The Neurotransmitter

UT Health Austin Pediatric Neurosciences at Dell Children's

Promoting Discovery and Innovation in the Pediatric Neurosciences

Dear colleagues:

Welcome to UT Health Austin Pediatric Neurosciences at Dell Children's. This issue of *The Neurotransmitter* provides a sense of the excitement surrounding our rapidly growing new program. We are committed to offering outstanding educational opportunities, promoting research and scholarly activity, and delivering exceptional multidisciplinary clinical care for all children with neurological disorders. We are always happy to hear from you.

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BERMANS ISKANDAR, MD, PRESENTS THE INAUGURAL TIMOTHY M. GEORGE MEMORIAL LECTURE IN PEDIATRIC NEUROSURGERY

Elizabeth Tyler-Kabara, MD, PhD, with Bermans J. Iskandar, MD

Bermans J. Iskandar, MD, Professor of Pediatric Neurosurgery at the University of Wisconsin, presented the first annual Timothy M. George Memorial Lecture in Pediatric Neurosurgery at Dell Children's Medical Center on November 12, 2021. Iskandar discussed the role of folate in central nervous system repair, folate-driven mechanisms of transgenerational epigenetic inheritance, and the importance of epigenetics in tissue regeneration and healing.

Timothy M. George, MD, was a professor of neurosurgery at Dell Medical School and a beloved pediatric neurosurgeon at Dell Children's Medical Center when he died unexpectedly at age 59 in 2019. Dr. George graduated from New York University Grossman School of Medicine before completing his neurosurgery residency at Yale University and his pediatric neurosurgery fellowship at Northwestern University. He joined the faculty of Duke University in 1996 and in 2006 moved to the then new Dell Children's Hospital. His research interests included Chiari malformation and the genetic mechanisms of neural tube defects. Tim was a superb pediatric neurosurgeon. His quiet confidence and unfailing empathy and compassion endeared him to colleagues and patients alike.

Timothy M. George, MD

HARDY DISCUSSES PROTECTIVE FACTORS IN PREVENTING PEDIATRIC-ONSET MULTIPLE SCLEROSIS

The diagnosis and treatment of multiple sclerosis has improved dramatically in the last several years, in both adults and children. Most discussions of multiple sclerosis center on secondary prevention with agents intended to prevent disease progression and limit the ultimate severity of neurological disability. Such disease-modifying treatments are particularly important for children, because children with multiple sclerosis have more years to accumulate lesions. What is not often discussed, however, is primary prevention strategies for multiple sclerosis.

In a *Frontiers in Neurology* article, **Duriel Hardy, MD**, and colleagues take a critical look at the difficult topic of multiple sclerosis risk factors that might be modified in the pediatric population. Concern about exposure to Epstein-Barr virus, inhalation of passive cigarette smoke, and exposure to other environmental toxins is bolstered by considerable statistical evidence. An increased body mass index also seems to increase the multiple sclerosis risk, albeit at a lower level. Although the studies are inconsistent, preliminary evidence suggests that breastfeeding protects against development of multiple sclerosis (possibly by avoiding molecular mimicry between cow milk proteins and brain antigens). Other possible protective factors include sun exposure and higher serum vitamin D levels. Although many of these factors are modifiable, altering them would require extensive public health changes.

Hardy D, Chitnis T, Waubant E, Banwell B. Preventing multiple sclerosis: the pediatric perspective. *Front Neurol* 2022;13:802380. doi: 10.3389/fneur.2022.802380

A SECOND OPINION

This eight-year-old girl was born at term via Caesarean delivery due to fetal tachycardia. After birth she was treated for suspected sepsis. Her early development was normal. She walked at 12 months, and her language and social development were normal. At age five, she developed right in-toeing and began tripping and falling. She later developed episodic posturing of the right arm, and her gait deteriorated. She complained of muscle soreness after increased activity, and she often experienced more difficulty in the afternoon and evening. She was diagnosed with cerebral palsy (CP) and began physical therapy and right leg bracing. The second opinion request was triggered by a further recommendation to proceed with botulinum injections.

The girl had mild thoracic scoliosis. Her mental status and cranial nerve functions were normal. Her tone fluctuated from low tone to tightness in the legs. The right foot was plantar flexed, adducted at midfoot with in-toeing. Her tendon reflexes were hyperactive in the right leg with a right Babinski sign. Her gait was unsteady and broad based, with right toe walking. She exhibited dystonia of both legs as well as intermittent posturing of the right arm (adduction of the shoulder, flexion at the elbow, and clenching of the fist).

Serum CK and thyroid function were normal. A 3T brain MRI was normal. Nerve conduction studies were normal, and electromyography showed no evidence of neuronal hyperexcitability.

See below for additional discussion.

REPETITIVE VALPROATE INFUSION SHOWS PROMISE IN REDUCING REFRACTORY CHRONIC HEADACHE PAIN

Sara Pavitt, MD, Assistant Professor of Neurology at Dell Medical School and Chief of the Pediatric Headache Center at Dell Children's, recently described the use of intravenous valproate in significantly reducing pain for children with chronic headache.

Pavitt and her colleagues summarized 45 children with refractory headache disorders who completed a standardized four-day inpatient repetitive valproate infusion protocol. Patients with chronic migraine had undergone a median of seven previous migraine prevention trials, and 85% had completed one or more previous intravenous therapies with other agents. One week after completing the valproate infusions, each patient began a new headache preventive agent. The baseline headache frequency did not change significantly for the cohort as a whole, but two-thirds of the patients experienced long-term improvement based on a combined analysis of headache frequency, headache intensity, and diminished use of acute pain medications.

Refractory migraine causes substantial discomfort and long-term disability. These children are seldom included in clinical trials, so there is a paucity of objective evidence to guide therapy. Based on this report, valproate infusions may be an encouraging option.

Pavitt S, Gelfand AA, Zorrilla N, Allen I, Riggins N. Efficacy and safety of repetitive intravenous sodium valproate in pediatric patients with refractory chronic headache disorders: a retrospective review. *Pediatr Neurol* 2022;128:52-57. doi: 10.1016/j.pediatrneurol.2021.12.008

DELL CHILDREN'S MEDICAL CENTER HOSTS THIRD ANNUAL PEDIATRIC NEUROSCIENCE SYMPOSIUM

Pediatric practitioners care for children with a wide range of neurological disorders, but a lack of extensive training in these conditions can make managing and treating them challenging. The Practical Pediatric Neuroscience Symposium was created to enhance knowledge of common and uncommon pediatric neurological conditions, with the goal of helping providers improve care for children with these conditions. The third annual symposium, held on May 21, 2022, at Dell Children's Medical Center, featured presentations by 10 Dell Medical School faculty members within the Pediatric Neurosciences Program. Topics ranged from primary care issues in neuromuscular disease to behavioral pain management for pediatric headache. Each interactive presentation provided specific techniques and evidence-based recommendations for diagnosis and management, including the roles of interprofessional teams in improving quality of life and treatment outcomes.

WOMEN IN NEUROSCIENCE (WiN) PROGRAM ENCOURAGES YOUNG WOMEN TO PURSUE NEUROSCIENCE CAREERS

WiNterns Dignity Butts and Bella Thomas scrubbed in and ready to observe neurosurgery.

Several members of our pediatric neurosciences team have embraced Women in Neuroscience (WiN), an Austin-based organization whose mission is to encourage young economically disadvantaged, first-generation, and underrepresented minority high school seniors or college women to pursue careers in neuroscience or neurology. WiN offers a $3,000 stipend to support eight-week summer internships (thus "WiNterns") during which each student works in a neuroscience-related research laboratory or on a clinical research project. Additionally, the program offers seminars and tutorials designed to facilitate professional development and leadership skills and provides ongoing mentorship.

WiN was established in 2018 to honor Harvey Nudelman, PhD, a neuroscience researcher and teacher who died from progressive supranuclear palsy. The organization partners with the University of Texas at Austin Department of Neuroscience, the Department of Neurology at Dell Medical School, Huston-Tillotson University, and the Ann Richards School for Young Women Leaders. **Audrey Brumback, MD, PhD**, who has been hosting WiNterns since the program began, teaches skills such as PCR genotyping of transgenic mice and quantification of behavior in mouse models of autism. In 2021, three students worked on **Dave Clarke, MD**'s Discrepancies and Disparities in the Care of Children with Epilepsy project. Among the program's seminars and tutorials was a half-day biomedical writing workshop taught by **E. Steve Roach, MD**, and tutorials by Brumback and Clarke.

For additional information on WiN, see www.neurowomen.org or follow the organization on Twitter at @helloneurowomen.

Dave Clarke, MD, with Hepsiba Barar (left) and Whittney Barry (right), WiNterns who worked on his pediatric epilepsy project.

VASCULAR AUTONOMIC LAB OPENS

Q-Sweat measurement system in the newly opened lab.

The Pediatric Neurosciences Program recently opened a vascular autonomic laboratory at Dell Children's Medical Center. The lab offers tilt-table testing with simultaneous electroencephalography, video, electrocardiography, and quantitative sudomotor axon reflex testing (QSART) for evaluating children with suspected positional orthostatic tachycardia syndrome (POTS), syncope, pseudosyncope, and other autonomic disorders. It is one of only two pediatric autonomic labs in the Southwest.

The laboratory is jointly overseen by **Manikum Moodley, MD**, who previously served as the director of the pediatric vascular autonomic lab at the Cleveland Clinic, and **Veda Vedanarayanan, MD**, who oversaw the Electromyography and Autonomic Laboratory at the University of Mississippi Medical Center. To refer patients for autonomic testing or consultation, call 512-628-1855 or email program coordinator **James Johnson, BSN, RN, CPN**, at jejohnson@ascension.org.

PEDIATRIC NEUROSCIENCES PROGRAM WELCOMES SEVERAL NEW COLLEAGUES

UT Health Austin Pediatric Neurosciences at Dell Children's has grown dramatically since it was founded in 2019. The multidisciplinary program features 15 child neurologists, three pediatric neurosurgeons, a pediatric physical medicine and rehabilitation specialist, six pediatric neuropsychologists, and a pediatric neuro-ophthalmologist. We recently welcomed several new colleagues to the program.

Raynah Lobo, MS, LCGC, is a licensed certified genetic counselor in the Pediatric Neurosciences Program and in the Dell Medical School Department of Neurology. She received her master's in genetic counseling from the University of Pittsburgh and her master's in microbiology at The Institute of Science, Mumbai. Her clinical and research interests include inborn errors of metabolism, genetic epilepsies, and neurocutaneous disorders. She is certified by the American Board of Genetic Counseling and is a member of the National Society of Genetic Counselors. Prior to joining our program, she served as a biochemical laboratory genetic counselor at Quest Diagnostics.

Christina Roth is the editor of the Pediatric Neurosciences Program. Roth joins the program with 15 years of experience in editing books, journal articles, web content, and government documents. Previously, she was an editor for a dental marketing company and the production manager for a book publisher, where she worked on multiple *New York Times* Best Sellers and was instrumental in a Wiley acquisition of over 1,000 titles. She has a Bachelor of Arts in English from Lipscomb University.

Yingchao Yuan is senior biostatistician in the Pediatric Neurosciences Program. Yuan received his Master of Arts in statistics at the University at Albany, SUNY. Before coming to Austin, he was a researcher for the New York State Department of Health and in data analytics for the New York State Office of Alcoholism and Substance Abuse Services.

Stephen Deputy, MD, Professor of Neurology at Dell Medical School, focuses on Tourette syndrome, tics, and other movement disorders. He received his medical degree from Northwestern University Feinberg School of Medicine in Chicago and completed residency training in pediatric neurology at the University of California, San Francisco. Deputy joins the Dell Medical School faculty after several years at Louisiana State University Health Sciences Center in New Orleans, where he won numerous student and resident teaching awards.

OUR COLLEAGUES IN THE NEWS

Edmond Receives Parks Medal From AAPOS

Jane C. Edmond, MD, Professor and Chair of the Department of Ophthalmology at Dell Medical School and a neuro-ophthalmologist in the Pediatric Neurosciences Program, recently received the Marshall M. Parks Bronze Medal from the American Association for Pediatric Ophthalmology and Strabismus (AAPOS). Marshall M. Parks medals are awarded to past AAPOS presidents and other individuals who have made noteworthy contributions to children's eye care. Edmond completed her two-year term as AAPOS president in 2020. Congratulations, Dr. Edmond!

Deputy Named Section Editor of *Pediatric Neurology*

Stephen Deputy, MD, Professor of Neurology at Dell Medical School, has been appointed as a section editor of *Pediatric Neurology*, with expertise in pediatric movement disorders, neuroembryology, and medical education. Deputy joined the Dell Medical School faculty in early 2022 after several years at Louisiana State University Health Sciences Center in New Orleans.

Hardy Named to the Editorial Board of *Pediatric Neurology*

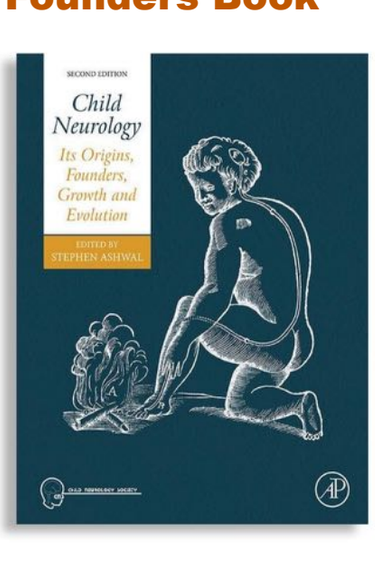
Duriel Hardy, MD, Assistant Professor of Neurology at Dell Medical School, was recently appointed to the Editorial Board of *Pediatric Neurology*. "Dr. Hardy's expertise in the neuroimmunologic conditions of children and young adults is exceptional," said Yasmin Khakoo, MD, Editor-in-Chief of *Pediatric Neurology*. "I look forward to working with him as the newest member of our editorial board."

Hardy joined the Pediatric Neurosciences Program in 2021 after completing his pediatric neurology residency and a fellowship in pediatric neuro-immunology at the Children's Hospital of Philadelphia and the Hospital of the University of Pennsylvania.

Freedman Selected to Oversee SUDEP Toolkit Development

Daniel Freedman, DO, Assistant Professor of Neurology at Dell Medical School, has been selected by the Child Neurology Foundation's Project Advisory Committee as the lead epileptologist to oversee the development of its SUDEP and Epilepsy Mortality Toolkit. Freedman will assist the committee by developing, implementing, and evaluating the toolkit, which will help reduce epilepsy-related deaths by promoting behavior change among providers, patients, and patient families. He will also advise the committee on institutional partnerships that will support the project through research.

Roach Included in the Second Edition of Child Neurology Founders Book



A biography of **E. Steve Roach, MD**, Professor of Neurology at Dell Medical School and Co-Chief of UT Health Austin Pediatric Neurosciences at Dell Children's, was included in the second edition of *Child Neurology: Its Origins, Founders, Growth and Evolution*. Commemorating the 50th anniversary meeting of the Child Neurology Society, the book includes biographies of individuals dating to the early 1800s who made seminal contributions to the development of child neurology as a discipline. Roach was cited for his early work in stroke in children and contributions to selected genetic diseases.

A SECOND OPINION: EPILOGUE

Based on her motor dysfunction and perinatal history, this girl was initially misdiagnosed with CP. When she failed to improve with physical therapy and leg bracing, localized botulinum toxin injections were recommended. However, there were several concerns about the initial CP diagnosis. Neonatal tachycardia and suspected sepsis do not provide very strong support for a CP diagnosis, and there was no evidence of residual perinatal brain injury on MRI. It is unlikely that severe CP would begin at age five and less likely still that the manifestations would become progressively worse. Finally, spontaneous fluctuation of the motor function should not occur with CP.

Diagnosis
Genetic studies confirmed a heterozygous pathogenic variant in the GTP-cyclohydrolase 1 (*GCH1*) gene, confirming the suspected diagnosis of dopa-responsive dystonia, or Segawa disease. Curiously, her asymptomatic mother has the same heterozygous mutation. Soon after starting levodopa/carbidopa therapy, the child's physical signs resolved and her gait normalized.

Segawa in 1976 described six families with fluctuating dystonia that responded to treatment with levodopa. They were later found to have a *GCH1* mutation, and the disorder can arise from either autosomal recessive or dominant mutations. The dominant mutations tend to have milder manifestations and more variable expression. Some adults have symptom onset in the fourth decade or even later.

Additional Reading

Segawa M, Hosaka A, Miyagawa F, Nomura Y, Imai H. Hereditary progressive dystonia with marked diurnal fluctuation. *Adv Neurol* 1976;14:215-233.

Wijemanne S, Jankovic J. Dopa-responsive dystonia—clinical and genetic heterogeneity. *Nat Rev Neurol* 2015;11:414-424.

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UT Health Austin Pediatric Neurosciences at Dell Children's is a clinical partnership between Dell Children's Medical Center and UT Health Austin, the clinical practice of the Dell Medical School at The University of Texas at Austin.

For additional program information:

UT Health Austin Pediatric Neurosciences at Dell Children's
Comprehensive Pediatric Epilepsy Program
Pediatric Neurosciences Blog