
Division Data Summary

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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
Madeline Chadehumbe, MD, Instructor  
**Research Interests:** neuromuscular disorders

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

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

Diego Morita, MD, Assistant Professor Clinical  
**Research Interests:** epilepsy, pharmacology

Tonya Phillips, MD, Associate Professor Clinical  
**Research Interests:** neonatal seizures

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

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

Charles Vorhees, PhD, Research 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

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**Clinical Staff Members**

- Tina Narayan, MD

**Trainees**

- Shannon Standridge, DO, PGYVI, Kansas City University
- Marc DiSabella, DO, PGY-V, Cooper University Hospital
- Pierre Fequiere, MD, PGY-V, Long Island College Hospital
- Steve Wu, MD, PGY-V, VanderBilt University
- James Collins, MD, PGY-IV, University of Cincinnati
Sarah Hopkins, MD,  PGY-IV,  University of Arkansas
Laurel Malinowski, MD,  PGY-IV,  University of Wisconsin
Alice Lawrence, MD,  PGYIII,  Milton S. Hershey Medical Center
Cameron Thomas, MD,  PGYIII,  University of Colorado
Shawn Aylward, MD,  PGYIII,  Southern Illinois University
Keith Ridel, MD,  PGYIII,  University of Cincinnati

Significant Accomplishments in FY08

Epilepsy Program
The Children’s Comprehensive Epilepsy Program is a nationally recognized leader in pediatric epilepsy with strengths in integrated multidisciplinary comprehensive clinical care, cutting edge clinical and basic research and patient education. The four major areas of focus include epilepsy pharmacology, epilepsy surgery, multimodality (MRI, fMRI, MEG) epilepsy imaging, and basic neuroscience. The pharmacology group (Drs. Glauser, Morita, Holland) aims to personalize care for children with new onset epilepsy by integrating multidisciplinary care, clinical research and patient education. The major research activities of this group include examination of the role of drug-gene interactions on the inter-individual variation in antiepileptic drug clinical response, laboratory studies of the functional significance of the genetic variations found, and study of parental adherence to prescribed medication regimens. Gene-drug interactions include research on the impact of variation in genes coding for drug metabolizing enzymes, drug transporters and drug receptors on clinical response to antiepileptic medications (pharmacogenetics) along with the impact of antiepileptic medications on gene expression (pharmacogenomics). The pharmacogenetics research is funded through an NIH U01 that is based at CCHMC and includes 31 other centers. The trial is a double blind, randomized, comparison trial of three antiepileptic medications focused on identifying the optimal initial therapy for children with absence epilepsy. The study is also designed to identify pharmacokinetic, pharmacodynamic, and pharmacogenetic factors that impact upon response to therapy. This landmark study has completed enrollment and will be announcing its results at the end of 2008.

The epilepsy surgery program, led by Drs. Lee and Mangano are undergoing a major expansion and expect to become a national leader in the surgical evaluation and management of children with treatment resistant epilepsy. The program is currently one of the busiest in the nation and utilizes a novel multimodality (MRI, fMRI, MEG) imaging approach to seizure lateralization and localization that aims to improve surgical outcome. The multimodality (MRI, fMRI, MEG) epilepsy imaging teams (Drs. Rose, Xiang, Vannest) also have active research programs focused using non-invasive imaging to better understand the interaction between epileptic seizures, brain development and brain activity. The basic neuroscience component of the epilepsy program focuses on determining the functional significance of the genetic variations found in the clinical pharmacogenetic studies (Dr. Holland) along with developing non-genetic biomarkers of epilepsy and response to therapy (Dr. Hallinan).

Tuberous Sclerosis
In the past year I have seen enhancement and extension of various research programs related to Tuberous Sclerosis Clinic. A trial of RAD-001 in giant cell astrocytomas has almost completed enrollment and shows great promise for reduction in tumor volume as well as improvement in seizures and cognition. The trial is to continue with RAD-001 for renal angiomyolipomas as well as with rapamycin for lymphangioleiomyomatosis and angiomyolipomas. The addition of Darcy Krueger, MD, PhD has enhanced our basic science program. In cooperation with Dr. George Thomas and Sara Kozma at Genome Research Institute. Dr. Krueger is performing basic science research on the role of mTOR in cognition and motor development. An NIH grant was submitted to fund CCHMC involvement in an infantile spasms consortium. The key aspect to this will be an evaluation of the efficacy of RAD-001 for infantile spasms, first in tuberous sclerosis patients, and later in infantile spasms for other causes. Novartis has agreed to fund the performance of a trial of RAD-001 in infantile spasms and tuberous sclerosis patients. A clinical trial is being planned for intractable epilepsy and tuberous sclerosis and cortical dysplasia using RAD-001 in collaboration with Baylor University College of Medicine.

Our Tuberous Sclerosis Clinic remains the largest in the United States following over 500 adults and children with the disorder. We have improved and extended services to individuals with tuberous sclerosis through educational programs, community support, and the first ever camp for tuberous sclerosis children. Our clinic remains the only true and multidisciplinary Tuberous Sclerosis Clinic with access to full range of medical care for both adults and children with the disorder.

The Headache Center
The Headache Center at Cincinnati Children’s Hospital Medical Center, Department of Neurology, was established in the fall of 1996. The Headache Center was organized as a multi-disciplinary clinic combining Child Neurologist, Child
Psychologist and Nurse Practitioners to diagnose and treat children with headache disorders. It is based within a growing academically and clinically based neurology department at Cincinnati's Children's Hospital Medical Center, and is affiliated with the University of Cincinnati College of Medicine and the Division of Psychology at CCHMC. Over the past 10 years, we have seen nearly 4000 children with the complaint of headaches. A clinical diagnosis and a standardized diagnosis using the International Classification of Headache Disorders, 2nd Edition, are also made for each of these children. A detailed questionnaire about the child’s headache has been developed and a computer-based database to accumulate medical information as well as response rate was designed and is continually updated. Treatment strategies include acute therapy for individual headache episodes, prophylactic therapy for preventing headache episodes and psychological intervention including biofeedback-assisted relaxation training as well as life style behavior adjustments. This multidisciplinary approach has been demonstrated to be highly effective, not only in the standard methods of measuring outcome, but also in using tools developed and validated at CCHMC to characterize disability and quality of life. The Headache Center has also been designed to develop and expand research into childhood headache disorders by examining new treatment options, improved characterization of childhood headache and response patterns, and understanding the genetic pathophysiology of childhood headaches. In this role, multiple studies and publications have been developed including one of the few NIH sponsored studies in headache examining genomic expression patterns, as well as an NIH sponsored study on treatment of chronic daily headache with combined pharmacologic and behavioral treatment. Education is also a key component with the Headache Center established the first pediatric fellowship for the study of childhood headaches in the country, the only pediatric headache fellowships out of the 1 established headache fellowships in the country certified by the United Council of Neurologic Subspecialties with both Drs. Hershey and Kabbouche board certified in Headache Medicine.

**Significant Publications in FY08**


This is the second report from our group of a new treatment for patients with tuberous sclerosis. This shows that mTOR inhibition works for angiomyolipoma. The previous report showed the same results for brain tumors in this condition.


First report on SCN3A mutation as likely cause of epilepsy in this patient

**Tillema, JM etal, Cortical reorganization of language functioning following perinatal left MCA stroke, Brain Lang. 2008, 105: 99-111**

Clear evidence of plasticity of the neonatal brain for language function after perinatal stroke.

**Division Highlights**

**Movement Disorders**

The Transcranial Magnetic Stimulation Laboratory - We continue to study motor cortex physiology in Tourette Syndrome and ADHD and have performed pioneering studies of the relationship between dopamine transporter genotype variations and physiological responses to dopaminergic and noradrenergic medications. See publications list. We also are co-investigators in a two-site, five year study, the first NIH funded study to combine TMS and fMRI to assess motor cortex and motor function in ADHD, with ongoing recruitment. We have recently purchased equipment which could allow for an exciting new venture in quantifying long term potentiation and depression in vivo in humans, using TMS, and have submitted a grant proposal to use this for Tuberous Sclerosis Complex.

**Movement Disorders**

Tourette Syndrome Genetics - We are one of two sites in a 5-year NIH-funded study to identify the prevalence of SLITRK1 mutations and other mutations in TS. Another NIH grant is in the planning phases.

**Neurology Basic Science Labs**

The Division officially launched the Animal Behavioral Phenotyping Core this past year under the direction of Drs. Vorhees and Williams (Website: http://www.cincinnatichildrens.org/research/cores/abc/default.htm). This is a new collaborative research facility available to investigators from all divisions of CCRF, any department of UC, and outside
institutions. The new core has already secured multiple CCRF and UC collaborators, one outside contract with a major pharmaceutical company, and has a pending contract with a start-up pharmaceutical company. The core specializes in the characterization of transgenic mice, but can also evaluate rats. The new core offers a wide range of behavioral assays for both species, many more than most comparable facilities at other universities. A new laboratory to expand the core’s testing capacity will begin construction in the near future.

Neurology Basic Science Labs
New Animal Model of Methamphetamine-induced Cognitive Impairment - Over the course of the last 10-15 years there has emerged clear evidence that methamphetamine (Meth) abusers, especially chronic users, develop cognitive impairments that remain long after these individuals enter treatment and even after they have been abstinent for 6 months, a year, or even longer. Attention, learning, and memory deficits have been reported in many studies of former chronic users. For 5-10 years, animal models of this problem have been under investigation as a means to understand these effects, uncover the mechanisms of action, and to use these models to develop interventions to treat these impairments. Meth is neurotoxic at high doses in humans and rodents. Unfortunately, in rodents few learning and memory effects have been found even after neurotoxic doses are given. The best model until now has been Meth-induced novel object memory impairments in rats. Recently, the reliability of this model has come into question. During the past year, the laboratories of Drs. Williams and Vorhees have found a new cognitive effect from high dose Meth treatment in the form of impairments in path integration (also called egocentric) learning. The effect has been replicated using different Meth dosing schedules and is both reliable and substantial. Further, the effect on the HPA axis was tested in sham versus adrenalectomized Meth or Saline treated rats and the impairment was unchanged. This proved that Meth-induced corticosterone release does not contribute to the learning impairment. Drs. Williams and Vorhees recently submitted a new grant application to NIH to perfect the model, expand its utility, test potential mechanisms of action in relation to neurotransmitters (dopamine, serotonin, and glutamate), and to test a potentially promising treatment to reverse the damage after it has occurred using a drug already marketed.

MEG Research
We have completed a study on high-frequency neuromagnetic signals in the developing brain. To our knowledge, this is the world's first high-frequency MEG database from healthy children. The database lays a foundation for identification of brain abnormality and functional developmental delay in children. primary clinical application and research interests are 1) determination of the seizure onset location in children with medically intractable epilepsy who are candidates for surgery and 2) localization of the normal functional brain regions subserving language and motor control so that these regions are preserved during epilepsy surgery. There are multiple methods for localization of abnormal and normal brain function with MEG; however, only a few sites worldwide study children with MEG. The optimum methods are not yet known for localization of the epileptic focus and normal brain function in children. Dr. Rose has just received approval for an IRB protocol: Algorithms for Improved Interpretation of Electromagnetic Brain Activity to evaluate and optimize these MEG methodologies for children. He is collaborating with researchers at the University of Cincinnati, Miami University, and Oakland University in these pursuits. A second research interest is in the synergistic value of comparing findings across multiple modalities (MEG, fMRI, SPECT, PET). Dr. Rose has been developing collaborations principally with CCHMC Department of Radiology in pursuit of these research goals. Dr. Rose is also collaborating with multiple colleagues within the Neurology Division on brain research using MEG and also EEG.

Division Collaboration

Collaboration with Division of Human Genetics
Collaborating Faculty: Greg Grabowski, MD ; Ying Sun, PhD
Collaborating on mouse knock-out models of lipid storage disease

Collaboration with Division of Anesthesiology
Collaborating Faculty: Steve Danzer, PhD
Collaborating on the dentate gyrus-specific floxed pten knock-out mouse model of autism with hypothesized increased seizure susceptibility

Collaboration with Imaging Research Center
Collaborating Faculty: Weihong Yuan, PhD; Scott Holland, PhD
Collaborating on a model of early onset hydrocephalus and the beneficial effects of shung surgery on cognitive and behavioral outcome in rats

Collaboration with Division of Anesthesiology
Collaborating Faculty: John McAuliffe, MD
Effects of early hypoxia-ischemia and anesthetics on cognitive outcome in mice

Collaboration with Division of Anesthesiology
Collaborating Faculty: Andreas Lepke, MD
Effects of early anesthesia exposure on apoptosis and cognitive development

Collaboration with Division of Allergy & Immunology
Collaborating Faculty: Marc Rothenberg, MD, PhD
Effects of NPS and its putative receptor GPRA in asthma and CNS function

Division Publications


21. Gilman DK, Palermo TM, Kabbouche MA, Hershey AD, Powers SW. Primary headache and sleep disturbances in 

22. Korostenskaja M, Kicic D, Kahkonen S. The effect of methylphenidate on auditory information processing in 


24. Modi AC, Morita DA, Glauser TA. One-month adherence in children with new-onset epilepsy: white-coat 

25. Spitzmiller RE, Phillips T, Meinzen-Derr J, Hoath SB. Amplitude-integrated EEG is useful in predicting 
neurodevelopmental outcome in full-term infants with hypoxic-ischemic encephalopathy: a meta-analysis. J 
Child Neurol. 2007; 22: 1069-78.

time-dependent effects of (+)-methamphetamine or forced swim on monoamines, corticosterone, glucose, 

27. Schaefer TL, Skelton MR, Herring NR, Gudelsky GA, Vorhees CV, Williams MT. Short- and long-term effects of (+)- 
methamphetamine and (±/−)-3,4-methylenedioxymethamphetamine on monoamine and corticosterone levels 

28. Miles MV, Patterson BJ, Chalfonte-Evans ML, Horn PS, Hickey FJ, Schapiro MB, Steele PE, Tang PH, Hotze SL. 
Coenzyme Q10 (ubiquinol-10) supplementation improves oxidative imbalance in children with trisomy 21. 

29. Skelton MR, Williams MT, Schaefer TL, Vorhees CV. Neonatal (+)-methamphetamine increases brain derived 
neurotrophic factor, but not nerve growth factor, during treatment and results in long-term spatial learning 

30. Skelton MR, Williams MT, Vorhees CV. Developmental effects of 3,4-methylenedioxymethamphetamine: a 


33. Vannest J, Szafarski JP, Privitera MD, Scheff BK, Holland SK. Medial temporal fMRI activation reflects memory 

34. McAuliffe JJ, Joseph B, Hughes E, Miles L, Vorhees CV. Metallothionein I,II deficient mice do not exhibit 
significantly worse long-term behavioral outcomes following neonatal hypoxia-ischemia: MT-I,II deficient mice 
have inherent behavioral impairments. Brain Res. 2008; 1190: 175-85.

35. Pan D, Sciascia A, 2nd, Vorhees CV, Williams MT. Progression of multiple behavioral deficits with various ages 

36. Siuciak JA, McCarthy SA, Chapin DS, Reed TM, Vorhees CV, Repaske DR. Behavioral and neurochemical 
characterization of mice deficient in the phosphodiesterase-1B (PDE1B) enzyme. Neuropharmacology. 2007; 53: 
113-24.

37. Vorhees CV, Schaefer TL, Williams MT. Developmental effects of +/-3,4-methylenedioxymethamphetamine on 

38. Vorhees CV, Skelton MR, Williams MT. Age-dependent effects of neonatal methamphetamine exposure on 


40. Markham LW, Kinnett K, Wong BL, Woodrow Benson D, Cripe LH. Corticosteroid treatment retards development 

41. Miles MV, Miles L, Tang PH, Horn PS, Steele PE, DeGrauw AJ, Wong BL, Bove KE. Systematic evaluation of 


Grants, Contracts, and Industry Agreements

Grant and Contract Awards

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Vorhees, C

Williams, M.
Effect of Lead, Manganese and Stress During Development  
National Institutes of Health  
R01 ES 015689  
09/18/06 - 06/30/11  
$242,750 / $1,250,000

Wong, B.  
Translational Research in Dystrophinopathies  
National Institutes of Health (University of Utah)  
R01 NS 043264  
04/01/06 - 03/31/11  
$12,981 / $78,663

Current Year Direct  $6,678,519

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Current Year Direct Receipts  $286,826

Total  $6,965,345