-deoxyuridine (50mg/kg, IP) was injected 2h prior to sacrifice on P21. Percent of brain atrophy was quantified and immunohistochemistry was performed for analyses of neural and glial markers.

Results: Microglial density was increased in the hilus of injured animals and correlated with severity of hippocampal injury irrespective of treatment. Severity of injury and performance on developmental behavioral milestones were not impacted by treatment. HCBC treatment showed a sex-dependent increase in subgranular zone (SGZ) proliferation in injured males (significant ipsilaterally; $p=0.041$; a trend contralaterally, $p=0.09$). Furthermore, the injury resulted in increased ipsilateral SVZ GFAP expression which was significantly suppressed in the treated males ($p=0.013$) while significantly increased contralaterally in females treated with HCBC ($p<0.003$).

Conclusion: Injection of CD34+ enriched HCBC after neonatal stroke increased proliferation of cells in the SGZ and decreased GFAP in the SVZ, and the response appears to be gender dependent. Future studies are needed to delineate mechanisms underlying this sex-dependent response to HCBC.

NN-18. Impaired brain structure and function in newborns with complex congenital heart disease prior to open heart surgery
Owen M, du Plessis A, Bouyssi-Kobar M, Clouchoux C, Limperopoulos C (Washington, DC)

Objective: To examine the relationship between abnormal neurological examinations and total and regional brain volumes in newborns with complex congenital heart disease (CHD) prior to open heart surgery (OHS).

Methods: 41 term newborns (38 ± 2.1 weeks; birth weight 3124 ± 505.23 grams) with CHD were prospectively studied using MRI and clinical neurological examinations preoperatively. Total brain and cerebellar volume, as well as white matter (p = 0.024) and subcortical gray matter (p = 0.020). Absent primitive reflexes were associated with decreased cerebellar volume (p = 0.035), as well as cortical (p = 0.027), and subcortical gray matter (p = 0.006). Microcephaly was associated with reductions in total brain volume (p < 0.001). All analyses controlled for age at MRI. Illness severity and CHD lesion type did not mediate outcome.

Conclusions: In newborns with CHD, abnormal preoperative neurological examinations are strongly associated with impaired global and regional brain volumes. These data suggest that the clinical neurological examination is a reliable marker of brain growth prior to OHS.

POSTERS: Stroke

S-1. The Quick Measure of Cognitive Status: A tool to monitor pediatric neurocognitive recovery
Ladenheim B (Valhalla, NY), Zenon V (Bronx, NY), Sinclair C (Bronx, NY), Matt J (Valhalla, NY)

Objective: Traumatic brain injury (TBI) can have devastating impact on neurodevelopment, particularly in young children. Measures currently used to assess cognitive function are either not validated for children, become invalid when administered too frequently, or are too cumbersome to administer to children. In addition, recovery often follows different timelines for different cognitive domains. The Quick Measure of Cognitive Status (QMOCS) was developed to address these issues.

The Rancho Level of Cognitive Functioning Scale (LCFS) monitors recovery by observation of behaviors. However, it does not give information about specific cognitive domains; information is collapsed to generate the score. QMOCS also generates a profile of the patient, but categorizes behaviors into specific domains and tracks each domain independently.

Methods: The QMOCS was administered at least once to 63 TBI patients between 3 months and 19 years. Results were compared to the cognitive portion of the WeeFIM (a reliable instrument widely used to measure outcomes) when available.

Results: Principal component analysis identified a cognitive subscale with four stable component loadings ranging from .77-.91. Significant cognitive improvement was shown (p < .0005) with test-retest correlation = .543 (p < .004) (N=26). Analyses showed good internal consistency (Cronbach alpha: test=.91, retest=.85) and test-retest reliability (intraclass correlation coefficient=.41, p=.002). Significant positive correlations to the WeeFIM were also found.

Conclusions: The findings support further testing with larger samples, multiple administrations, and comparisons to other, standardized, measures of cognitive function. This might lead to the refinement of a tool that will serve as a valuable measure in monitoring recovery in pediatric TBI patients.

S-2. Obstructive sleep apnea associated with sickle cell-related cerebral vasculopathy: a retrospective analysis
Nasif LM, Glaze DG, Ramocki MB, Airewele G, Suzrez JI, Mueller BU (Houston, TX)

Objective: To study the association of cerebral vasculopathy (OSA), a stroke risk factor in adults, in children with sickle cell disease (SCD).

Results: Principal component analysis identified a cognitive subscale with four stable component loadings ranging from .77-.91. Significant cognitive improvement was shown (p < .0005) with test-retest correlation = .543 (p < .004) (N=26). Analyses showed good internal consistency (Cronbach alpha: test=.91, retest=.85) and test-retest reliability (intraclass correlation coefficient=.41, p=.002). Significant positive correlations to the WeeFIM were also found.

Conclusions: The findings support further testing with larger samples, multiple administrations, and comparisons to other, standardized, measures of cognitive function. This might lead to the refinement of a tool that will serve as a valuable measure in monitoring recovery in pediatric TBI patients.

S-2. Obstructive sleep apnea associated with sickle cell-related cerebral vasculopathy: a retrospective analysis
Nasif LM, Glaze DG, Ramocki MB, Airewele G, Suzrez JI, Mueller BU (Houston, TX)

Objective: To study the association of cerebral vasculopathy with obstructive sleep apnea (OSA), a stroke risk factor in adults, in children with sickle cell disease (SCD).
Method: We retrospectively studied children with SCD (ages 2–16 years) using the EMR and sleep center database (1999–2010). Children in the OSA group (SCD and apnea-hypopnea index ≥1 on polysomnography) were compared to control children (SCD and no chronic pulmonary disease, sleep-related breathing disorders, prior clinical stroke, chronic transfusions, or hydroxyurea therapy). OSA subjects were excluded if they had prior clinical stroke, chronic transfusions, or hydroxyurea therapy at the time of polysomnography. Findings on transcranial Doppler imaging (TCDi) and brain MRI were compared using SPSS v18.0, assessing mean, standard deviation, and significance.

Results: OSA subjects (n = 22) had higher TCDi velocities (MCA 146.6 vs. 112.6 cm/sec, p < 0.002; ICA 102.9 vs. 82.1 cm/sec, p < 0.026) compared with controls. While 36% (8/22) of OSA subjects had no MRI performed, silent strokes were identified in 41% (9/22) of the OSA group (compared with an expected 22–35% from historical literature). Daytime oxygen saturation (SaO2) for the OSA and control groups were statistically different [97% (95–99%) vs. 99% (98–100%); p = 0.014 but were within normal values. The OSA group had a mean nocturnal SaO2 of 95% (range 88–98%); SD = 3.1).

Conclusion: These data suggest that OSA may contribute to cerebrovascular disease in children with SCD, shown by elevated TCDi velocities and increased incidence of silent strokes. Prospective studies are necessary to determine if OSA is an independent risk factor for sickle cell-related stroke.

**POSTERS: Translational Research**

**T-1. Safety and tolerability of intermittent theta burst transcranial magnetic stimulation in children**

**Wu SW, Huddleton D, Lewis A, O’Malley J, Gilbert DL**

(Cincinnati, OH)

Objective: Intermittent Theta Burst Stimulation (iTBS) is a low intensity, high frequency repetitive Transcranial Magnetic Stimulation (TMS) technique that has been used for examining cortical function. This technique was first developed and has been used mostly on adult subjects. Here, we report the safety and tolerability of iTBS in school age children.

Methods: Healthy and Tourette Syndrome children ages 8–17 years were recruited after parental consent. Open questions and a structured sixteen-question review of systems were performed before and after iTBS. Single-pulse TMS was administered using a Magstim BiStim™ (Wales, UK) figure-8 coil to measure Resting and Active Motor Thresholds (RMT, AMT), and to assess cortical excitability before and after iTBS. A Magstim Rapid2™ (Wales, UK) figure-8 coil was placed over the left primary motor cortex to deliver iTBS, consisting of three 50 Hz magnetic pulses repeating every 200 milliseconds for 2 seconds (one cycle) and each cycle repeating every 10 seconds for 20 times, using a stimulation intensity of 80% AMT.

Results: Thirty-nine children completed the study (mean age = 12.1 years, SD = 2.7 years, 26 boys, 13 girls). Only one child complained of a subjective sensation of finger twitching. However, neither the investigator nor the parent observed any actual twitching or seizure in this child. This complaint resolved later in the same day. No other adverse events were reported.

Conclusion: iTBS is a repetitive TMS protocol that can be used to study cortical function. A single session of iTBS in children appears to be safe and well tolerated.

**T-2. Role of gestational inflammation induced by group B streptococcus in perinatal brain lesions and subsequent cerebral palsy**

**Bergeron J, Girard S, Brochu M-E, Fortier L-C, Sebire G**

(Sherbrooke, QC)

Objective: Bacterial infections during pregnancy, including those induced by group B streptococcus (GBS), are associated with development of cerebral lesions of human newborns. Even though GBS infection is one of the most frequently encountered pathogen exposures during pregnancy, the role of the inflammatory process triggered by this infection/inflammation on the fetal brain remain unknown. According to our hypothesis, GBS-induced inflammation plays a noxious role in the occurrence of perinatal brain damage.

Methods: Pregnant rats were injected every 12 hours with inactivated GBS (10⁹ CFU) or with saline from gestational day 19 until the end of gestation. Forebrains were removed at post-natal day 9 to perform immunohistological studies. Behavioral tests assessing spontaneous (Open field) and forced motricity (Rotarod) were used to detect and measure motor deficiencies.
**Results:** Pregnant rats exposed to inactivated GBS had significant weight loss compared to controls. The number of pups per litter from GBS exposed dams was reduced, and the surviving pups showed an intrauterine growth retardation. Histological studies disclosed a loss of astrocytes and microglial cells within the periventricular white matter of GBS exposed pups. Preliminary results of spontaneous motor behavior showed a decreased motor activity in pups exposed to GBS as compared to control animals.

**Conclusion:** We showed for the first time that the inflammatory response triggered in pregnant rat by exposure to inactivated GBS – without any infection - affects brain's development and induces motor disabilities. This animal model will be used to uncover the mechanistic processes linking gestational inflammation to perinatal brain damage.
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