Division Photo

First Row: Shannon Standridge, Jing, Xiang, Michael Miles, Ton deGrauw, Cindy Molloy, Jennifer Vannest, Anna Byars; Second Row Diego Morita, Donald Gilbert, Charles Vorhees, Barbara Hallinan, Tracy Glauser, Ki Lee, Mark Schapiro, Paul Horn

Division Data Summary

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<th>Research and Training Details</th>
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Significant Publications


We found a high risk of seizure recurrence (66%) in this group of 150 children. Abnormal EEG and abnormal MRI did not predict seizure recurrence.

Hershey AD, Burdine D, Liu C, Nick TG, Gilbert DL, Glauser TA, Assessing quality and normalization of
This is part of our effort to use blood genomics for the study of neurological disorders. This paper addresses sensitivity and specificity issues in patients with migraine and new onset epilepsy.

Miles MV, Miles L, Tang PH, Horn PS, Steele PE, DeGrauw TJ, Wong BL, Bove KE, systematic evaluation of muscle coenzyme Q10 content in children with mitochondrial respiratory chain enzyme deficiencies, Mitochondrion, 2008, 8:170-180

A study of CoQ10 content in muscle of children with clinical and biochemical evidence of mitochondrial disease. Low total CoQ10 was associated with Electron Transport Chain deficiencies.


Our first paper on high frequency brain oscillations in children: developmental patterns. This is the basis for our current studies of high frequency brain oscillations in children with epilepsy.


Evaluation of a practice guideline to obtain sleep deprived EEG's in new onset epilepsy. We found that sleep deprivation increases the yield of abnormalities on the EEG from 32% to 44% compared to routine EEG's.

Division Highlights

Vorhees CV, PhD and Williams MT, PhD

Ongoing studies of the effects of neonatal +methamphetamine exposure on learning and behavior in rats. Our studies address the critical period and dose of drug exposure on learning/behavior. A number of papers was published on this throughout the year.

Division Collaboration

Collaboration with cardiology; pulmonary medicine; rehabilitation; orthopedics; endocrinology

Collaborating Faculty: R. Spicer, MD, L. Cripe, MD; R. Amin, MD; M. McMahon, MD; T. Do, MD; M. Rutter, MD

Multispecialty clinic in neuromuscular disorders, B. Wong, MD, clinical trials, clinical research

Collaboration with nephrology; cardiology; psychiatry

Collaborating Faculty: J. Bissler, MD; T. Knilans, MD; D. Nelson, MD

Tuberous Sclerosis program (D. Franz, MD and D. Krueger, MD). Multispecialty clinic, translational and clinical research studies.

Collaboration with psychology

Collaborating Faculty: S. Powers, PhD and others

Headache Center (A. Hershey, MD, M. Kabbouche, MD). Multispecialty clinic, clinical trials, translational and clinical research, improvement science

Collaboration with radiology; nuclear medicine; neurosurgery

Collaborating Faculty: J. Leach, MD; M. Gelfand, MD; F. Mangano, MD

Epilepsy Surgery Program (K. Lee, MD, K. Holland, MD, PhD). Multispecialty clinical service, outcome studies, integration of imaging and neurophysiology techniques to improve localization of seizure focus, mapping of cognitive function

Collaboration with psychology; genetics; clinical pharmacology

Collaborating Faculty: A. Modi, PhD; G. Grabowski, MD; A. Vinks, PhD

Epilepsy pharmacology (T. Glauser, MD, D. Morita, MD). clinical pharmacology, pharmacogenetics, pharmacodynamics, pharmacogenomics, adherence to Anti-Epileptic Drugs.

Faculty Members

Antonius DeGrauw, MD, PhD, Professor; Director Neurology Division

Research Interests: Neurodevelopment, mitochondrial disorders
Todd Arthur, MD, Assistant Professor Clinical
Research Interests: Brain concussion

Anna W Byars, PhD, Associate Professor Clinical
Research Interests: Cognitive effects of epilepsy

David Franz, MD, Professor Clinical; Director Tuberous Sclerosis program
Research Interests: Tuberous sclerosis

Donald Gilbert, MD, Associate Professor Clinical; Director Movement Disorders program
Research Interests: Tourette syndrome, Transcranial Magnetic Stimulation (TMS)

Tracy A Glauser, MD, Professor Clinical; Director Comprehensive Epilepsy program
Research Interests: Epilepsy, pharmacology

Barbara Hallinan, MD, Assistant Professor Clinical
Research Interests: CSF steroid profiles

Andrew Hershey, MD, Professor Clinical; Director Headache Center
Research Interests: Migraine, blood genomics

Katherine Holland-Bouley, MD, PhD, Assistant Professor Clinical
Research Interests: Ion channels and epilepsy

Sejal Jain, MD, Assistant Professor Clinical
Research Interests: Epilepsy, sleep

Marielle A Kabbouche, MD, Assistant Professor Clinical
Research Interests: Migraine

Darcy Krueger, MD, Assistant Professor Clinical
Research Interests: Tuberous Sclerosis

Ki Lee, MD, Associate Professor Clinical; Director EEG lab, EMU
Research Interests: Epilepsy surgery

Cindy Molloy, MD, Assistant Professor Clinical
Research Interests: Autism

Diego Morita, MD, Assistant Professor Clinical
Research Interests: Epilepsy, pharmacology

Douglas Rose, MD, Professor Clinical; Director MEG lab
Research Interests: Magneto-EncephaloGraphy (MEG)

Mark Schapiro, MD, Professor Clinical; Director Neurology Residency program
Research Interests: Neurodevelopmental disorders

Mary Sutton, MD, Assistant Professor Clinical
Research Interests: Neuro-oncology

Shannon Standridge, DO, Assistant Professor Clinical
Research Interests: Outcomes study, epilepsy

Jennifer Vannest, PhD, Research Assistant Professor
Research Interests: Speech and language development

Charles Vorhees, PhD, Professor; Director Animal Neurobehavior Core
Research Interests: Drugs/toxicants and brain development

Kristen Wesselkamper, MD, Assistant Professor Clinical
Research Interests: Improvement science

Michael Williams, PhD, Research Associate Professor
Research Interests: Drugs/toxicants and brain development

Brenda Wong, MD, Associate Professor Clinical; Director Neuromuscular program
Research Interests: Duchenne's Muscular Dystrophy, Spinal Muscular Atrophy

Jing Xiang, MD, PhD, Research Associate Professor; Director MEG Research program
Research Interests: MEG

Clinical Staff Members

- Tina Narayan, MD
- Irina Rybalsky, MD
Trainees
- Marc DiSabella, DO, PGY-VI, Cooper University Hospital
- Pierre Fequiere, MD, PGY-VI, Long Island College Hospital
- Steve Wu, MD, PGY-VI, Vanderbilt University
- James Collins, MD, PGY-V, University of Cincinnati
- Sarah Hopkins, MD, PGY-V, University of Arkansas
- Laurel Malinowski, MD, PGY-V, University of Wisconsin
- Alice Lawrence, MD, PGYIV, Milton S. Hershey Medical Center
- Cameron Thomas, MD, PGYIV, University of Colorado
- Shawn Aylward, MD, PGYIV, Southern Illinois University
- Keith Ridel, MD, PGYIV, University of Cincinnati
- Jan-Mendelt Tillema, MD, PGYIII, St. Radboud University Nijmegen, The Netherlands
- Laura Lehman, MD, PGYIII, University of Cincinnati
- Jeffrey Tenney, MD, PGYIII, University of Massachusetts Medical School
- Jamie Fountain, MD, PGYIII, Albany Medical College

Significant Accomplishments

Childhood Absence Epilepsy: RX, PK-PD Pharmacogenetics

The Childhood Absence Epilepsy Study (NS045911) is a 32 center, 453 patient, double blind, randomized parallel group study developed and directed by Tracy A. Glauser, MD, director of the Comprehensive Epilepsy Center in the Division of Neurology. This study, the largest NIH funded pediatric epilepsy trial ever conducted, aimed to identify the optimal anticonvulsant used for the initial treatment of children with untreated childhood absence epilepsy, a common pediatric epilepsy syndrome. The study sought to determine the pharmacogenetic factors underlying the inter-individual variation in drug response along with defining and contrasting the effects of ethosuximide, lamotrigine, and valproic acid monotherapy on cognition (attention), behavior and quality of life. Enrollment completed just 4 months after the original projected date. Multiple important study milestones were reached during the past year including finishing the primary objective on time, breaking the study medication blind, and analyzing double blind data.

The study found differences between the three commonly used medications based on seizure control and effects on attention. Publication of these clinical trial results is expected soon. Detailed neuropsychological testing performed prior to starting medication was used to construct novel models on how attention, memory, and executive function affect academic achievement. Blood levels of study medications obtained throughout the study have led to development of new population pharmacokinetic models. Over 100 new polymorphisms were discovered in genes coding for the neuronal T-type calcium channels; the relationship of these polymorphisms to drug response is being examined. The trial cohort is being followed to assess whether the best short term medication is also the best long term medication. The findings of this landmark study have already begun to alter clinical care around the world for this common pediatric epilepsy syndrome.

Childhood Epilepsy: Factors affecting Adaptation

Children with epilepsy have high rates of comorbidities such as mental health problems and academic underachievement. Most research has focused on children who had seizures for many years, which has made it difficult to know what factors contribute to the mental health and academic problems. Drs DeGrauw and Byars joined with researchers at Indiana University to study 350 children with first recognized seizure FRS). They followed them prospectively for 36 months to identify factors that predict behavioral adjustment and academic achievement. We published a series of articles on this population over the past 3 years with the following conclusions: MRI abnormalities were found in 14.4% of children with a FRS who are otherwise developing normally. A second unprovoked seizure occurred in 76% of children with a FRS. 13% of children with a FRS had persistent seizures during the first 36 months. Children with a FRS who have an IQ of ≥70 have lower neuropsychological functioning in language, processing speed, attention/executive/construction, and verbal memory and learning than their healthy siblings at baseline, 18 months, and 36 months. Children with persistent seizures during the first 36 months after seizure onset have the greatest decline in neuropsychological functioning. Children with seizures had significantly more sleep problems than normal and these were related to cognitive problems. Bedtime difficulties, daytime somnolence, and parasomnias were the most frequently occurring sleep problems. Approximately one fourth of children with a FRS are in the at-risk range for depression symptoms at baseline. Children with a FRS have more total behavior problems than their siblings at baseline, 18 months, and 36 months. The individual areas of greatest difficulty are attention problems and somatic complaints. It is our hope that this study will result in better management of these co-morbidities in children with
Headache Center

The Center continues to advance characterization, pathophysiology, management and outcome of pediatric and adolescent patients with headache.

The characterization has been expanded into an investigation of features and etiologies in the differences between boys and girls with migraine and now includes the description of the development of menstrual migraine in adolescents. The use of genomic expression analysis contributes to our understanding of the pathophysiological changes that underlie the development of migraine and expression of acute migraine attacks. We have identified preliminary biomarkers for patients at risk of development of medication overuse headaches and we are moving forward with the identification of other subgroups. One of these groups is patients with cutaneous allodynia with central sensitization. This characteristic has been noted to contribute to the progression of headaches in adults. To date we have only been able to characterize this through patients clinical recognition of these symptoms. To better understand this we have begun testing using quantitative sensory testing to better understand the level of allodynia in patients both during the acute headache attack and inter-ictally. The neurophysiological basis of acute migraine attack is being investigated using MEG. We have tested adolescents having an acute migraine for both motor cognitive ability and mis-matched negativity. Both of these test have demonstrated altered cortical functioning during an acute attack providing a foundation for further understanding the neurophysiological basis of migraine.

These acute studies can be performed due to the development and continuation of the acute headache care unit. This unit has greatly enhanced our ability to manage children and adolescents with acute headache exacerbations. These tools are also being advanced through our NIH sponsored study evaluating the benefit of coping skills training in children with chronic migraine.

Division Publications


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### Grants, Contracts, and Industry Agreements

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<td>Genome Wide Association Study of Autism&lt;br&gt;Autism Speaks</td>
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<td><strong>VANNEST, J</strong></td>
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<td>The Neural Basis of Language in Neurodevelopmental Disorders&lt;br&gt;Jerome LeJeune Foundation</td>
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<td>Developmental Effects of Methamphetamine-Like Stimulant&lt;br&gt;National Institutes of Health&lt;br&gt;R01 DA 006733</td>
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### Training Program in Teratology
National Institutes of Health  
T32 ES 007051  
07/01/07 - 06/30/12  
$285,190 / $1,432,850

### Genetic Differences in PCB-Induced Behavior
National Institutes of Health (University of Cincinnati)  
R21 ES 015335  
12/15/07 - 11/30/09  
$52,120 / $112,720

### WILLIAMS, M.
#### Effect of Lead, Manganese and Stress During Development
National Institutes of Health  
R01 ES 015689  
09/18/06 - 06/30/11  
$244,562 / $1,250,000

### WONG, B.
#### Spinal Muscular Atrophy Foundation Biomarker Pilot Study
Spinal Muscular Atrophy Foundation  
10/01/08 - 09/30/09  
$34,231 / $34,231

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