



FRIENDS OF DOERNBECHER

2019 Friends of Doernbecher Grant Recipients

Stephen A. Back, MD, PhD

Proposal: Defining the Impact of Hypoxia from Apnea of Prematurity on Learning and Memory Mechanisms in the Preterm Brain

Award: \$43,784

Premature birth rates continue to rise in the U.S. with at least 380,000 new preterm babies born each year. Brain injury is the leading cause of life-long chronic complications in newborns who survive premature birth. About half of these children develop global challenges with motor abilities, learning and memory, mathematics, reading, attention and socialization. These children also have markedly higher rates of autism and major mental illnesses including anxiety disorders, depression and schizophrenia. These major challenges persist into adulthood with a staggering long-term impact on these children, their families and society. The cause of these devastating disabilities remains unclear, but has been widely attributed to loss of brain cells due to low oxygen delivery (hypoxia) to the brain. My lab has challenged this dogma through a series of key discoveries that demonstrated that immature nerve cells (neurons) in the preterm brain are actually remarkably resistant to death from hypoxia. Rather, we discovered that neurons persistently fail to mature normally. As a result, the brain's "wiring diagram" is disrupted, which sets off a "domino effect" of persistent changes in brain structure and function that synergistically increase the lifelong challenges of prematurely born babies.

With prior Friends' support, we began to study the hippocampus, which is responsible for learning and memory. We determined that memory circuits in the preterm hippocampus are persistently disrupted after only one half hour of hypoxia. We propose to build on these important findings to provide critically needed information to improve the management of preterm infants during intensive care. Although preterm babies often stop breathing multiple times a day (apnea of prematurity), the long-term impact of these transient episodes of hypoxia on brain development is unknown. We will determine: (1) how a limited number of brief repetitive episodes of hypoxia influence learning and memory circuits in the preterm brain and (2) determine if normalization of learning and memory circuits can be achieved with agents already in wide clinical use that may be repurposed to promote improved nerve cell firing disrupted by sustained or intermittent hypoxia.

Debora Burger, RN, MSN

Proposal: CPR for Caregivers of Children of all Ages at Doernbecher Children's Hospital

Award: \$11,920

The Childbirth and Early Parenting Education Program are interested in expanding and incorporating CPR and safety training for caregivers of all ages of children at DCH. The program currently runs an Infant Safety and CPR class. With additional funding the program could run an additional Child Safety and CPR class. The current class is 3 hours long with 5 hours of instructor time for set up and take down. They offer spaces for 24 couples to attend per month and are

currently mostly full. The instructors are employed on 0.1 contracts (except one who is 0.2), the hours they work are very flexible and dependent on when classes are scheduled. All of them teach a number of other classes but have time in their schedule to accommodate new classes if there is additional funding.

Aaron Cunningham, MD and Mubeen Jafri, MD

Proposal: Venous thromboembolic prediction algorithm in pediatric trauma: a pilot study

Award: \$46,237

Morbidity from deep vein thrombosis (DVT) and its consequences, collectively referred to as venous thromboembolism (VTE), is a significant problem in trauma, but the specific risk in children is poorly understood. The morbidity of VTE is substantial and reducing these occurrences, can lessen the impact of injury, decrease the exposure to blood thinners and save children's lives. Specifics regarding which children are low- or high-risk have not been clearly established and current expert management guidelines are developed from limited data and therefore not uniformly implemented. Our group developed a clinically applicable model (VTE risk tool) to predict the risk of VTE in traumatically injured children and the main barrier to clinical implementation is high quality data from a prospective study. Prior work in our group demonstrated that the VTE prediction tool has better diagnostic accuracy and implementation would expose 88% less children to blood thinners than current society guidelines. Therefore, we propose a prospective pilot study of our model to risk stratify pediatric trauma patients at Doernbecher Children's Hospital. Additionally, we plan to apply ultrasound surveillance to a moderate-high risk cohort, to determine if screening in this risk-stratified group will allow for early detection of VTE.

Randall Jenkins, MD

Proposal: Toxic Exposures in the Neonatal Intensive Care Unit

Award: \$18,423

Prompted by over twenty-year clinical experience observing unexplained high blood pressure in premature infants, our group has been investigating the source of such hypertension. We published an initial report of infants developing hypertension at about 40 weeks' postmenstrual age. These infants had clinical characteristics consistent with a derangement in how sodium is regulated in the kidney, suggesting an exposure as a potential source of the hypertension. With seed funding from the Friends of Doernbecher in 2014, we published a manuscript (January 2019) detailing plastic softeners found in the neonatal intensive care unit (NICU) as a potential source for this unexplained hypertension. The report associated infants' exposure to di-2-ethylhexyl phthalate (DEHP)—an additive to polyvinyl chloride to make the plastics soft and flexible—to the high blood pressure observed. We found DEHP in NICU medical devices and now we seek to determine the extent to which each of these putative sources impact the health and safety of these vulnerable infants. This study proposes to measure the amount of DEHP that leaches from neonatal IV bags, tubing, and respiratory equipment in a lab setting that replicates clinical conditions. The results from this study will help estimate health risks to premature infants exposed to this potential toxin in currently used supplies and devices. Data acquired from this study should allow us to obtain major funding for a definitive study to show the extent to which DEHP exposures in neonates produce an outcome of hypertension and is a significant health risk to premature infants in the NICU.

Juan Piantino, MD

Proposal: Linking Glymphatic Pathway Impairment and Post- Concussive Headaches in Youth with Traumatic Brain Injury.

Award: \$42,362

In the United States, mild traumatic brain injury (mTBI) occurs in 692 out of 100 000 children younger than 15 years.¹ Headache is the most common symptom reported following mTBI in youth. In these patients, headaches without the added burden of traumatic brain injury, are associated with disability and poor quality of life. In addition, missing school and other activities due to headaches and other post-concussive symptoms can cause significant academic and social challenges for youth in this critical period of development. The mechanisms underlying the pathogenesis of post-concussive headaches (PCH) remain poorly understood. Without this knowledge, it will remain difficult to create interventions to reverse the long-term consequences of PCH.

Bethany M. Sloane, PT, DPT

Proposal: An evaluation of the effect on gait in hemiplegic cerebral palsy and stroke with the use of Constraint-Induced Movement Therapy

Award: \$18,274

"The Lower Extremity Constraint Induced Movement Therapy (CIMT) Program at the Child Development & Rehabilitation Center (CDRC) has been incredibly helpful on several fronts. Over the past two years our daughter, who has hemiplegia, has built strength in her leg and stability in the way she walks and runs so that she falls far less than in the past. This is the number one most noticeable change." – CDRC parent

Children with a diagnosis of hemiplegic cerebral palsy or stroke experience disuse of one side of their body, which can progress into muscle weakness, abnormal movement patterns, muscle tightness, and delays in gross motor function. Clinicians at the CDRC have begun a pilot program that consists of constraining a child's intact lower limb in order to encourage increased use of their involved side by using a solid ankle-foot orthotic (AFO). This type of intervention has been proven successful in the literature for upper limb function, but it has not been studied or recorded for the lower limb. Currently clinicians have observed that the use of the constraint on the child's intact lower limb has encouraged weight shifting over to their involved side for squatting, using their involved side as their lead leg with stair climbing and kicking activities, and has improved the symmetry of walking patterns.

Our hypothesis is that normalizing the symmetry of movement as an effect of CIMT can be seen immediately in one or more of the gait parameters recorded by a trained physical therapist and by sensitive three-dimensional motion analysis equipment. Our aims are to prove that CIMT for the LE is an effective intervention, prove that you can start seeing changes in gait symmetry and movement quality during and following intervention, and that families will report perceived benefits, risks, results and difficulties of this intervention.