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The Neurotransmitter UT Health Austin Pediatric Neurosciences at Dell Children's

Promoting Discovery and Innovation in the Pediatric Neurosciences



The University of Texas at Austin

Dear colleagues:

Welcome to UT Health Austin Pediatric Neurosciences at Dell Children's. Our program is 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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HOW DO EPILEPSY CENTER CHARACTERISTICS AFFECT EPILEPSY SURGERY UTILIZATION?



Kristen Arredondo, MD

Nearly a third of people with epilepsy continue having seizures despite adequate trials of multiple antiseizure medications. Many of these individuals with medically refractory epilepsy benefit from various palliative and potentially curative surgical procedures. Although the number of centers offering surgery for epilepsy has increased dramatically in the last couple of decades, surgical treatment remains underutilized. **Kristen Arredondo** and colleagues analyzed data from the National Association of Epilepsy Centers (NAEC) to determine how epilepsy center characteristics affected access to different types of epilepsy surgery and surgery volumes. The dataset included information from 206 adult epilepsy center directors and 136 pediatric epilepsy center directors.

Arredondo and colleagues provide a wealth of useful information. Geographic location of the center, center accreditation level, institution type, demographics, and available resources influenced the access and the rates of potentially curative and palliative surgical interventions. The likelihood of undergoing potentially curative procedures (e.g., temporal lobectomy, extratemporal resection, hemispherectomy or hemispherotomy, and laser interstitial thermal therapy) was higher in centers with image-guided robotics and magnetoencephalography. Except for hemispherectomy and hemispherotomy, potentially curative procedures were more likely to occur in centers with a greater number of epilepsy specialists with at least two years of epilepsy fellowship training. Extratemporal resection, hemispherectomy, and hemispherotomy were all more likely to occur in pediatric centers than in adult centers, and hemispherectomy or hemispherotomy was only attempted in level 4 centers.

There are multiple reasons why surgical treatment of epilepsy is underutilized. Better understanding of the resources that make surgery for refractory epilepsy more feasible and the barriers that impede it may help us provide optimal care for more people.

Arredondo KH, Ahrens SM, Bagić AI, et al. on behalf of the NAEC Center Director Study Group. Association between characteristics of National Association of Epilepsy Centers and reported utilization of specific surgical techniques. *Neurology* 2023;100:e719-e727. https://doi.org/10.1212/WNL.00000000201526

AUTISM RESEARCH PROGRAM RECEIVES ADDITIONAL NIH GRANT



Audrey Brumback, MD, PhD

The important role of genetics in autism development has become increasingly obvious. Many genes implicated in autism are so fundamental to basic neurobiology that species as diverse as worms and humans share them. After discovering that natural variability in autism-related genes correlates with alterations in worm social behavior, **Audrey Brumback, MD, PhD**, pediatric neurologist and an assistant professor in the Department of Neurology, and Jon Pierce, PhD, in UT Austin's College of Natural Sciences, hypothesized that these changes could provide a way to rapidly screen potential treatments for individuals with specific genetic causes of autism.

Leveraging *C. elegans* as a minimum animal model, Brumback and Pierce can screen thousands of FDA-approved drugs to quickly and inexpensively identify personalized treatment for autism based on a patient's genetic profile. They were recently awarded a three-year, \$500,000 R01 grant from the National Institute of Mental Health entitled "High-Throughput Interrogation of Autism Risk Genes: From Molecules to Behavior" to uncover the molecular mechanisms by which autism genes influence worm social behavior.

This new grant builds on another recent \$1,500,000 grant from the National Institute of Mental Health for "Functional Architecture of the Mediodorsal Thalamus." For this work, Brumback's team will use mice to map the structure and function of a part of the thalamus that is thought to affect conditions such as autism, attention-

deficit/hyperactivity disorder, and schizophrenia. The thalamus is typically considered a relay center that facilitates the transfer of incoming sensory messages to the brain cortex, using the incoming sensory information to modulate the activity of cortical neurons. As one of the largest thalamic nuclei, the mediodorsal thalamus reciprocally connects with multiple cortical and subcortical brain regions, provides a strong projection to the medial prefrontal cortex, and coordinates the activity of cortical microcircuits there during prefrontal-dependent behaviors.

Despite the importance of the mediodorsal thalamus in a range of behaviors and human disease, little is known about the physiology of the neurons in this region or how they influence behavior. In preliminary work, Brumback discovered that two populations of neurons in the mediodorsal thalamus have distinct structural and functional profiles. Based on her preliminary work and how these two thalamic circuits connect differently to the rest of the brain, she hypothesizes that each circuit is responsible for a different aspect of behavior: one circuit is responsible for social or emotional behaviors, while the other circuit modulates cognitive functions like attention and working memory.

In the funded studies, Brumback's team will directly test this model using a neuromodulation approach called optogenetics. Using flashes of light delivered directly into the brain via a fiber optic probe, she will activate or inactivate specific populations of neurons with millisecond precision while mice perform a battery of behavioral tasks. By turning each of the proposed circuits on or off during different types of behavior, she can test which circuit is important for each type of behavior. The team will also determine how individual neurons in these two thalamic circuits integrate synaptic inputs from different brain regions. The team's future work will decipher how these and other thalamic circuits are altered in autism and whether they can be modified to treat cognitive or social emotional symptoms.

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



M. Omar Iqbal, MD

The fourth annual Practical Pediatric Neuroscience Symposium, held on May 13, 2023, at Dell Children's Medical Center, featured presentations by 10 Dell Medical School faculty members from the Pediatric Neurosciences Program. Topics ranged from neuro-ophthalmological disorders to spina bifida and neurogenetics. 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. The symposium was created to enhance knowledge of pediatric neurological conditions to help general pediatric providers improve care for children with these conditions.

A SECOND OPINION

This 36-week gestation baby was transferred from another hospital because of metabolic acidosis, respiratory distress, and abnormal movements. His mother's pregnancy was complicated by maternal diabetes, premature rupture of membranes, and a three-day history of vaginal bleeding. He was born limp, lethargic, and cyanotic, with Apgar scores of 3 and 7 at one and five minutes. On day two of life, he developed metabolic acidosis and required intubation because of apnea. He exhibited abnormal facial movements and posturing that were suspected to represent seizures.

Phenobarbital and levetiracetam were halted after continuous electroencephalography showed no epileptiform discharges during the abnormal movements. Blood cultures and cerebrospinal fluid analysis were unremarkable aside from the spinal fluid protein of 240 mg/dL. An inborn error of metabolism was initially suspected because his serum ammonia was dramatically elevated at 1284 µg/dL. Urine organic acids, plasma amino acids, serum pyruvate, and carnitine were normal. However, next-generation DNA sequencing of serum confirmed evidence of Ureaplasma urealyticum, and he began azithromycin.

His hospital course was complicated and prolonged. His ammonia level increased to 1374 μ g/dL despite infusion of sodium benzoate and sodium phenylacetate, and he began continuous kidney replacement therapy. At one week of age, he was documented to have multifocal cerebellar hemorrhages on ultrasound and computed tomography. He developed a thrombosis of the right external iliac and right common femoral veins and was anticoagulated with careful monitoring of the cerebellar hemorrhages. By three weeks of age, his condition had improved and his ammonia level had fallen to 63 μ g/dL.

What caused this child's hyperammonemia? Why did he develop cerebellar hemorrhages?

See below for additional discussion.

ELECTED AND SELECTED

Pavitt Appointed Associate Chief of Pediatric Neurology



Sara Pavitt, MD, Chief of the Dell Children's Pediatric Headache Center, was appointed Associate Chief of Pediatric Neurology on June 1, 2023. Pavitt joined the program two years ago and oversaw the expansion of the pediatric headache program, created our Pediatric Neuroscience Wellness Committee during the pandemic, and created an exceptional pediatric headache fellowship. Pavitt will be responsible for integrating our neurology practitioners with the Dell Children's Medical Center outpatient clinic staff, overseeing the expanding inpatient coverage, facilitating clinical research, and developing our program's promotional and outreach strategies to increase access to care for children in Central Texas.

Clarke Participates in Health Improvement Leadership Program



Dave Clarke, MD, Chief of the Dell Children's Comprehensive Pediatric Epilepsy Center, has been selected to participate in Dell Medical School's Courageous Leadership for Health Improvement, a 15month experiential professional development program for individuals committed to health equity and improvement. The program is designed to cultivate courageous leadership, influence systems, and drive nonpartisan policies and programs that affect health and community wellness. As part of the inaugural cohort, Clarke will participate in mentorship opportunities, health justice immersion experiences, and monthly didactic sessions with local, state, and national leaders. "It has been a dream to engage with thought leaders such as Dr. Jewel Mullen, Associate Dean for Health Equity at Dell Medical School, in reducing disparities nationally," Clarke said. "I am grateful for this opportunity to continue my longtime work with the National Association of Epilepsy Centers on

Bosques Presents at International PM&R Conference

expanding access to epilepsy care."



Glendaliz Bosques, MD, Chief of Pediatric Rehabilitation Medicine and Associate Professor of Neurology at Dell Medical School, was an invited faculty speaker for the 17th World Congress of the International Society of Physical and Rehabilitation Medicine, held June 4-8, 2023, in Cartagena, Colombia. Bosques presented "Toe Walking: Mimickers of Cerebral Palsy" as an invited topic for the Spanish content session "Holistic Approach to the Pediatric Patient," coordinated by the Asociación Colombiana de Medicina Física y Rehabilitación (ACMFR). She also presented "Pediatric Considerations for Spasticity Management" during a workshop entitled "The Art and Science of Performing Chemical and Cryoneurolysis for Spasticity Management."

Roach Named to Distinguished Educators Academy



Congratulations to **E. Steve Roach, MD**, Chief of UT Health Austin Pediatric Neurosciences at Dell Children's, for being selected as a member of Dell Medical School's **Sue Cox, M.D. Academy of Distinguished Educators**. The academy was created to recognize Dell Medical School's most outstanding educators and educational leaders, to support the medical school's growing community of teachers, and to foster excellence at the leading edge of medical education. Roach will be inducted at the annual Dell Med Educational Innovation, Research & Awards Symposium on October 2, 2023.

Moodley Honored as Lecturer at Nelson Mandela School of Medicine Conference



Manikum Moodley, MD, Chief of the Pediatric Multiple Sclerosis Center and Co-director of the Dell Children's Neurofibromatosis Clinic, presented "The Pathogenesis of NF1: Genetic and Molecular Discoveries and Novel Drug Therapy" at the 2023 KZN Specialist Network Conference in Durban, South Africa, organized by the University of KwaZulu-Natal Nelson R. Mandela School of Medicine. Moodley, who received his medical degree and completed his initial training in pediatrics at the medical school, was selected based on his significant contributions to the field of child neurology. He is the third Nelson R. Mandela School of Medicine graduate invited to give the international guest lecture at the annual conference.

Freedman and Vedanarayanan Receive Teaching Awards



Daniel Freedman, DO, and **Vandana Vedanarayanan, MD**, assistant professors in the Department of Neurology, were recently honored with the 2023 Dell Medical School child neurology faculty teaching awards. Freedman was selected by the pediatric and adult neurology residents for their best resident teacher award. Vedanarayanan received the medical student teaching award, given to the child neurology faculty member with the highest average teaching scores from the students who spent time in our program. Congratulations, Drs. Freedman and Vedanarayanan!

Four Providers Named Castle Connolly Top Doctors





We are proud to announce that four of our pediatric neuroscience providers were named Castle Connolly Top Doctors: **E. Steve Roach, MD, Dave Clarke, MD**, **Elizabeth Tyler-Kabara, MD, PhD**, and **Jane Edmond, MD**. Castle Connolly Top Doctors are peer nominated through surveys sent out to tens of thousands of doctors. Those results are rigorously vetted by a research team of Castle Connolly physicians based on several factors. Castle Connolly Top Doctors represent the top 7% of all U.S. practicing physicians.

PEDIATRIC NEUROSCIENCES WELCOMES NEW COLLEAGUES

UT Health Austin Pediatric Neurosciences at Dell Children's has grown dramatically since it was founded in 2019. The multidisciplinary program now features 19 child neurologists, 17 advanced practice providers, two pediatric neurosurgeons, two pediatric physical medicine and rehabilitation specialists, eight pediatric neuropsychologists, and a pediatric neuro-ophthalmologist. We recently welcomed two new colleagues to the program.



Chelsey Ortman, MD, joins our Comprehensive Pediatric Epilepsy Center as an assistant professor of neurology at Dell Medical School. Ortman earned her medical degree from Mercer University School of Medicine in Macon, GA. After her pediatrics and child neurology training at the University of Pittsburgh Medical Center, she completed fellowships in pediatric epilepsy and advanced clinical neurophysiology at Baylor College of Medicine/Texas Children's Hospital in Houston. She is board certified in neurology with special qualification in child neurology and is a member of the American Clinical Neurophysiology Society, American Epilepsy Society, Child Neurology.



Leah Ferrante, MD, joins the Pediatric Neurosciences Program as an assistant professor in the Department of Neurology. After receiving her medical degree from West Virginia University School of Medicine, she completed a pediatrics residency and a neurodevelopmental disabilities residency at Baylor College of Medicine. Most recently, she completed a fetal and neonatal neurology fellowship at The University of Texas Southwestern Medical Center. She is certified in neurology with special qualification in child neurology and is board eligible for certification in neurodevelopmental disabilities. She is a member of the Texas Neurological Society, Newborn Brain Society, American Academy of Pediatrics, and American Academy of Neurology.

NORTH CAMPUS EPILEPSY CENTER CELEBRATES GRAND OPENING





Dell Children's Medical Center North hospital and medical office building (courtesy of Ascension Texas)

On April 12, 2023, the Dell Children's Medical Center North Campus in North Austin celebrated a community open house featuring Austin mayor Kirk Watson and leadership from Dell Children's Medical Center. The campus's medical office building houses the newest clinic of the Dell Children's Comprehensive Pediatric Epilepsy Center, which provides neurology and neurosurgery consultations, neuropsychology evaluations, and EEG studies. Services will continue to expand throughout the year. Read about the open house in the *Austin American-Statesman* and CBS Austin.

CHILDREN'S TUMOR FOUNDATION NF CLINIC NETWORK RENEWS NEUROFIBROMATOSIS CLINIC AFFILIATE CLINIC STATUS



The Dell Children's Neurofibromatosis Clinic has once again received Affiliate Clinic Status approval as a member of the NF Clinic Network of the Children's Tumor Foundation. The NF Clinic Network recognizes clinics that provide comprehensive medical care to individuals with NF, foster patient education, and encourage participation in clinical research trials and the NF registry. Our NF clinic is co-directed by pediatric neurologist **Manikum Moodley**, **MD**, former co-director of the Cleveland Clinic Neurofibromatosis Center, and pediatric neuro-oncologist Virginia Harrod, MD, PhD. **Karla Robles Lopez**, **MD**, PhD, from the Pediatric Neurosciences Program staff serves as the clinic coordinator.

A SECOND OPINION: EPILOGUE

This child was first suspected to have seizures, but continuous electroencephalography showed no epileptiform discharges even during the movements. His serum ammonia level was dramatically elevated, but subsequent testing failed to identify an inborn error of metabolism. The cause of his hyperammonemia was quickly clarified by the presence of Ureaplasma urealyticum. These organisms release substantial amounts of ammonia during urea hydrolysis, sometimes leading to clinical hyperammonemia.^{1,2}

The reason for the multifocal cerebellar hemorrhages is less certain. Cerebellar hemorrhages have been documented in children with organic acidemias.³⁻⁵ Propionic, methylmalonic, and isovaleric acidemia typically present in babies as acute metabolic decompensation and encephalopathy, often associated with hyperammonemia. We suspect that severe hyperammonemia, whatever its origin, may promote cerebellar hemorrhage in neonates. However, most of these children are seriously ill, so it is possible that other factors could be responsible.

When seen at 13 months of age, the child was thriving. He had experienced no seizures or periods of lethargy. He was starting to walk, playfully interacting, and saying several typical words.

Final Diagnosis (1) Severe hyperammonemia due to Ureaplasma urealyticum sepsis and (2) bilateral cerebellar hemorrhages, possibly related to hyperammonemia.

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- 3. Dave P, Curless RG, Steinman L. Cerebellar hemorrhage complicating methylmalonic and propionic acidemia. *Arch Neurol* 1984;41:1293-1296.
- 4. Velasco-Sanchez D, Gomez-Lopez L, Vilaseca MA, et al. Cerebellar hemorrhage in a

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patient with propionic acidemia. *Cerebellum* 2009;8:352-354.5. Fischer AQ, Challa VR, Burton BK, McLean WT. Cerebellar hemorrhage complicating

Register for the International Pediatric Headache Didactic Series

The International Pediatric Headache Didactic Series, a partnership between Dell Children's Pediatric Headache Center and Texas Children's Hospital Headache Clinic, is held every first and third Friday from 11:00 a.m. - 12:00 p.m. CT throughout the 2023-2024 academic year. CME credits are available. Sign up for the series or fill out

the speaker interest form if you are interested in speaking.

The University of Texas at Austin Dell Medical School is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The University of Texas at Austin Dell Medical School designates this live activity for a maximum of 1.00 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The Neurotransmitter, 2023, Issue 2

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