Nemours Summer Undergraduate Research Program

Project Title: *Remedy to Diabetes Distress (R2D2): A scalable screen to treat program for school-age families*

Work Location: Jacksonville, FL

Mentor(s): Susana R. Patton, PhD, ABPP, CDCES; Jessica Pierce, PhD

2021 Summer Research at Nemours

NSURP Project 1

PROJECT DESCRIPTION

BACKGROUND:
Diabetes Distress (DD) is a psychological state characterized by fear, guilt, anger, and sadness related to living with or caring for someone with type 1 diabetes mellitus (T1D). Research suggests that both children with T1D and their parents are vulnerable to experiencing DD and the American Diabetes Association Standards of Care recommend clinic-based screening for DD in parents and children starting at age 8. Unfortunately, there are no practical screen-to-treat programs for DD for clinics to adopt. Our team has recently received a R01 grant to study DD in families of school-age children and to develop a scalable and effective screen-to-treat program. For this R01, we are employing the ORBIT Model for Behavioral Intervention Development. This model proposes a phased design approach using a series of small, cost-effective studies to determine a treatment's acceptability before embarking on a large clinical trial. In summer 2021, we will pursue two projects that comprise Phase 1 of our R01. The first project is a brief longitudinal study to establish cut-points for clinically-relevant DD in parents and school-age children. The second project uses crowdsourcing methodology to obtain family input on a new mHealth treatment to reduce DD in school-age families. The participating NSURP trainee would assist with both projects thereby receiving a diverse clinical research experience.

HYPOTHESIS:
Cut-Point Study: The scores marking a shift in the linear or quadratic association between child/parent DD and measures of resilience, adherence, and HbA1c will form clinically-relevant cut-points for DD.

Crowdsourcing Project: Parent feedback will establish the initial acceptability of our new mHealth intervention.

SPECIFIC AIM:
Projects address Aim 1 of the R01: Define and refine our new screen-to-treat program (R2D2) for DD in school-age families in order to maximize feasibility and acceptability.

METHODOLOGY:
Cut-Point Study: We will recruit ~126 families (child age 8-12 years-old). Parents will provide informed consent; youth will provide assent. Parents and children will complete measures of DD, resilience, and adherence. We will also measure children's glycated hemoglobin (HbA1c). COVID-19 design considerations: To eliminate in-person study visits families will complete surveys via REDCap and we will use mail-in HbA1c kits. An NSURP trainee would: 1-help to send out surveys and HbA1c kits for study visits, 2-help with data management, and 3-attend weekly project research meetings via Teams. He/she could shadow coordinators during recruitment/consent.

Crowdsourcing Project: We will recruit 50 parents. We will obtain informed consent and then invite parents to join a closed social network community on Yammer.com. On Yammer, we will post potential treatment content and questions (open-ended and rating-based) and parents will be able to view and reply to our posts and to each other's responses. COVID-19 design considerations: We will use an internet-based crowdsourcing design to enable parents to participate from home. An NSURP trainee would: 1-help with posting questions/content to our Yammer network, 2-help to monitor the discussion for each post, 3-learn about qualitative coding methodology, 4-help develop our coding manual, and 5-code parents' responses for thematic content. He/she could contribute creatively to the design of our mHealth intervention.

Project Title: *Capacity of Urinary Bladder in Children with Neurogenic Bladder*

Work Location: Jacksonville, FL

Mentor(s): Chetan Shah MD, MBA

2021 Summer Research at Nemours

NSURP Project 2

PROJECT DESCRIPTION

BACKGROUND:

Children often undergo Ultrasound and voiding cystourethrogram (VCUG) studies. VCUG studies require estimate of capacity of urinary bladder. Various formula/table/chart exist for these estimates. Many of these estimates are from 1950s to 1980s and are from children who do not have neurogenic bladder. Children who are developmentally delayed or children who do not have bladder control due to various reasons including anomalies of the spine may have a large, dysfunctional urinary bladder. Their bladder capacity may be much larger than other children. Empirically, radiologists and urologists multiply the estimated capacity from various charts by a factor of 2 or 3, to estimate bladder capacity in children with neurogenic bladder. Although these estimates are critical in their evaluation of bladder by VCUG or by urodynamic studies, most are being used empirically and requires evidence-based data.

Ultrasound allows us to measure the bladder volume directly. For VCUG, radiopaque contrast is instilled in the urinary bladder till the patient voids spontaneously on the examination table. Ultrasound is usually done when patient has a good size bladder, not necessarily full to the point that patient cannot hold any longer. However, measuring bladder volume in children with neurogenic bladder at Ultrasound will probably be more accurate than using estimates based on children with normal urinary bladder. Furthermore, the various estimates available for bladder capacity in children vary widely when compared with each other. There is a need for more recent, more robust estimates of bladder capacity in children.

HYPOTHESIS:

Children with neurogenic bladder may have higher bladder capacity than other children. Commonly used estimates of bladder capacity may not apply to these children. We may be able to develop bladder capacity estimates for children with neurogenic bladder that can be used to perform VCUG studies in them.

SPECIFIC AIM:

1. To compare volume of the urinary bladder at Ultrasound and VCUG.
2. To compare urinary bladder volume noted on Ultrasound with estimates of urinary bladder capacity from various formula based estimates.
3. Develop an estimate of urinary bladder capacity in children with neurogenic bladder, poor bladder control and developmental delay.
4. Compare urinary bladder volume in children with neurogenic bladder with that of other children.

METHODOLOGY:

Retrospective evaluation of Ultrasounds and VCUG on children performed over the past 5 years will be studied. Variables examined will include volume of pre-void urinary bladder at the time of Ultrasound, cauterization status at the time of examination, reason for examination, surgical history, referring office, height, weight, patient demographics, history of neurogenic bladder/poor bladder control/developmental delay, history of vesicoureteric reflux, volume of contrast injected at the time of VCUG. Microsoft Excel and SPSS will be used for analysis and statistics calculations. Statistical analysis including chi square and t-tests will be performed.

Project Title: *Impact of microbial milieu in mother's milk on the immature intestinal epithelium and the development of necrotizing enterocolitis*

Work Location: Orlando, FL

Mentor(s): Jennifer Liedel, MD

2021 Summer Research at Nemours

NSURP Project 3

PROJECT DESCRIPTION

BACKGROUND:

Necrotizing enterocolitis (NEC) is a condition that affects up to 10% of all admissions to the neonatal intensive care unit (NICU). It causes inflammation and necrosis in the intestine, resulting in significant complications in many of those who survive. There is no single identifiable factor that causes NEC to develop, rather it results from multiple factors intrinsic to the infant that are modulated by environmental stressors. One intervention that has been shown to protect against the development of NEC is provision of mother's own or donor breast milk to preterm infants. Breast milk is a complex mixture of nutrients and bio-active factors, including white blood cells, bacteria and cytokines. My previous studies focused on the intestinal epithelial barrier and breast milk, evaluating the role of milk-derived pro and anti-inflammatory cytokines on barrier function and intestinal inflammation in immature cellular and animal models. The results demonstrated that the cytokine milieu of the milk does, in fact, impact the function of the intestinal barrier. When pro-inflammatory cytokines were present at elevated concentrations, the intestinal barrier was negatively-impacted and inflammation was present. Small-scale studies have also evaluated the breast milk microbiome and protein content. These studies suggest that the microbial profile of the milk stimulates the infant immune response. Further, intestinal microbiome studies have demonstrated a shift toward more pathogenic bacterial composition in infants prior to the development of NEC. However, the interplay between the milk microbiome, milk cytokine profile, and the combined effect on the infant has not been evaluated.

HYPOTHESIS:

Dysfunction of the intestinal barrier and subsequent NEC within infants results from a shift in the intestinal microbiota to a more pathogenic profile, which is directly influenced by elevated levels of proinflammatory cytokines and the bacterial composition of mother's milk. The microbiota shift directly impacts intestinal barrier function, predisposing to NEC.

SPECIFIC AIM:

1. Characterize the microbiota in breast milk fed to hospitalized infants and describe the impact on the development of NEC.
2. Identify immune factors within human milk and the mechanisms by which they may lead to intestinal epithelial injury underlying NEC.

METHODOLOGY:

For all studies, small aliquots of milk from mothers of hospitalized infants will be collected on a timed basis. Additional clinical data about perinatal history, feeding, infection, and general clinical condition of the infant will be collected. The breast milk samples will be evaluated by ELISA analysis to determine cytokine content, flow cytometry to determine cellular content, and unbiased 16s ribosomal RNA gene sequencing to determine the microbial composition. Once analyzed, remaining milk aliquots will be utilized for in vitro cellular studies to correlate the milk to intestinal epithelial cell integrity. The results will also be correlated to clinical factors to determine if the characteristics of the milk are predictive of NEC. These studies will elucidate the mechanisms underlying the barrier dysfunction that leads to NEC in the premature infant.

Evaluation of results: Once the data has been collected, statistical analysis will be completed. In order to ensure accurate representation of the data and logical conclusions, statisticians will be utilized.

Nemours Summer Undergraduate Research Program

Project Title: *Incidence and Risk factors of Gastrostomy Tube Placement in Infants Following Surgery for Complex Congenital Heart Disease*

Work Location: Orlando, FL

Mentor(s): Sreekanth Viswanathan, MD, MS; Darlene Calhoun, DO; Peter Wearden, MD; Adam Lowry, MD; Arianna Ahiagbe, MD

2021 Summer Research at Nemours

NSURP Project 4

PROJECT DESCRIPTION

BACKGROUND:

Congenital heart disease (CHD) is the most common birth defect occurring in nearly 1% of newborns. About 25% of newborns with CHD undergo cardiac surgery annually, especially those with *critical CHD*. Many infants with complex CHD do not develop the skills to feed orally enough to meet their energy demands and are discharged home on gastrostomy tube (G-tube). Various studies suggest that the proportion of neonates with CHD requiring G-tube at hospital discharge ranges from 30-45%. Oral feeding difficulties (*dysphagia*) is a significant contributor to the prolonged hospital length of stay (LOS). G-tube placement as an additional surgical procedure has its own anesthetic and infectious risk. Dysphagia during the hospital stay and following hospital discharge is one of the most significant parental concerns/stressors, sometimes even overshadowing cardiac concerns. Thus, there are several reasons to improve the quality and efficiency of oral feeding skills and to minimize the need for tube feeding in infants with complex CHD. However, the current understanding of the etiopathogenesis of dysphagia in infants with complex CHD is limited.

SPECIFIC AIM/OBJECTIVES:

To determine the incidence and risk factors for G-tube placement in infants with complex CHD at Nemours Children's Hospital. The *rationale* for the study is that recognition of modifiable risk factors for dysphagia may allow the opportunity for early interventions to improve the oral feeding outcomes and fewer G-tubes at hospital discharge.

METHODOLOGY:

To attain the study objectives, we will conduct a *single-center retrospective cohort study* of all infants under 6 months of age who have undergone a cardiac surgical procedure for CHD at Nemours Children's Hospital, Orlando, Florida, from 2012 to 2020. Infants will be excluded if they had gastrointestinal surgical conditions, significant genetic or congenital anomalies, orofacial anomalies, or cardiac anomalies that did not require surgery. Electronic medical records (EMR) of all infants less than 6 months of age during their first admission to the cardiac intensive care unit (CICU) during the study period will be reviewed to identify eligible infants. EMR will be reviewed for demographics, cardiac lesion based on echocardiogram and procedural records, feeding milestones, growth metrics, laboratory and imaging data, and LOS. Infants placed on G-tube feeding (GTF group) will be compared to infants who have reached independent oral feeding (IOF group) prior to hospital discharge to determine the risk factors for G-tube placement. All data will be stored using REDCap, a secure, web-based application designed to support data capture for research studies. The study will be undertaken under an approved IRB protocol at Nemours Children's Hospital in Orlando, Florida.

STATISTICS:

Differences between the GTF and IOF groups will be analyzed using appropriate univariate analysis. A multivariable logistic regression model will be built by including all the risk factors that are found to be significantly associated with G-tube placement and those that are considered clinically relevant covariates. A $p \leq 0.05$ will be considered statistically significant.

Project Title: *Correlation of tracheal narrowing seen with CTA of the chest and other imaging modalities in children and adults with Mucopolysaccharidosis IVA*

Work Location: Wilmington, DE

Mentor(s): Lauren Averill, MD

NSURP Project 5

PROJECT DESCRIPTION

BACKGROUND:
Mucopolysaccharidosis IVA (MPS IVA) is rare autosomal recessive lysosomal storage disease characterized by progressive skeletal dysplasia and respiratory issues with difficult airway management during anesthesia. Patients with MPS IVA develop progressive respiratory difficulty due to a combination of factors, including restrictive chest deformity, obstructive airway disease (both supraglottic and subglottic large airways), and weakness from spinal cord compression. Recent investigations have shown worsening tracheal narrowing and deviation with advancing age in individuals with MPS IVA. Specifically, computed tomography angiography (CTA) of the chest has been used in MPS IVA to provide detailed imaging of the trachea, surrounding soft tissues including arteries, and the bony thorax. This information can help inform airway management during anesthesia and possible need for tracheal reconstructive surgery. However, it is not known which patients are at higher risk for developing critical airway narrowing and should be selected for CTA assessment, a study that imparts cost as well as radiation and intravenous contrast exposure.

HYPOTHESIS:
Imaging studies obtained during routine care of patients with MPS IVA can serve as screening tools to identify those individuals who are at risk for severe tracheal narrowing and would benefit from CTA of the chest.

SPECIFIC AIM:
The specific aim is to correlate the appearance of the trachea on chest radiographs, spine radiographs, and cervical spine MRI with the appearance of the trachea on CTA of the chest in patients with MPS IVA. By identifying the most useful modalities and imaging techniques, the use of CTA of the chest in MPS IVA can be used in a targeted manner.

METHODOLOGY:
Via retrospective chart review, MPS IVA patients with CTA of the chest who have other imaging studies within one year of CTA will be included. Tracheal measurements and qualitative assessment will be performed using each modality available and correlated with tracheal measurements and qualitative assessment using CTA previously reported by this group. Utility of each modality as a screening tool for the trachea will be determined.

Project Title: *The Effectiveness of Serial Casting in the Treatment of Recurrent Equinovarus in Children with Arthrogryposis*

Work Location: Wilmington, DE

Mentor(s): Reid Nichols, MD; Chris Church, MPT

2021 Summer Research at Nemours

NSURP Project 6

PROJECT DESCRIPTION

BACKGROUND:
Lower limb contractures and muscle weakness are common in children with arthrogryposis and result in foot deformities and gait deviations. The most common foot deformity in arthrogryposis is equinovarus. Foot deformities in children with arthrogryposis are most frequently treated with surgical intervention, but more recently conservative management with casting and physical therapy has been encouraged. Conservative management is routinely used in children with idiopathic clubfoot (equinovarus) with excellent results.

Serial casting has changed the way idiopathic clubfeet are treated leading to outcomes with improved foot mobility, while drastically reducing invasive surgical procedures. The clubfoot in children with arthrogryposis is typically more stiff than the idiopathic clubfoot so has traditionally been treated surgically, but improved outcomes with conservative treatment would offer great clinical benefit to this population by delaying or reducing the need for invasive surgical procedures.

HYPOTHESIS:
Foot deformity will improve and a positive outcome will be reported following conservative management of foot deformities in children with arthrogryposis.

SPECIFIC AIM:
To evaluate the effectiveness of serial casting to treat equinovarus foot deformities in children with arthrogryposis utilizing passive range of motion (PROM), parent reported outcomes, and dynamic foot pressure during ambulation.

METHODOLOGY:
Children with arthrogryposis treated with serial casting due to recurrent equinovarus foot deformities will be evaluated retrospectively comparing evaluations pre, post/short term (ST; within 6 months), and post/longer term (LT; 6 months to 1 year) serial casting. Serial casting includes the application stretching casts worn for 7-10 days followed by repeated casting for a total of 2 to 8 weeks. Outcome data include results from PROM, pedobarograph, and the Pediatric Outcomes Data Collection Instrument (PODCI) as reported by parents. Post-casting outcomes will be compared to pre-operative presentation using ANOVA with bonferroni corrections.

The student will be responsible for the retrospective review of the data and will assist in the data analysis and write up of the project for publication. Additionally the student will be encouraged to observe weekly in the orthopedic clinic or operating room to expand their knowledge of the care of children with arthrogryposis and other pediatric diagnoses leading to foot deformities.

Nemours Summer Undergraduate Research Program

Project Title: *Understanding Maternal Purpose in Life in the Transition to Motherhood and its Associations with Postpartum Depression, Parenting, and Infant Development*

Work Location: Wilmington, DE

Mentor(s): Danielle Hatchimonji, PhD; JJ Cutuli, PhD

2021 Summer Research at Nemours

NSURP Project 7

PROJECT DESCRIPTION

BACKGROUND:

Maternal PPD (depression in the infant's first year of life) affects roughly 13-17% of mothers and is associated with risk for poor cognitive, behavioral, and health outcomes for children. This project examines factors that influence the relationship between maternal postpartum depression (PPD) symptoms and developmental outcomes for infants. Our ultimate goal is to develop more effective interventions to promote resilience for new mothers and their babies.

SPECIFIC AIMS AND HYPOTHESES:

1. **Investigate the mediating role of parenting practices in the association between postpartum depression symptoms and infant development in the first year of life.** We expect that PPD symptoms will be negatively associated with infant development and that negative parenting practices will explain this relationship. These relationships would suggest that a mother's PPD symptoms may lead to poorer parenting, which may then lead to poorer development for the infant.
2. **Identify factors that buffer against or exacerbate the negative association of postpartum depression symptoms with parenting practices.** We expect that for mothers who have PPD symptoms, if they also have social support and/or a purpose in life (a meaningful life goal), they may demonstrate less negative parenting practices than mothers without these protective factors. We also expect women with both PPD symptoms and a history of adverse life experiences may demonstrate more negative parenting practices than mothers without a these experiences.
3. **Assess purpose and its development for new mothers over course of the first year after their child's birth.** Because purpose in new mothers has been largely unexplored, we will assess the longitudinal development of purpose over the three study time points. We hypothesize that purpose among new mothers will increase over the first year of their child's life.

METHODOLOGY:

We will recruit first-time mothers and their infants (birth through two months old) to complete assessments via phone interview at 0, 6, and 12 months. Research staff will use a structured assessment using standardized measures of depression, parenting, and child development. Summer 2021 will include Time 2 and Time 3 follow-up assessments and opportunities for data analysis.

Project Title: *Implementing Family Psychosocial Risk Screening for Pediatric Health Equity*

Work Location: Wilmington, DE

Mentor(s): Anne E. Kazak, PhD

2021 Summer Research at Nemours

NSURP Project 8

PROJECT DESCRIPTION

BACKGROUND:
Childhood cancer affects multiple levels of the social ecology, including social determinants of health (e.g. financial and resource issues, child and family problems). The 2015 Standards of Psychosocial Care in Pediatric Cancer outline optimal psychosocial care, starting with a standard devoted to assessment of psychosocial healthcare needs. With support from the American Cancer Society (ACS-RSG-13-015) we validated in English and Spanish a brief family psychosocial risk screener, the Psychosocial Assessment Tool (PAT), now ready for broad implementation. Use of the PAT across children's cancer programs nationally can achieve the assessment Standard and deliver psychosocial care matched to family need for all patients, especially those most impacted by health inequities. This grant is funded by the American Cancer Society (RSH-19-022).

OBJECTIVE/HYPOTHESIS:
The PAT is being implemented across a national sample of 18 pediatric cancer programs in a comparative effectiveness study, guided by the Interactive Systems Framework for Dissemination and Implementation, comparing two Strategies. It is hypothesized that implementation will be more successful at the patient/family, provider, and institutional level when Training (Strategy I) is combined with Implementation Expanded Resources (Strategy II). The trial is informed by input from Stakeholders and will result in a web-based Toolkit for dissemination nationally.

SPECIFIC AIMS:
1. We first refined the two implementation strategies using semi-structured interviews with 18 stakeholders from parent advocacy groups, providers, pediatric oncology organization representatives, healthcare industry leaders
2. Now we are comparing the two theoretically based and empirically informed strategies to implement the PAT in English and Spanish using a cluster randomized controlled trial
3. Based on the results of the trial and feedback from stakeholders, we will integrate feasible and effective strategies to develop and disseminate a PAT Implementation Toolkit.

METHODOLOGY:
This mixed methods implementation research includes qualitative interviews with the Implementation Team to refine the strategies (Aim 1). Sites will be randomized to cohort (3) and strategy (2) for the trial (Aim 2). Outcomes include adoption and penetration of screening (patient/family), staff job satisfaction/burnout (provider), and cost effective use of resources consistent with family risk (institution). Based on results of Aims 2, with input from the Implementation Team, a web-based Toolkit will be developed for dissemination (Aim 3).

Student research opportunity: In 2021 the research will focus on Aim 2. Students will have the opportunity to learn about and be involved with an implementation science project. They will work with project staff in collecting data on implementation of the PAT from cancer programs around the country. They will gain experience in data management and the conduct of a randomized clinical trial across multiple sites related to psychosocial care in pediatric cancer and implementation science. Students may also utilize the qualitative stakeholder data to learn about qualitative research methods. This is a great opportunity for students interested in careers in medicine, nursing, psychology, social work or public health.

Project Title: *Is Standing Function Improved after Orthopedic Surgery in Youth with CP at GMFCS Levels III/IV?*

Work Location: Wilmington, DE

Mentor(s): Nancy Lennon, MS, PT; Chris Church, MPT

2021 Summer Research at Nemours

NSURP Project 9

PROJECT DESCRIPTION

BACKGROUND:

During adolescent growth and the transition to adulthood, youth with cerebral palsy (CP) classified at Gross Motor Function Classification (GMFCS) Levels III and IV are at risk for losses in standing function. Such losses increase the potential for harmful secondary consequences including prolonged sitting, increased sedentary time, compromised bone health, reduced cardiovascular health, and increased incidence of pain and depression (Verschuren 2018). Preserving weight-bearing ability for transfers and therapeutic standing is an important and practical goal, with the potential for significant positive effects on caregiving needs and opportunities for daily activity and participation for youth at GMFCS levels III /IV.

Orthopedic surgery is a common treatment in youth with spastic cerebral palsy to address a variety of problems. Youth with spastic CP undergo lower extremity surgery to improve gait, upper limb surgery to improve hand use, and spine or pelvic surgery to relieve pain/discomfort (Miller 2020). For youth whose ambulatory function is marginal, surgery may be performed to preserve weight-bearing function for transfers and therapeutic standing. The success of such treatment approaches is unclear as documenting functional mobility outcomes for youth with severe gross motor impairments is inconsistent in both clinical practice and research literature. This project will examine the impact of orthopedic surgery on standing function in marginally ambulatory youth with CP using objective measures from the gait analysis lab.

HYPOTHESIS:

Youth with CP classified at GMFCS levels III and IV will demonstrate improved standing function after orthopedic surgery as documented by objective measures from the gait analysis lab .

SPECIFIC AIM:

1. To describe the standing function of youth with CP classified at GMFCS levels III and IV using objective data from the gait analysis lab including dimension D of the GMFM-88, the Transfer & Basic Mobility and Pain subtests of the Pediatric Outcomes Data Collection Instrument (PODCI), the Functional Mobility Scale (FMS) and gait velocity
2. To evaluate change in standing function one to two years after orthopedic surgery in youth with CP classified at GMFCS levels III and IV using objective data from the gait analysis lab including dimension D of the GMFM-88, the Transfer and Basic Mobility and Pain subtests of the Pediatric Outcomes Data Collection Instrument (PODCI), the Functional Mobility Scale (FMS), and gait velocity

METHODOLOGY:

We will perform a retrospective review of standing function in youth classified at GMFCS level III and IV before and after orthopedic surgery by identifying data collected in the gait analysis lab between January 2010 and January 2020. Filtering patients according to GMFM-D will identify eligible records. All data will be extracted from a secure database in the gait analysis lab. Summary statistics of outcome measures will be used to describe standing function before orthopedic surgery. Parametric tests will be used to identify changes pre versus post-operatively. Multiple regression analysis will be used to predict whether pre-op gait speed accounts for any variation in functional standing outcomes after surgery. We will also collect data on the use of assistive devices and orthoses in this group of patients and characterize the influence of adaptive equipment on standing function.

Project Title: *Physiological evaluation and prevalence estimation of auditory sensitivity in children and adolescents with ADHD*

Work Location: Wilmington, DE

Mentor(s): Kyoko Nagao, PhD

2021 Summer Research at Nemours

NSURP Project 10

PROJECT DESCRIPTION

BACKGROUND:

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurodevelopmental disorder. Previous studies suggest that abnormal auditory sensitivity is common in ADHD and persists into adulthood, but the cause of altered auditory sensitivity is still not clearly understood. Auditory sensitivity issues are currently evaluated based on self- or parent-report.

Auditory sensitivity can be hypersensitive (sensitive to sounds) or hyposensitive (insensitive to sounds), but the prevalence of auditory sensitivity among children with ADHD has not yet been established. Auditory hypersensitivity can result in symptoms such as fatigue and concentration difficulties. Auditory hyposensitivity has not been studied much because patients may not be aware of their symptoms. However, insensitive to loud sounds could increase a risk of noise-induced hearing loss. In this study, we use auditory physiology measures known as acoustic reflex to evaluate auditory sensitivity among patients with ADHD.

HYPOTHESIS:

1. Some children with ADHD have impaired subcortical function that causes malfunction of their acoustic reflex system and results in altered loudness perception.
2. The prevalence of atypical auditory sensitivity is higher in children with ADHD than in typically developing children.

SPECIFIC AIM:

1. Evaluate auditory sensitivity in children and adolescents with ADHD using acoustic reflex testing.
2. Estimate prevalence of auditory hypersensitivity and hyposensitivity in children and adolescents with ADHD.

METHODOLOGY:

1. Two groups of participants (ADHD and control groups) will be recruited for this study. We will collect a variety of hearing function tests (including acoustic reflex test), cognitive tests, a mix of sound exposures, and sensory profile questionnaires from each participant. We will compare results between patients with ADHD and controls.
2. Online questionnaires addressing sensory sensitivities, sound exposure, and medical and demographic information will be used to collect data from children and young adolescents with and without ADHD for this study. We will estimate prevalence of hyper- and hypo-sensitivity among patients with ADHD and compare them with the estimated prevalence in individuals without ADHD. We will also analyze factors such as birth sex, comorbid disorders, medication use type/status, and socio economic status.

Project Title: *Analysis of proteome of peripheral extracellular vesicles in rabbit models of intimal hyperplasia by mass spectrometry*

Work Location: Wilmington, DE

Mentor(s): Valerie Sampson, PhD; Madeline Jeshurin, BS

2021 Summer Research at Nemours

NSURP Project 11

PROJECT DESCRIPTION

BACKGROUND:
Intimal hyperplasia (IH) is the expansion of the vascular intimal region after intervention, which can lead to stenosis and eventual failure of vascular grafts or interventional procedures such as angioplasty or stent placement. To determine a possible cause for the development of intimal hyperplasia, a proteomics-based approach will be used to assess the small extracellular vesicle (sEV) protein composition from peripheral blood from rabbit models after carotid transection and anastomosis surgery. sEVs are nanovesicles that are secreted by cells and are largely responsible for intercellular communication through the delivery of bioactive molecules, such as proteins, messenger RNAs (mRNAs), microRNAs (miRNAs), DNAs, lipids, and metabolites.

HYPOTHESIS:
Proteome profiles of plasma sEVs secreted by rabbits after carotid transection and anastomosis surgery indicate intimal hyperplasia.

SPECIFIC AIM:
The goal of this study is to determine markers of intimal hyperplasia contained in the sEVS in a rabbit open surgical model.

METHODOLOGY:
We will analyze the proteomes of sEVS secreted by rabbit open surgical models on post-operative day 21 by mass spectrometry analysis and compare proteome profiles with sEVs from normal animals and assess differenced that indicate intimal hyperplasia.

Project Title: *Pre-Op Psychosocial Assessment and Surgical Admissions in Youth with Cerebral Palsy Undergoing Spine and Hip Reconstruction*

Work Location: Wilmington, DE

Mentor(s): Carrie Sewell-Roberts, LCSW; Nancy Lennon, MS, PT; M. Wade Shrader, MD

2021 Summer Research at Nemours

NSURP Project 12

PROJECT DESCRIPTION

BACKGROUND:

Parenting a child with cerebral palsy (CP) is stressful (Majnemer et. Al 2012). Primary caregivers experience the most significant stress at the child's initial diagnosis and when anticipating a major treatment intervention such as orthopedic surgery (Park et. Al 2010; Parkes et. Al. 2009). More than 90% of children with CP undergo at least one orthopedic surgery (Rang 1990). Primary caregivers worry about pain, rehab needs after surgery, finances, and delayed recovery. Anxiety is exacerbated in families with pre-existing socioeconomic stressors and low social support. Such pre-existing stress risk factors often go unidentified until families arrive for surgery. Medical teams can mitigate stress by providing support and connecting families to resources that will alleviate burdens on primary caregivers. Identifying ways to provide this support to families before hospital admission may lessen stress for parents, and assist in ensuring a more successful course for the surgery, inpatient stay, and acute recovery.

One way to identify stress and risk factors before an orthopedic surgery is for a social worker to conduct a pre-operative psychosocial assessment. A psychosocial assessment involves asking the primary caregiver questions regarding family composition and support system, housing, transportation and financial situation and needs, behavioral health concerns, and educational and therapy needs. Healthcare systems that provide psychosocial support and resource navigation to families during times of stress report improved hospital outcomes related to discharge and post-operative care (Jones et. al., 2010). Helping families to access services that lessen the financial burden of medical care, or help them acquire respite care or additional social support, can reduce caregiver stress load and lead to better health outcomes for both patients and their caregivers.

HYPOTHESIS:

Participation by families in a pre-op psychosocial assessment will be associated with improved surgical episodes as measured by lesser cancellation rates, shorter hospital length of stays, lower 30-day readmission rates, and higher completion of post-discharge follow-ups.

SPECIFIC AIM:

1. To examine specific quality metrics associated with the surgical perioperative planning phase, acute hospital stay, and 30-day post-operative period for youth with CP at GMFCS levels IV and V who undergo hip and spine surgeries.
2. To identify relationships between family participation in pre-op psychosocial assessment and quality metrics including timely completion of surgery, inpatient length of stay, 30-day readmission rate, and frequency/nature of post-discharge follow-up.

METHODOLOGY:

Medical records will be retrospectively reviewed from February 2017 through February of 2020 to identify all patients with cerebral palsy or like conditions, classified at GMFCS level IV or V, who have undergone hip or spine reconstruction surgery within the CP Division of Orthopedics. Data on demographics and medical conditions will be collected for patient cases that meet inclusion criteria. Objective outcome data on surgical scheduling delays, length of hospital stay, discharge follow-up contacts, and readmission within 30 days will be compiled. Statistical analyses will include summary statistics, univariate and multivariate analyses. Analyses will control for the presence of chronic medical conditions to identify associations between pre-op psychosocial assessment and the hospital admission metrics listed above.

Project Title: *Sleep Better; Breathe Better*

Work Location: Wilmington, DE

Mentor(s): Abigail Strang, MD; Kimberly Canter, PhD; Aaron Chidekel, MD

NSURP Project 13

PROJECT DESCRIPTION

BACKGROUND:
Children with chronic respiratory disease, including asthma and cystic fibrosis (CF), are at risk for disrupted sleep for several reasons. These sleep disruptions can negatively affect both physical and mental health. Despite this known relationship, the effect of using standardized behavioral strategies to improve sleep in children with respiratory disease is understudied.

HYPOTHESIS:
Children with asthma and CF who complete a brief, modularized sleep intervention will report improvements in sleep health and respiratory health measured by standardized questionnaires, lung function testing, and self-reported sleep logs.

SPECIFIC AIM:
1. Collect baseline information about sleepiness, sleep needs, behaviors and beliefs in children with asthma and CF
2. Explore the effect of a brief, modularized sleep intervention in children with asthma and CF on sleep and respiratory symptoms
3. Explore the acceptability and feasibility of a brief, modularized sleep intervention in children with asthma and CF

METHODOLOGY:
Patients with asthma and CF aged 9-17 will be recruited to participate in the study during routine appointments in the pulmonology clinic, either in-person or via telemedicine. Participant baseline characteristics will be collected using standardized surveys, self-reported sleep logs, and chart review. The sleep intervention modules and follow-up assessments of sleep and respiratory parameters will be administered by the research team at set time points both in-person and utilizing telemedicine platforms. Changes in outcomes from baseline to post-intervention will be analyzed.

Pending Covid-19 restrictions at the time of the study, these research procedures will be modified to allow for either remote study consenting and data collection or safe social distancing for participants and research staff including NSURP student in the clinic environment.

Project Title: *Cardiopulmonary Exercise Testing (CPET) in Adolescents to Identify Preclinical Cardiovascular Abnormalities after Open Heart surgery for Congenital Heart Disease*

Work Location: Wilmington, DE

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PROJECT DESCRIPTION

BACKGROUND:

Long term symptom-free survival is expected in patients who underwent surgical repair of complex congenital heart disease (CHD) during childhood. However, the higher incidence of cardiovascular complications is reported in adults with repaired CHD, mainly due to either residual hemodynamic abnormalities or lack of regular exercise involvement. We have been advocating cardiopulmonary exercise testing (CPET) as an excellent screening tool to identify those who are at risk for future cardiovascular complications. In addition to its diagnostic value, CPET can provide a unique opportunity to educate the patients with the mechanism of beneficial effects of exercise to general health.

Exercise performance consists of cardiac function (cardiac function), lung function (oxygenation and ventilation), blood (oxygen carrying capacity; hemoglobin), vascular function (vasodilatation), and skeletal muscles. We will delineate how these factors contribute to the overall exercise capacity.

HYPOTHESIS:

Preclinical cardiovascular abnormalities can be screened by CPET in asymptomatic adolescents who underwent open heart surgery for complex CHD.

SPECIFIC AIM:

1. Assess exercise performance by CPET in different type of repaired CHD including tetralogy of Fallot (TOF), truncus arteriosus (TA), transposition of the great arteries (TGA), and s/p Fontan operation for single ventricle (retrospective analysis of existing database). By using peak CPET parameters and submaximal parameters simultaneously, we will address 1) stroke volume reserve and heart rate dependency, 2) skeletal muscle mass, 3) exercise economy, and 4) exercise endurance capacity.
2. Correlate CPET-derived data regarding functional cardiovascular reserve with hemodynamic data obtained by noninvasive imaging study (echocardiogram).

METHODOLOGY:

1. Retrospective chart review of adolescents (age ≥ 12 years old) who were studied CPET (with cycle ergometer) after undergoing reparative cardiac surgery for complex congenital heart disease during childhood and age- and sex-matched controls. Complex CHD patients include; i) tetralogy of Fallot and truncus arteriosus (right ventricular volume overload group), ii) transposition of the great arteries, and iii) single ventricles with Fontan patients.
2. Application of new method of CPET analysis ("Two-way CPET analysis†") with a) peak CPET parameters: peak oxygen consumption (pVO2), peak heart rate (pHR), peak work rate (pWR), peak minute ventilation (pVE), peak oxygen pulse (pOP), and peak respiratory quotient (pRQ), and b) submaximal CPET parameters: ventilator anaerobic threshold (VAT), oxygen uptake efficiency slope (OUES), and submaximal slopes including HR and VO2 (ΔVO2/ ΔHR: stroke volume), heart rate (ΔHR/ ΔWR: heart rate dependency), WR and VO2 (ΔVO2/ ΔWR: exercise economy), and ventilator efficiency (ΔVE/ ΔCO2).
    a) Heart rate dependency and Stroke volume reserve (ΔHR/ ΔWR and pOP)
    b) Skeletal muscle effects (pVO2, VAT, OUES, and ΔVO2/ ΔHR)
    c) Chronotropic competence (pVO2 and pOP)
    d) Exercise endurance: submaximal parameters (VAT, OUES, and ΔVO2/ ΔHR) and pVO2
    e) Exercise economy and peak exercise performance (ΔVO2/ ΔWR and pVO2)
3. Echocardiographic analysis of global left ventricular function.
4. Statistical analysis of the data: Pearson correlation coefficient analysis for two-way CPET analysis, one way ANOVA for multiple comparison, and unpaired Student t-test for 2 comparison.

Summer students are also encouraged to shadow actual CPET with attending cardiologists in the Exercise Laboratory.