NRC *newsletter*

The Neuroanatomy of Bilingualism in Childhood

Kelly A. Vaughn, PhD

Vaughn

Abstract: In Houston, over 50% of children (ages 5-17) speak a language other than English, but this population (i.e., bilingual children) remains understudied in research on language network development in the brain. We compared cortical thickness data from bilingual and monolingual children (ages 9-10) in the Adolescent Brain and Cognitive Development study, a large NIH-funded project that aims to track brain and cognitive development in nearly 12,000 children across adolescence. We found that bilingual children had thinner cortex than monolingual children across a widespread network of brain regions, and thicker cortex in specific language and cognitive networks was associated with higher English proficiency and more English use for bilinguals. Results of this research suggest that cortical structures may develop differently for bilingual and monolingual children; therefore, additional theories are needed that reflect the unique brain development of bilingual children.

The fact that we were all born unable to speak or understand language, and we are now, as adults, capable of communicating and understanding complex ideas is an amazing developmental feat. What may be even more impressive is that some people who, like all of us, were born unable to speak or understand language, go on to speak, write, read, and understand *multiple* languages. In Houston, over 50% of children (ages 5-17) speak a language other than English (U.S. Census Bureau, 2019). Developmental neuroscientists now have theories about how the brain supports language development, with a focus on early connections from the temporal to frontal lobe – supporting bottom-up auditory/sensory processing of language – and later connections from the frontal to temporal lobe, through the parietal lobe – supporting top-down analysis of language (Friederici et al., *Nat. Hum. Behav.* 1:713, 2017; Skeide & Friederici, *Nat. Rev. Neurosci.* 17:323, 2016). Still, we do not yet have well-defined theories about how the brain supports *bilingual* (i.e., multiple language) development.

There is reason to believe that bilingual brain development may be different than monolingual brain development. A recent study compared measures of brain structure from bilingual and monolingual children between the ages of 3 and 21 years

Neuroimaging Predictors of Psychological Health after Pediatric Traumatic Brain Injury

Dana M. DeMaster, PhD & Linda Ewing-Cobbs, PhD

DeMaster   **Ewing-Cobbs**

Abstract: Traumatic Brain Injury (TBI), a disorder of brain connectivity, is associated with significant long-term psychological health consequences. In clinical practice, an early intervention model is found to decrease health consequences of TBI. There is growing awareness that pediatric TBI results in reduced health-related quality of life with effects on psychological health persisting years following the initial injury. Nevertheless, there is a paucity of information regarding the characteristics of these problems and their association with injury characteristics and demographic variables, such as age at injury. It is important to identify specific characteristics that might influence brain structure and development and result in increased risk for adverse neuropsychological outcomes after pediatric TBI. This article provides an overview of ongoing research at the UTHealth Children's Learning Institute investigating links between atypical prefrontal-limbic circuitry and behavioral outcomes following pediatric TBI.

Each year in the United States, approximately 1.5 million children seek medical treatment for Traumatic Brain Injury (TBI). TBI, a disorder of brain connectivity, is associated with significant long-term psychological and physical health consequences. Pediatric TBI may disrupt the typical course of brain development, leading to cascading effects on health-related quality of life. Unfortunately, it remains difficult to predict which children are at greatest risk for health and behavioral problems after a TBI because both neuroimaging and health outcomes have a high degree of heterogeneity. Consequently, targeted investigation of the impact of injury on both brain networks and behavioral outcomes at different stages of development may improve prediction of children likely to experience persistent neurobehavioral symptoms.

Injury-Related Changes to Brain Networks

Our research team at UTHealth McGovern Medical School's Children's Learning Institute, including Drs. Linda Ewing-

UTHealth | Neuroscience Research Center
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Health Science Center at Houston

Director's Column

From the Director, John H. Byrne, PhD

Providing educational opportunities for children has always been one of the greatest joys of the UTHealth Neuroscience Research Center's outreach efforts. No one knows this feeling better than the faculty and staff at the Children's Learning Institute (CLI) at UTHealth whose pivotal work provides life-changing effects for children and their families every day. The CLI was formed from several programs in 2003 by the founding director, Susan H. Landry, PhD, the Albert and Margaret Alkek Endowed Chair in Early Childhood and Michael Matthew Knight Memorial Professor. Designated as the Texas State Center for Early Childhood Development, the CLI has received enormous support and funding from the state of Texas, as well as many other federal institutions. Currently lead by Co-Directors April Crawford, PhD, associate professor of pediatrics, and Tricia Zucker, PhD, professor of pediatrics, an extensive focus on clinical research has continued to serve as the foundation of the CLI's initiatives, programs, and resources.

We are pleased to highlight neuroscience research at the CLI in this edition of the NRC Newsletter, which features scientific articles by Drs. Linda Ewing-Cobbs, Dana DeMaster, and Kelly Vaughn. In one featured article, co-authored by Linda Ewing-Cobbs, PhD, professor, and Dana DeMaster, PhD, assistant professor, provides an overview of ongoing research at the CLI investigating links between atypical prefrontal-limbic circuitry and behavioral outcomes following pediatric traumatic brain injury (TBI). Indeed, the primary research goals of Dr. Ewing-Cobbs has included the examination of the trajectory of neuroanatomical changes, psychological health, and behavioral outcomes following TBI. This research has allowed her to characterize physical and psychological health needs as they relate to decisions for public health policies and guidelines following TBI. Her work also expands to translational studies using cellular therapies to repair neural damage after injury. Dr. Ewing-Cobbs also serves on the Executive Committee of the NRC and as the Director of Clinical Programs for the CLI where she oversees the operations of multidisciplinary clinics and provides diagnostic assessment services to children and adults with acquired or developmental differences

As described in the featured article, pediatric TBI research is also an important part of Dr. DeMaster's research program which investigates typical and atypical pediatric brain development using neuroimaging techniques such as MRI, fMRI, and DTI. Her work examining neuroplasticity, structural brain development, and childhood brain maturation as it relates to injury, learning and memory has greatly contributed to the overall research programs at the CLI. She is a principal investigator on an NIH-funded project investigating the impact of PALS (Play and Learning Strategies) intervention on brain development in toddlers who were born prematurely. Drs. Susan Landry (see below) and Johanna Bick (University of Houston) are also PIs on this grant.

In another featured article is by Kelly Vaughn, PhD, assistant professor of pediatrics, who has also been a part of this PALS intervention team, and has worked with Drs. Ewing-Cobbs and DeMaster to investigate the neural outcomes of pediatric TBI using neuroimaging techniques. In this edition of the Newsletter however, she focuses on her primary research investigating the neuroanatomy of bilingualism in childhood, and the relationship between language and cognitive development in bilingual children. As co-investigator on the project Adolescent Brain Cognitive Development (ABCD) funded by the US Department of Education Institute of Education Sciences (IES), Dr. Vaughn has collaborated with PIs, Susan Landry, Tricia Zucker, PhD (see below) and Maria Carlo, PhD (University of South Florida) to examine the combined impacts of classroom intervention and PALS intervention on Spanish-English bilingual development. Dr. Landry's research has extensively examined neurological development from prenatal and infancy stages through adolescence and adulthood, in cases of normal development, injury, diseases, and disorders. She has also greatly contributed to projects examining best practices for parent-child and early childhood classroom intervention studies.

Tricia Zucker, PhD is a former classroom teacher whose research focusses on the development and evaluation of innovative classroom curricula and professional development resources. Dr. Zucker currently directs trials funded by the IES, "Developing Talkers: Building Effective Teachers of Academic Language Skills," "Reading Rules," and "Teaching Together." In addition, she directs a current IES Postdoctoral Research Training program. Furthermore, research funded by the National Science Foundation, in partnership with the Children's Museum in Houston, is allowing Dr. Zucker to modify approaches aimed at sparking an early interest in science, technology, engineering and math (STEM) for pre-kindergarten children.

While we cannot highlight all the incredible research happening at the CLI, we invite you to visit their website to learn more about their ongoing and influential research-based programs. The CLI also makes their education resources available through their website, including Child Progress Monitoring Tools & Assessments, Continuous Quality Improvement Tools, Curriculum & Activities for School and Home, Professional Development & Training, and State Early Learning Guidelines Training Resources.

This year, we enjoyed the return of our largest event, "Brain Night for Kids," held annually at The Health Museum. Like most in-person events over the last few years, this program has previously been canceled due to COVID-19 concerns. This particular event is an important component of our "Brain Awareness Week" efforts, a small part of the annual global campaign organized by the Dana Foundation. We hope you enjoy looking through some of the photos from this joyful and exciting evening.

In addition, we saw the return of an in-person annual Public Forum, moderated by Vineeth John, MD, MBA, professor and vice chair for education in the department of psychiatry and behavioral sciences, where he is the director of the Geriatric Psychiatry Section. The timely` topic was on Alzheimer's Disease and Related Dementias. Finally, we enjoyed a long-awaited visit from Cameron Carter, MD, a distinguished professor and presidential chair in neuroscience at the University of California at Davis. We look forward to reporting on these two events in the next issue of the *Newsletter*.

old (Pliatsikas et al., *Brain Struct. Funct.* 225:2131, 2020). Results revealed an interaction between language group (i.e., bilingual/monolingual) and age. Specifically, until early adolescence (i.e., ages 10-13), bilinguals had thinner cortex than monolinguals across multiple frontal, temporal, parietal regions, but from mid-adolescence through early adulthood, bilinguals had thicker cortex than monolinguals in the same regions. These findings suggest that brain development is not identical between bilinguals and monolinguals, but they also raise additional questions about the bilingual experiences and skills that lead to these language group differences.

To address these questions, my collaborators and I compared measures of brain structure from bilingual and monolingual children between the ages 9 and 10 who were part of the NIH-funded Adolescent Brain and Cognitive Development (ABCD) study (https://abcdstudy.org) (Vaughn et al., *Neuroimage* 243:118560, 2021). The data from the ABCD study is publicly available to researchers through annual data releases on the National Institute of Mental Health (NIMH) Data Archive (https://nda.nih.gov/). We reduced the sample to participants with usable MRI data and usable English vocabulary data. Then, we identified bilingual children as those whose parents reported that their native language was not English or a language other than English was used in their home at least half of the time. We identified monolingual children from the larger sample as those whose parents reported that their native language was English; English was used more than any other language in the home; and the child was never enrolled in a dual language program at school. We further restricted the bilingual sample to children who self-reported speaking a language other than English, and we further restricted the monolingual sample to children who self-reported that they only speak English. Then we selected a subsample of bilinguals and monolinguals who were matched on age, sex, pubertal status, parent education, household income, non-verbal IQ, and handedness. This led to a final sample of 678 bilingual children and 678 monolingual children.

We conducted statistical analysis using the analysis of covariance (ANCOVAs) method to compare cortical thickness from bilinguals and monolinguals while controlling for age, sex, pubertal status, household income, parent education, non-verbal IQ, and handedness. This addressed the question of how the brain structure of bilingual and monolingual children differed at ages 9-10 while controlling for many other potential confounds. Then, we conducted multiple regression within bilinguals focused on English vocabulary and English use (scale of 0-8, where 0 = child only uses the other language with family and friends; and 8 = child only uses English with family and friends), while controlling for the same covariates described above. This model allowed us to determine which, if any, of the differences in brain structure between bilinguals and monolinguals could be explained by level of English skill (i.e., vocabulary) and amount of English use with family and friends.

Our results indicated widespread cortical thickness differences between bilingual and monolingual children, even after controlling for potential confounds. Of the 70 cortical regions examined, 47 differed significantly between bilinguals and monolinguals. The largest effect sizes were observed in the bilateral superior temporal gyri, bilateral parietal regions (e.g., paracentral gyrus, postcentral gyrus, supramarginal gyrus), bilateral occipital regions (i.e, pericalcarine gyrus and lateral occipital gyrus), and left frontal regions (i.e., inferior frontal gyrus and middle frontal gyrus, anterior cingulate cortex). For the majority of these differences, bilinguals had thinner cortex than monolinguals. Further, bilinguals with higher levels of English vocabulary had thicker cortex in frontal and temporal regions, which are typically associated with the "language network" in the brain (Friederici & Gierhan, *Curr. Opin. Neurobiol.* 23:250, 2013). In addition, bilinguals who used English more often with family and friends had thicker cortex in some temporal, parietal, and frontal regions, reflecting both the language network and a top-down cognitive network (Abutalebi & Green, *J. Neurolinguistics* 20:242, 2007; Friederici et al., *Nat. Hum. Behav.* 1:713, 2017; Friederici & Gierhan, *Curr. Opin. Neurobiol.* 23:250, 2013; Green & Abutalebi, *J. Cog. Psych.* 25:515, 2013; Skeide & Friederici, *Nat. Rev. Neurosci.* 17:323, 2016). **Figure 1** shows the language network and the top-down cognitive network in the left hemisphere.
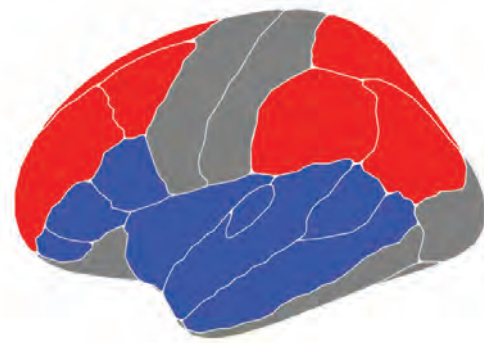

Figure 1. *Regions of the brain involved in the "language network" (blue; Friederici & Gierhan, Curr. Opin. Neurobiol. 23:250, 2013) and a top-down cognitive network (red; Abutalebi & Green, J. Neurolinguistics 20:242, 2007; Green & Abutalebi, J. Cog. Psych. 25:515, 2013). Both networks seem to be related to bilingual experiences and skills, but more research is needed to understand how these networks develop during childhood.*

These findings lead to two main conclusions. The first is that there are widespread differences in cortical thickness between bilinguals and monolinguals that are not fully explained by English vocabulary or English use and cannot be attributed to the other confounding variables we controlled for (i.e., age, sex, pubertal status, parental education, household income, non-verbal IQ, and handedness). The second is that having higher English vocabulary and using more English with family and friends is related to thicker – more monolingual-like – cortex in regions of the brain related to language. This reinforces the idea that the language network in the brain may develop differently for bilingual and monolingual children, and therefore theories are needed that reflect the unique brain development of bilingual children.

grants&awards

Tatiana Barichello, PhD, associate professor of psychiatry and behavioral sciences, and Rodrigo F. Morales, PhD, associate professor of neurology, received a multi-year grant from the National Institutes of Health (NIH)/National Institute on Aging (NIA) for a project titled, "Infection-driven mechanisms associated with Alzheimer's disease pathology."

Alexandra Czap, MD, assistant professor of neurology, won the Society for Vascular and Interventional Neurology Junior Investigator Award, as well as the award for Best Abstract.

William Dowhan, PhD, professor and John S. Dunn Chair in Biochemistry and Molecular Biology, received the 2022 Anatrace Membrane Protein Award at the Biophysical Society national meeting in February. Dr. Dowhan was recognized for his seminal contributions to understanding lipid regulation of integral membrane protein topology.

Valentin Dragoi, PhD, professor of neurobiology and anatomy and Rochelle and Max Levit Distinguished Professor in the Neurosciences, received a grant from the NIH/National Eye Institute (NEI) for a 5-year project titled, "The impact of sleep on network coding and perceptual performance." This grant will examine how sleep influences the processing and coding of sensory information in non-human primate visual cortex.

Albert J. Fenoy, MD, associate professor of neurosurgery and Director of the Deep Brain Stimulation Program, received a R01 grant from the NIH/National Institute of Neurological Disorders and Stroke (NINDS) for a project titled, "Elucidating the temporality of structural and functional connectivity changes in essential tremor after successful deep brain stimulation to the dentato-rubro-thalamic tract."

Gabriel R. Fries, PhD, assistant professor of psychiatry and behavioral sciences, received funding through the American Foundation for Suicide Prevention (AFSP) Young Investigator Grant for a project titled, "The neuronal transcriptome of suicide in bipolar disorder." This study will investigate the transcriptomic alterations in postmortem prefrontal cortex from bipolar disorder subjects who died of suicide or of other causes and integrate those with methylomic and genomic markers.

Angela Heads, PhD, associate professor of psychiatry and behavioral sciences, was awarded a Texas Developmental Center for AIDS Research grant for HIV Prevention research for her project, "Removing barriers to effective HIV prevention strategies for individuals with problematic substance use or substance use disorders."

The McGovern Medical School honored four faculty members with the 2021 Women's Faculty Forum Excellence Awards, two of which are NRC Members. Angela Heads, PhD, associate professor of psychiatry and behavioral sciences, received the John P. and Kathrine G. McGovern Distinguished Faculty Award – Clinical Service. Ruth Heidelberger, MD, PhD, professor of neurobiology and anatomy and Frederic B. Asche Chair in Opthalmology, received the John P. and Kathrine G. McGovern Distinguished Faculty Award from the Women Faculty Forum – Research. These awards celebrate outstanding contributions made by women faculty at McGovern Medical School.

Melba Hernandez-Tejada, PhD, DHA, associate professor of psychiatry and behavioral sciences, received a grant from the VA-Victims of Crime Act Formula Grant Program for her project titled, "Serving elder abuse survivors via elder to elder support + home-based telehealth."

Benson Irungu, PhD, assistant professor of psychiatry and behavioral sciences, received a grant from the NIH/National Institute on Drug Abuse (NIDA) for a project titled, "A software product that empowers individuals affected by substance use disorders and their care teams with health and social resources."

Amanda Jagolino-Cole, MD, associate professor of neurology, received the 2021-22 American Board of Psychiatry and Neurology (ABPN) Faculty Innovation in Education Award. The award supports the development of innovative education and/or evaluation projects that promote effective residency/fellowship training or lifelong learning of practicing psychiatrists and neurologists.

NRC Members Vasanthi Jayaraman, PhD, professor of biochemistry and molecular biology, and Theresa M. Koehler, PhD, Chair of the Department of Microbiology and Molecular Genetics, as well as Juan Fueyo, MD, professor of neuro-oncology at MD Anderson Cancer Center, were named 2021 American Association for the Advancement of Science (AAAS) Fellows. AAAS Fellows are elected by their peers, a tradition that began in 1874 in order to recognize invaluable contributions to science and technology.

Eunhee Kim, PhD, assistant professor of neurosurgery, received a grant from the Brain Aneurysm Foundation to support a project titled, "The role of KRAS mutation in aneurysm formation and rupture in brain arteriovenous malformations." She also received a Cerebrovascular Research Grant from the Aneurysm and AVM Foundation (TAAF) for a project titled, "Targeting KRAS signaling in brain arteriovenous malformations."

Deborah Little, PhD, professor of psychiatry and behavioral sciences and director of research for the Trauma and Resilience Center, received a grant from the Department of Defense Awarding Office – USAMRAA for a project titled, "Expanding the characterization and application of clinical MRI markers in Gulf War illness."

Louise McCullough, MD, PhD, professor and Roy M. and Phyllis Gough Huffington Distinguished Chair in the Department of Neurology, and Fudong Liu, MD, associate professor of neurology and Director of Translational Stroke Research, were awarded a grant from the NIH to study sex differences in COVID-19 outcomes. This study aims to identify patients at risk for developing chronic consequences of COVID-19 infection and discover potential underlying mechanisms leading to neuropsychiatric symptoms.

Louise McCullough, MD, PhD, received the 2021 C. Miller Fisher, MD Neuroscience Visionary Award from the American Heart Association/American Stroke Association (AHA/ASA) at the 16th Annual NorthEast Cerebrovascular Consortium Summit in October. The award is given annually to an individual in the field of neuroscience who has significantly influenced the ASA's mission, made clear and lasting contributions to neuroscience,

and made major contributions to the identification and/or treatment of stroke patients.

Rodrigo F. Morales, PhD, associate professor of neurology, has been awarded a grant from the US Department of Agriculture (USDA)/ Animal and Plant Health Inspection Service (APHIS) for a project titled, "In vitro and in vivo evaluation of CWD prions in feral swine." The goal of this project is to identify the presence of infectious prions in biological samples derived from wild feral swine using PMCA (Protein Misfolding Cyclic Amplification) and bioassays.

Eunsu Park, PhD, instructor of neurosurgery, received the Stroke Basic Science Award at the American Stroke Association's (ASA) International Stroke Conference 2022 for his research uncovering the underlying pathology of brain arteriovenous malformations.

Swati Pradeep, DO, assistant professor of neurology, was honored by the Harris Health System for "ServiceFIRST Standard of Behavior - Friendliness, Integrity, Responsibility, Satisfaction, and Teamwork."

Anjail Z. Sharrief, MD, MPH, associate professor of neurology and Director of Stroke Prevention, UTHealth Institute of Stroke and Cerebrovascular Disease, was awarded a grant from the NIH/National Institute on Minority Health and Health Disparities to test whether telehealth improves racial disparities in outcomes for stroke survivors. This study is a collaborative effort among the Cizik School of Nursing, School of Public Health, School of Biomedical Informatics, and Institute for Stroke and Cerebrovascular Disease.

Faculty members in the Louis A. Faillace, MD, Department of Psychiatry and Behavioral Sciences have received grants from the Baszucki Brain Research Fund, partnering with the Milken Institute, aimed at funding innovative research in bipolar disorder. **Jair Soares, MD, PhD**, professor and Pat R. Rutherford, Jr. Chair in Psychiatry, received a grant for his project titled, "Developing brain imaging analysis expertise for personalizing transcranial electric stimulation in anhedonia treatment of patients with bipolar depression." **Marsal Sanches, MD, PhD**, associate professor, and Alexandre Paim Diaz, MD, PhD, are co-investigators on the project. **Rodrigo Machado-Vieira, MD, PhD**, professor, received a grant for his project titled, "A randomized, placebo controlled trial of the fatty acid amide hydrolase inhibitor palmitoylethanolamide in bipolar depression." **Gabriel Fries, PhD**, received a grant for his project titled, "Targeting accelerated aging in bipolar disorder: calorie restriction mimetics as a novel treatment strategy."

Argy Stampas, MD, associate professor of physical medicine and rehabilitation and Spinal Cord Injury Medicine Research Director at TIRR Memorial Hermann, received funding from Mission Connect, a project of TIRR Foundation, for a project titled, "Can urine biomarkers characterize the developing neurogenic bladder in acute spinal cord injury?"

Antonio L. Teixeira, MD, PhD, professor of psychiatry and behavioral sciences, and **Venugopal Venna, PhD**, assistant professor of neurology, received a grant from the NIH/NIA for a project titled, "Kynurenine pathway in the pathogenesis of post-stroke depression in aged mice."

Andrey Tsvetkov, PhD, assistant professor of neurology, was awarded the Glenn Foundation for Medical Research Breakthroughs in Gerontology (BIG) Award from the American Federation for Aging Research (AFAR). Collaborating with **Nitin Tandon, MD**, professor and chair ad interim of the Vivian L. Smith Department of Neurosurgery, this award supports projects that offer significant promise of yielding transforming discoveries in the fundamental biology of aging. The project is titled, "G-quadruplex RNA and G-quadruplex RNA helicases in senescent astrocytes."

Jiaqian Wu, PhD, associate professor of neurosurgery, received a renewal of her R01 grant from the NIH/NINDS titled, "Identifying novel molecular targets for chronic SCI." The major goal of this project is to identify novel potential therapeutic targets for chronic spinal cord injury (SCI) gliosis using purified astrocytes in mouse contusive SCI models, and test their functions. In addition, she is co-investigator on an award from the NIH/NINDS for a project titled, "Role of TFEB in Tauopathy," working with the project's PI, Hui Zheng, PhD, from Baylor College of Medicine.

Jin Yoon, PhD, assistant professor of psychiatry and behavioral sciences, received a two-year grant from the National Institute on Alcohol Abuse and Alcoholism for a project titled, "Assessment of pioglitazone to address stress reactivity and alcohol use disorder." Co-Investigators include **Scott Lane, PhD**, professor and vice chair for research, and **Michael Weaver, MD**, professor and medical director at the Center for Neurobehavioral Research on Addictions, in the Department of Psychiatry and Behavioral Sciences.

Degui Zhi, PhD, associate professor at UTHealth School of Biomedical Informatics, received funding from the NIH/NIA for a grant titled, "Genetics of deep learning-derived neuroimaging endophenotypes for Alzheimer's disease." Collaborators on the project from the School of Biomedical Informatics include **Han Chen, PhD**, **Luca Giancardo, PhD**, and **Assaf Gottlieb, PhD**, as well as **Myriam Fornage, PhD**, from the Institute of Molecular Medicine, and Shuiwang Ji, PhD, from Texas A&M University.

Graduate Students & Postdoctoral Fellows

Lais Bhering Martins, PhD, a postdoctoral fellow under mentorship of **Antonio L. Teixeira, MD, PhD**, professor of psychiatry and behavioral sciences, was selected for the 2022 International Society for CNS Clinical Trials and Methodology (ISCTM) New Investigator Award Program. Ana Paula Costa, PhD, and Lais Bhering Martins, PhD, postdoctoral fellows from the same department also recently received separate New Investigator Awards from the ISCTM. Acceptance into this society includes a two-year mentorship, the ability to attend conferences, and a review on how they are conducting their respective studies.

My future research aims to examine these relationships longitudinally across childhood and adolescence, as brain structure at ages 9-10 does not tell the complete story about childhood language network development. While the ABCD study is a great source of longitudinal MRI data from a large sample of American children, the study was not designed to examine bilingual development, so some of the goals of my future research are to include more information about the age at which children were first exposed to their second language; language assessments that provide information about both English and the other language (e.g., Spanish); and functional neuroimaging methods (e.g., fMRI) that can capture neural responses during a language task in order to fully understand how different bilingual experiences and skills relate to brain development.

About the Author

Kelly A. Vaughn, PhD *is an assistant professor of pediatrics at the UTHealth Children's Learning Institute. She received an undergraduate degree in Psychology from High Point University and a master's degree in Psychology from the University of Houston (UH). She then obtained a doctorate degree in Developmental, Cognitive, and Behavioral Neurosciences from UH. During her graduate training, her research focused on how the brain supports language and cognition in adult bilinguals and monolinguals. She then received postdoctoral training in pediatric neuroimaging under the mentorship of Dr. Dana DeMaster at UTHealth. Dr. Vaughn's current research is broadly focused on supporting the development of bilingual children. She is interested in the neural underpinnings of typical and atypical language development and the relationship between language development and cognitive development for bilingual children.*

In*the*Spotlight
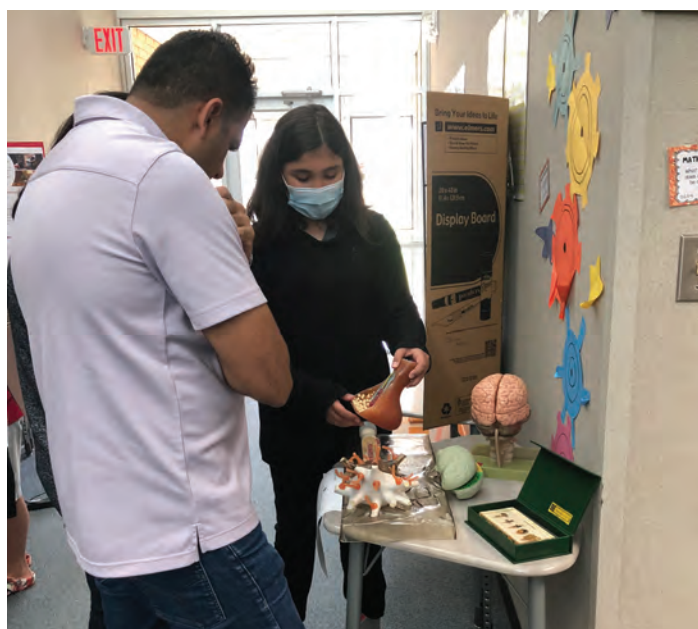
Inspired by UTHealth Brain Night for Kids, Tuba Askoy, a graduate student at MD Anderson Cancer Center, and her daughter created a smaller version of this program for their local school. They utilized pieces from the NRC's Lending Library to educate their school community about brain awareness. These materials are available for all UTHealth NRC Members to use for teaching and outreach opportunities, and are used throughout the year.

Cana Quave (center), a graduate student in the laboratory of **Fabricio H. Do Monte, PhD (left)**, assistant professor of neurobiology and anatomy, received the Terry J. Crow, PhD Scholarship in Neuroscience. Quave received the scholarship for his outstanding scholastic achievements. Mr. Quave's thesis research investigates the neural mechanism by which drugs of abuse encourage risk-taking behavior. Pramod Dash, PhD, (right) Chair of the Department of Neurobiology And Anatomy, presented the award to Mr. Quave.

Faculty judges from UTHealth, Baylor College of Medicine, and Rice University.

Rabab Al-Lahham, PhD, received third place for her poster in the postdoctoral fellow category.

Undergraduate, graduate, and medical students, as well as postdoctoral fellows and research scientists, presented their recent findings at the Poster Session.

Dr. Jack Byrne, Director of the UTHealth NRC, presents the Dee S. and Patricia Osborne Endowed Scholarship in the Neurosciences to Rachel van Drunen, who received the 1st place prize for a poster by a UTHealth Graduate Student.

UTHealth graduate students Kathryn Snyder (left) and Samantha Debes (right) received second and third place prizes, respectively, and were presented with their award by Dr. Jack Byrne.

27TH ANNUAL NEUROSCIENCE POSTER SESSION

Saturday, December 4, 2021 | UTHealth Cooley University Life Center

The NRC was pleased to host the 27th Annual Neuroscience Poster Session this year after needing to cancel the multi-institutional event last year due to COVID-19 concerns. Faculty, postdoctoral fellows, graduate and medical students, as well as undergraduate students, from three Houston institutions gathered to present and discuss their neuroscience research. The large group included the Departments of BioSciences, Psychology, and Electrical and Computer Engineering at Rice University, the Department of Neuroscience at Baylor College of Medicine, and the UTHealth Neuroscience Research Center.

Eighty-three research posters were presented to faculty judges from each institution and prizes were awarded for the best poster presentations in each category. For a complete list of winners, please visit our website.

Local businesses and restaurants generously provided door prizes and gift certificates for those presenting posters. Congratulations to all of the winners from the 27th Annual Neuroscience Poster Session!

news&information

Please visit our website for a list of recent publications from UTHealth NRC Faculty Members.

McGovern Medical School at UTHealth has recently been designated as a NORD (National Organization for Rare Disorders) Rare Disease Center of Excellence, joining a highly select group of medical centers nationwide whose goal is to foster knowledge sharing between experts across the country, connect patients to appropriate specialists regardless of disease or geography, and improve the pace of progress in rare disease diagnosis, treatment, and research.

The University of Texas System launched the new The University of Texas Education and Research Center at Laredo. Through this new initiative, the UTHealth School of Biomedical Informatics is offering graduate programs to students and professional development and training opportunities for health care providers in the region.

The Faillace Department of Psychiatry and Behavioral Sciences will hosted their 2022 UTHealth Houston Psychiatry Update Conference, titled "Hot Topics: Child and Adolescent Psychiatry," in April. Various topics in child psychiatry were discussed, including attention-deficit/hyperactivity disorder (ADHD), Autism spectrum disorder (ASD), mood and anxiety disorders, and pediatric trauma research. Karen Wagner, MD, PhD, from UTMB Health in Galveston will be one of the keynote speakers at the conference.

The McGovern Medical School Women Faculty Forum hosted a virtual edition of its fourth annual International Day of Women and Girls in Science Symposium in February. The symposium highlighted accomplished faculty including NRC member, **Patricia Butler, MD**, Professor Emerita in the Faillace Department of Psychiatry and Behavioral Sciences.

Alexandra Czap, MD, assistant professor of neurology, and **Sunil Sheth, MD**, associate professor of neurology, from the UTHealth Houston Institute for Stroke and Cerebrovascular Disease were recently elected to the Society of Vascular and Interventional Neurology's (SVIN) Board of Directors. The mission of SVIN is to advance the fields of vascular and interventional neurosciences to improve outcomes of patients with stroke and cerebrovascular diseases via research, innovation, and education. Other representatives from the Stroke Institute serving on SVIN committees include Louise **McCullough, MD, PhD**, and **Amanda Jagolino, MD**.

Joao de Quevedo, MD, PhD, professor of psychiatry and behavioral sciences, was recently promoted to fellow status in the American College of Neuropsychopharmacology (ACNP),

an international professional organization comprised of leading brain scientists.

Amanda Helminiak, MD, assistant professor, and Callie McCool, MD, fourth-year child psychiatry fellow in the Faillace Department of Psychiatry and Behavioral Sciences, were recently elected to the Alpha Omega Alpha Honor Medical Society (AOA). The AOA is a national medical honor society that recognizes medical professionals for their dedication to the profession and the art of healing.

Stella Kim, PsyD, assistant professor of neurology, was appointed as an officer to serve a 3-year term for the Society for Clinical Neuropsychology, Division 40 of the American Psychological Association Women in Neuropsychology Committee.

Micah Knobles, MD, assistant professor of psychiatry and behavioral sciences, was recently elected to his second term as president of the Houston Psychiatric Society, a local professional association for psychiatrists in the Greater Houston area.

Marsal Sanches, MD, PhD, associate professor, along with colleagues from the Faillace Department of Psychiatry and Behavioral Sciences, have established a specialized bipolar disorder clinic, offering various types of clinical treatment including vagus nerve stimulation, medication in clinical trials, and other treatments.

Jair Soares, MD, PhD, professor and Pat R. Rutherford, Jr. Chair in Psychiatry, was recently named the president of the American Association of Chairs of Departments of Psychiatry (AACDP). AACDP represents chairs in departments of psychiatry of medical schools across the United States, regardless of size with a mission to promote excellence in psychiatric education, research, and clinical care. In addition, the organization advocates for health policy to create appropriate and affordable psychiatric care for all.

GQ Zhang, PhD, vice president and chief data scientist for UTHealth, **Samden Lhatoo, MD**, professor and the John P. and Kathrine G. McGovern Distinguished Chair in neurology, and **Shiqiang Tao, PhD**, assistant professor and assistant director for the Texas Institute for Restorative Neurotechnologies, recently developed the Epilepsy Tracking and Optimized Management Engine (EpiToMe) platform which will allow doctors to streamline and better manage care of epilepsy patients.

Cobbs, Dana DeMaster, and Kelly Vaughn, contributed several reports using diffusion tensor and/or functional MRI data gathered seven weeks following TBI of varying severity in children ages 8 to 15 years. These reports examined disrupted integrity and connectivity of large-scale topological brain network organization following TBI and investigated the relation of neuroimaging metrics to a variety of neurobehavioral outcomes. Neuroimaging data were also acquired from an age-matched healthy control group and an extracranial injury group (EI). Children in the EI group experienced a bodily injury seven-weeks prior to testing and provide a comparison group with similar characteristics of injury such as premorbid behavioral problems and nonspecific effects of traumatic injury, including post-traumatic stress.

We applied graph theory to developmental MRI diffusion data and found reduced network efficiency that clustered around later-to-develop prefrontal and limbic neurocircuitry after pediatric TBI, and to a lesser degree after extracranial injuries compared to healthy children (Watson et al., *Neuroimage Clin.* 21:101673, 2019). In collaboration with Dr. Marina Vannuci at Rice University, we applied a novel method of characterizing brain connectivity networks based in Bayesian statistics. The approach, Bayesian Multi-Subject Vector Autoregressive Modeling, used white matter integrity as priors to evaluate effective connectivity, defined as the time-dependent relationship in fMRI activity between two brain regions. We examined the default mode network (DMN), which consists of the posterior cingulate cortex, precuneus, inferior parietal lobule, orbitofrontal cortex, medial prefrontal cortex, parahippocampal gyrus, and the inferior temporal gyrus. Because the DMN involves relatively long-distance and interhemispheric connections, it may be particularly vulnerable to injury. Activity in the DMN has been observed to be lower when individuals are actively engaged in a task, but higher during wakeful rest. Healthy controls had unique positive connectivity that mostly emerged from the inferior temporal lobes while children with TBI had unique effective connectivity among "orbitofrontal" and "parietal regions" (see **Figure 1**). Connectivity in these regions differed by TBI severity and was associated with persisting symptoms of anxiety and post-concussion symptoms (e.g. headache, sleeplessness, fatigue; Vaughn et al., *Eur J Neurosci.* 55:318, 2022).

Injury-Related White Matter Microstructure and Psychological Health

After experiencing injury to the brain or body, a significant portion of patients develop post-traumatic stress symptoms and/or new behavior problems. We used diffusion tensor tractography (DTT) to explore the effect of pediatric injury on limbic prefrontal pathways in relation to psychological health outcomes. DTT allows quantitation of the nature and extent of microstructural changes in both white and gray matter in relation to developmental changes, stress, and physical injury. DTT metrics include fractional anisotropy (FA) and mean diffusivity (MD). In healthy tissue, age-related increases in myelination causes axons to be more tightly packed, which results in increased FA in white matter. Reduced or lower FA is associated with processes of axonal degeneration and demyelination
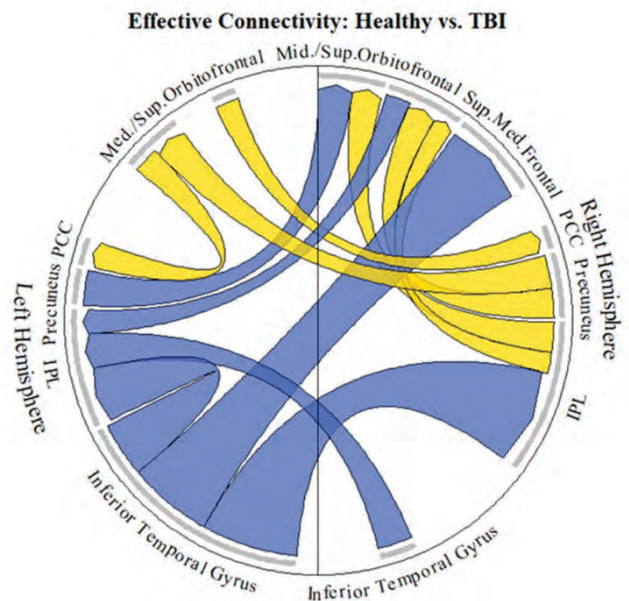

Figure 1. *Connectogram showing unique connectivity for 8-15-year-olds 7-weeks following mild-severe TBI (yellow) and aged-matched healthy control group (blue). The width of each line reflects relative connectivity strength such that wider lines indicate region pairs with higher connectivity. The origin of each connection pair is indicated with a flat end; whereas, the pointed end indicates the termination point.*

but likewise could correspond to white matter that has not reached peak myelination. MD decreases in gray matter with normal neural maturation; in turn, elevated MD is an indicator of axonal damage. We used DTT to characterize diffusivity of the amygdala and hippocampus and FA of prefrontal-limbic white matter pathways that connect them to each other and to targeted prefrontal cortical regions. We targeted prefrontal-limbic pathways because developmental-neuroscience literature clearly implicates prefrontal-limbic network development as a mechanism shaping self-regulation, including emotion regulation, in both typically-developing children and children at-risk for psychopathology. Our results indicate lower FA in children with TBI or EI compared to healthy controls in several pathways originating in the amygdala and hippocampus that connected with medial and lateral orbitofrontal cortex. Moreover, children with TBI had lower FA when compared to those with EI in pathways coursing to the nucleus accumbens which suggests microstructural changes resulting from head trauma. We then examined whether white matter microstructure of these fronto-limbic pathways predicted child outcomes (post-traumatic stress symptoms or new behavioral problems). We also tested if age at injury moderated child outcome effects because an injury to the brain when it is still developing can change the architecture of neural networks. Results specific to post-traumatic stress symptoms and behavior problems outcomes are provided below.

Post-traumatic stress symptoms occur in 25–57% of injured children; yet, little is known about how different types of injuries and age at injury affect neural structures associated with post-traumatic stress response. Working to address this knowledge gap, our team has found that higher hyperarousal, avoidance, and re-experiencing symptoms were associated with higher FA in amygdala to pre-frontal and hippocampus to amygdala pathways (see **Figure 2**). Interestingly, white matter microstructure and

post-traumatic stress symptoms were similar between TBI and EI groups suggesting that the experience of being injured, rather than the type of injury, is a primary predictor of post-traumatic stress symptoms. With regard to age at injury, the team found that hyperarousal symptoms associated with pediatric injury increased with age. Furthermore, when age and hippocampal microstructure were investigated as predictors of hyperarousal symptoms the pattern was non-linear, such that for children, but not adolescents, hippocampal injury (higher mean diffusivity) predicted higher self-reported arousal (Ewing-Cobbs et al., J *Neurotrauma* 36:1738, 2019). One possibility is that alteration in hippocampal microstructure in the weeks following physical injury may proceed hippocampal volume reduction reported by studies of children and adults with diverse childhood trauma exposures, including those with TBI (DeMaster et al., *Brain Behav* 7:e00832, 2017).
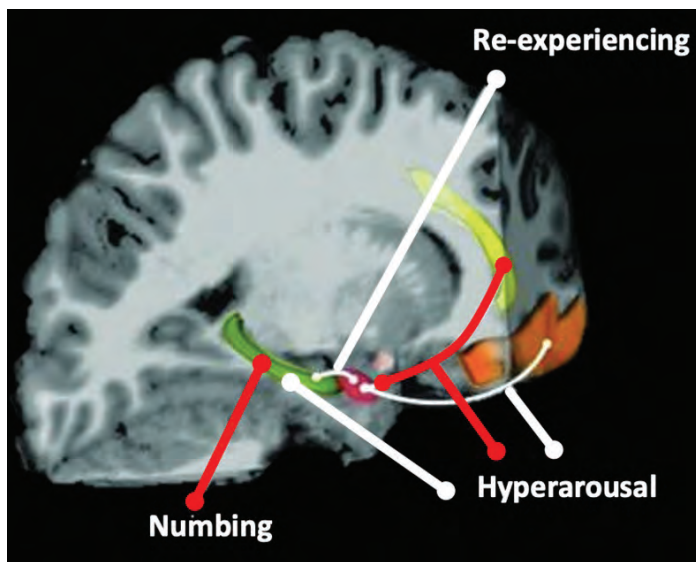

Figure 2. *Post-traumatic stress symptoms showed specific relations with limbic microstructure (white). Pathways with significant interactions of age and DTI metrics on post-traumatic stress scores are in red. Higher FA in the left hippocampus to amygdala pathway was associated with lower re-experiencing in the EI group and higher avoidance in the TBI group. For both injury groups combined (i.e., EI & TBI), hyperarousal was linked to higher FA of bilateral pathways connecting the amygdalae with orbital PFC, left amygdala to rostral anterior cingulate bundle, as well as to MD of bilateral hippocampi. Avoidance was also related to higher FA of the right hippocampus to amygdala tract. Numbing was predicted specifically by elevated left hippocampal MD. Amygdala-red, hippocampus-green, orbital PFC-orange, rostral anterior cingulate bundle-yellow. Modified from Ewing-Cobbs et al. J Neurotrauma 36:1738, 2019.*

Behavior problems are typically categorized as internalizing problems, such as anxiety and depression that are directed inward, and externalizing problems, such as oppositionality or conduct problems directed toward the external environment. One of our ongoing studies is testing if fronto-limbic white matter predicts parental reports of increased behavioral problems 7 months after injury. Results indicated lower FA in multiple pathways was associated with a greater increase in externalizing problems, and to a lesser extent internalizing problems, after TBI but not

extracranial injury (pathways include hippocampus-medial prefrontal cortex and hippocampus-parahippocampal cingulate). These findings suggest that pediatric injury, particularly TBI, alters relations between white matter microstructure and risk for subsequent behavioral problems relevant to mental health. Age also moderated the relation of injury group (TBI vs. EI) to white matter for left hemisphere pathways from the hippocampus to amygdala and from the hippocampus to parahippocampal cingulate. In both cases, strong age-related increase in white matter integrity was higher in the EI compared to those who sustained TBI. Future research should investigate if age at injury moderates the relation between frontal-limbic white matter and behavioral problems after pediatric TBI.

Heterogeneity is a known characteristic of TBI recovery in pediatric patients. As a result, research specifically targeting the mechanisms (e.g., disrupted neurocircuitry) responsible for diminished health outcomes is required to advance early prevention and intervention efforts. Converging research indicates that an early model of clinical intervention reduces impact of TBI on developmental, neuropsychological, and health outcomes. However, it is neither feasible nor cost-effective to provide intervention to patients at low risk for negative outcomes. A solution is to identify vulnerability factors, such as age at injury or type of injury, that are known to modulate child outcome. Understanding how brains reorganize post-injury will facilitate the creation of tailored interventions and improved treatments for children with a history of TBI, and thus expedite the recovery of cognitive function and improve psychological health outcomes.

About the Author

Dana M. DeMaster, PhD *is an Assistant Professor at the Children's Learning Institute (CLI). She completed her undergraduate degree in Cognitive Science from Hampshire College, and received both her master's and doctorate degrees in Psychology from the University of California, Davis. After completing a postdoctoral fellowship at UTHealth, she became a faculty member in the Department of Pediatrics and CLI. Her research program examines developmental improvements in learning and memory in infant and child populations through three branches of research: neuroplasticity in infants and young children, impact of brain injury, and implementation of new analytical methodology.*

Linda Ewing-Cobbs, PhD *is a member of the UTHealth NRC Executive Committee, a professor of pediatrics, Director of Clinical Programs at the CLI, and Psychologist at the Dan L. Duncan Children's Neurodevelopmental Clinic. She received her undergraduate degree in Psychology from Tulane University, and both a master's a doctorate degree in Clinical Neuropsychology from the University of Houston (UH). She completed a postdoctoral fellowship in Clinical Neuropsychology at UH before joining the UTHealth Department of Psychiatry and Behavioral Sciences in 1985. She moved to the Department of Pediatrics in 1994 as an assistant professor and rose to the rank of professor by 2004. Dr. Ewing-Cobb's research includes neuropsychological outcome studies examining the trajectory of brain, psychological health, and behavioral outcomes with traumatic brain injury (TBI); cellular therapies to repair neural damage after TBI; quantifying treatment response for both biological and educational interventions; and characterizing physical and psychological health needs that can impact public policy decisions.*

Brain Night for Kids

Brain Night for Kids was held on March 17, 2022 at The Health Museum in Houston. The UTHealth Neuroscience Research Center welcomed over 300 people for a fun-filled evening exploring neuroscience concepts with elementary school-aged children from the local community. Faculty, staff, postdoctoral fellows, graduate and medical students led diverse activity tables which sparked an interest in young children and their caregivers alike. For more information, please visit our website. We hope to see you at the event again next year!

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