Basim Ahmad
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Title: Attitudes Towards and Rates of Cancer Screening in Chronic Kidney Disease (CKD), Dialysis and Kidney Transplant Patients
Sponsor: Dr. Mariana Markell
Undergraduate Medical Education, Nephrology
Co-Advisor:
Location: SUNY Downstate Medical Center

Fellowship period: Yes
Involve any? Yes

Review Board Type: IRB
Study#: 763663-14
Dates: 01/09/2020
Title: Comparison of Factors Affecting Nutrient Intake in Kidney Transplant Recipients, Patients with CKD or ESKD and Local Controls: Relationship of Blood Levels of Phosphorous, Calcium, Vitamin D and Hgb and Body Composition Analysis by InBody S10 Bioimpedance Machine. A Cross-sectional Study.
Site: SUNY downstate medical center suite C.
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: During my undergraduate years, I spent a year as an intern at the Applied Technology Laboratory for Advanced Surgery (ATLAS) at Roswell Park Cancer Institute in Buffalo, NY. I assisted with research involving the efficiency of the operating room during robot-assisted surgery, and on risk factors for post-operative complications following robot assisted cystectomies. In my time at the lab, I participated in literature review, assisted with editing of publications, transcribed videos of the operating room during radical cystectomies, collected various forms of data, and designed spreadsheets to collect data. The data collection I worked on included inputting survey forms from the surgical team, collecting patient data from the EHR for retrospective research, and documenting details from video recordings of surgery such as stitch counts and tool changes. I learned about the process of research, and the work that is required to create and publish each paper. Following this year, I worked intermittently with the lab to help with editing and review of some of the publications I am listed as a coauthor for.

Career goals: My current career goals involve being involved in both the clinical and academic aspects of medicine. Although I do not know definitively what specialty I would like to be, I have a few fields I am currently interested in, such as oncology, emergency medicine, and dermatology. I feel that it is important to me to be involved both in helping patients in a clinical setting, but also advancing care through research. Ideally, I would be working in an academic hospital that will allow me to teach and be a mentor for the next generation of medical professionals. I feel by being involved in research, I will stay involved in the advancement of medicine. This involvement will allow me to make sure that my patients receive the best care that is possible at their time of treatment, and will allow me to make sure that future medical students are educated in a way that helps them understand the ever-evolving field of medicine. I would like to have a career that will leave a lasting impact on medicine, and one that allows me to provide the greatest quality care possible to the patients I work with.

Description: Background:
Patients with CKD who undergo Dialysis or Kidney Transplant may be at a higher risk for developing cancer than the general population, and face a higher mortality from cancer as well [1-5]. Some studies claim that cancer risk may increase from 10-80% after dialysis [6]. The large range of this prediction is suspected to be related to poor coverage and cancer follow up in the US and

Europe, leading to lower reported rates of cancer [6]. Patients with early stage CKD may have higher risks of certain types of cancer as well, although studies into the subject do not all show statistically significant increases [7, 8].
Screening and early diagnosis have been shown to reduce the mortality of cancer [9, 10]. As CKD patients continue to survive longer, it becomes more important to screen for cancer. Several studies have shown CKD patients participate less in breast cancer, cervical cancer, and colorectal cancer screening [7, 11, 12]. One study measured the beliefs and attitudes of CKD patients about screening and discovered themes in their aversion to colorectal cancer screening. However, it may lack external validity because it had a small sample size of 38 patients who were predominantly white (31/38) and all from Australia and New Zealand. They found five major themes in aversion to screening: invisibility of cancer, prioritizing kidney disease, preventing the crisis of cancer, cognitive resistance, and pragmatic accessibility [12]. In later stages of CKD, there are fewer benefits of cancer screening due to treatment being less likely to extend life expectancy. This justifies the low rates of cancer screening in those patients, however it does not explain the overall trend. Cancer screening should be based off the specific circumstances of the patient to avoid unnecessary harm and maximize its effects [13].
Additionally, studies have shown that CKD patients have low health literacy surrounding their condition, particularly patients of low socioeconomic status and those of nonwhite ethnicities [14]. Lower health literacy leads to lower rates of preventative care, such as cancer screenings [15, 16]. As far as we are currently aware, there are no studies that specifically measure incidence of preventative screening and attitudes about screening within CKD patients of these low socioeconomic, nonwhite populations.
Goals of the Project:
Cancer screening and early diagnosis are important to reducing the overall impact of cancer. The previous studies of cancer screening in CKD patients have had either limited patient populations or did not include more than one stage of CKD patients. There is also very limited research into the reasons patients may not want to receive screening, and what can be done to promote screening. Additionally, the population of Brooklyn, NY provides a unique patient group to study, which may treat their healthcare differently than other groups that have been studied.

We will seek to understand how these patients' attitudes towards cancer, and what affects their decision whether or not to participate in cancer screening. If the populations who would benefit from screening are not receiving it, this may demonstrate a need for greater advocacy by their physicians for cancer screening. If the patients are against screening, finding their thoughts on why they do not receive screening will help physicians advocate for screening in an effective way.
Methods and Analyses:
A random convenience sample of 90 patients will be recruited from the CKD (30) and kidney transplant clinics (30) at Downstate, as well as the dialysis unit (30) at Parkside. A control group of 20 patients will be recruited from an associated family medicine clinic.
A survey will be administered to address the patient's knowledge about various cancers, their beliefs about risk factors for cancer and the relationship of cancer to kidney disease, their past experiences with cancer both personally and in their friends and family, and their adherence to the USPSTF cancer screening recommendations. They will also be asked about common risk factors for cancer including smoking and occupational exposure as well as immunosuppression, infectious diseases and length of time with ESRD (if relevant). Chart review will be performed to examine risk factors for cancer, cancer history and record of cancer screening. Demographic data including age, education status, income, race and ethnicity, as well as other factors will be recorded. Associations will be evaluated using Pearson r or Spearman rho as appropriate, between group comparisons by t-test or Chi-Square analysis. Descriptive statistics will include mean and standard error. All analyses will be performed using SPSS. A group size of 20 should give a $p<0.05$ for a moderate sized effect for between group comparisons. It is unlikely that the n will be large enough for a logistic regression to be performed using the identified risk factors.

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Make ups: N/A

Saad Ahmed
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Title: Nocturia Treatment: What Works and Why
Sponsor: Dr. Jeffrey Weiss
Urology
Co-Advisor:
Location: Brooklyn VA Hospital

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: My previous research experience comes from my undergraduate career at the City College of New York. I first participated in bench research to perform synthesis of nanoparticles made of polymer material and metal. The first goal of this research was to synthesize nanoparticles with varying parameters, such as size and shape. The second goal of this project was to develop a hybrid system, consisting of both polymer and metal nanoparticles, that would allow us to consider and combine different mechanisms of energy transfer. These mechanisms of energy transfer include fluorescence in the polymeric nanoparticles and plasmon resonance in the metal nanoparticles. Ultimately, this would allow us to develop a smarter system with an efficient mechanism of energy transfer, that could have applications in drug delivery and therapeutics. I worked on this project for approximately two years and culminated in my honors research project.
Next, I also conducted research at the Albert Einstein College of Medicine. There, my research included determining synthetic routes to achieve an anti-viral nucleotide, which was dubbed ddHCTP (3'-deoxy-3',4'-didehydro-cytidine-triphosphate) . This work was based on the initial discovery of the mechanism of action of Viperin, an anti-viral protein. Specifically, it was found that this protein led to the synthesis of ddHCTP from cytidine triphosphate, which led to chain termination of growing viruses. Through this research, it was found that ddHC, the unphosphorylated form of ddHCTP, could be converted into ddHCTP by endogenous kinases. Finally, this research culminated in poster presentation and ongoing research in the lab hopes to develop pharmacologic applications of this anti-viral compound.

Career goals: My career goal is to specialize in the field of urology because it is a combination of both surgery and medicine. The surigical aspect will allow me to treat patients with another healing modality. Furthermore, working as a urologist also includes patient interaction and patient care, which is what drove me to the field of medicine in the first place. In addition, I find the field of urology fascinating because it brings together so many disciplines, including metabolism, reproductive health, endocrinology, nephrology, and many others. Next, since it is also a surgical field, it is always at the forefront of medicine and constantly evolving. This will give me the opportunity to be a lifelong learner. Finally, I hope to work in an academic setting where I can not only care for patients, but also contribute to urology research. This is important to further the field of urology, keep making contributions, and bridge research and patient care.

Description: My proposed research for the Summer will be a continuation of the work done by members of the Weiss lab. Specifically, the research project will focus on examining the database consisting of voiding diaries from patients who have been treated for lower urinary tract symptoms at the Brooklyn Veterans Affairs urology clinic. The research will focus on entering data regarding on specific attributes of these patients, such as other health conditions and medications. Next, the research will also focus on determining which medications and behavior modifications have aided these patients in nocturia treatment. Similar, another path to explore would be the possibility of a synergistic effect of behavior modification and medication in nocturia treatment. This is all done in hopes of determining optimal treatments for patients suffering with nocturia and improving patient care.

Make ups: N/A

Kyrillos Akhnoukh
Email: Kyrillos.akhnoukh@downstate.edu
Phone: 7184194812
Title: Effect of Selective Serotonin Reuptake Inhibitors (SSRIs) on Bleeding in the Setting of Hip Fracture Surgery
Sponsor: Dr. Afshin Razi
Maimonides Medical center, Brooklyn, NY: Orthopedics department
Co-Advisor: Erez, Orry, M.D.;Swiggett, Samuel M.D., Orthopedic research resident
Location: Maimonides Medical Center Brooklyn, New York

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: I have one year of research which spanned from June 2018 to June 2019. I was a research assistant in Dr. Greenbaum's biochemistry lab at CUNY Hunter College. During the summer I worked 30 hours a week and during the fall and spring semesters, I worked in the lab for 20 hours a week along with taking classes. The lab's focus was on determining the mechanics of a splicesome in the splicing of pre-mRNA to mature mRNA. My project was to determine the role of the protein RBM22 in the stabilization and folding of the splicesome. I utilized many lab techniques and protocols which include: spectrometry, Fast pace liquid chromatography, denaturing gel electrophoresis, and non-denaturing gel electrophoresis. I also had to transform bacteria to grow the desired protein and then culture, isolate, and purify the desired protein. I presented a research poster on my work in the lab at the undergraduate research symposium at Hunter College in April of 2019.

Career goals: Upon completion of medical school here at SUNY Downstate, I hope to match with an orthopedic residency program within NYC. Upon completion, I hope to become a practicing orthopedic surgeon in the New York City area where I can provide care as a physician to the community here. I have traveled to Kenya as a volunteer on a medical mission trip, where I was able to shadow and assist physicians, dentists, and pharmacists in the free clinics set up around the country. I hope to also travel back to the underserved countries as a practicing physician to assist in any way possible whenever I have the time.

Description: General Background:

SSRI medications are commonly prescribed in the elderly population to combat depression and anxiety. Hip fractures are one of the most common traumatic injuries in this population as well, and routinely need to undergo operative intervention to provide stabilization for appropriate rehabilitation. Increased bleeding and increased levels of blood transfusions can cause increased morbidity in this population and ideally should be avoided if possible. If patients are on SSRIs during an admission for a hip fracture, it would be important to know if this subsegment of patients is at an increased risk for 1) bleeding during the procedure or post-operatively, and 2) are at an increased risk for blood transfusions.

Specific aims and research plan of your proposed project:

•Examine levels of hemoglobin/hematocrit in patients both on SSRIs pre-operatively and those who are not on these medications with a diagnosis of a hip fracture (femoral neck fracture, intertrochanteric fracture, subtrochanteric fracture)

Determine if there is a larger drop in H&H post-operatively in patients on SSRIs than those that are not on SSRI medications

Compare rates of blood transfusion between patients on SSRI medications vs. those who are not in the same cohort

Methods and statistical analysis:

-Subjects: Retrospective internal database review of patients diagnosed with a hip fracture that underwent surgery at MMC between 2015 and 2017.

-Inclusion criteria: All patients diagnosed with a hip fracture that underwent surgery (CPT code: 27130,27235, 27236, 27236,27245) between 2015 and 2017 at MMC.

-Exclusion criteria: Patients with no laboratory studies post-operatively. Patients under 50 years of age

-Design: Retrospective case control study conducted by orthopaedic surgery department

-Data Collection Procedures: Internal database of hip fractures has previously been compiled under MMC IRB approval 2018-12-11. This study will utilize this database to identify study subjects. Chart review in SCM will be needed to identify hemoglobin and hematocrit levels for patients pre-operatively and post-operatively, as well as look in the medication list to see if these patients were taking SSRIs for any medical reason.

-Data Analysis: Data will be analyzed according to appropriate data standards with the help of the MMC statistician.

-Sample Size: 752 patients are included in the hip fracture database, which will compromise the study and control group.

References to prior publications:

Andrade C, Sandarsh S, Chethan KB, Nagesh KS. Serotonin reuptake inhibitor antidepressants and abnormal bleeding: a review for clinicians and a reconsideration of mechanisms. The Journal of Clinical Psychiatry. 2010 Dec;71(12):1565-1575. DOI: 10.4088/jcp.09r05786blu.

Dalton, S.O., Sørensen, H.T. & Johansen, C. SSRIs and Upper Gastrointestinal Bleeding. CNS Drugs 20, 143–151 (2006). https://doi.org/10.2165/00023210-200620020-00005

George Mawardi, Tim M. Markman, Rahatullah Muslem, Minoosh Sobhanian, Maureen Converse, Holly B. Meadows, Walter E. Uber, Stuart D. Russell, Rosanne Rouf, Bhavadharini Ramu, Daniel P. Judge, Ryan J. Tedford, Brian A. Houston, SSRI/SNRI Therapy is Associated With a Higher Risk of Gastrointestinal Bleeding in LVAD Patients, Heart, Lung and Circulation, 2019, ISSN 1443-9506, https://doi.org/10.1016/j.hlc.2019.07.011.

Roose SP, Rutherford BR. Selective Serotonin Reuptake Inhibitors and Operative Bleeding Risk: A Review of the Literature. J Clin Psychopharmacol. 2016;36(6):704–709. doi:10.1097/JCP.0000000000000575

Xavier Delavenne, Patrick Mismetti, Laurent Bertoletti,

Bleeding risk under selective serotonin reuptake inhibitor (SSRI) antidepressants: A meta-analysis of observational studies, Pharmacological Research, Volume 118, 2017, Pages 19-32, ISSN 1043-6618, https://doi.org/10.1016/j.phrs.2016.08.017.

These scholarly articles all show a direct correlation between the use of SSRI and increased bleeding risk. There is no published literature on the use of SSRI and hip surgery, specifically, which is the focus of this study. There has been research on the use of SSRI and GI bleeding, but not hip surgery. So, there is a general correlation with increased risk of bleeding but a need to find out more specifically how it affects the course of bleeding in hip surgeries.

Make ups: N/A

Tabrez Alam
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Title: The Impact of Previous Hand/Upper Extremity Surgery on Patient-Reported Outcome Measures.
Sponsor: Dr. Steven Koehler
Department of Orthopaedic Surgery
Co-Advisor:
Location: BSB 3-7

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: 1299140
Dates: 10-09-2018
Title: Developing the HAND-Q: Phase 2 Field Test
Site: SUNY Downstate
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: I have had considerable experience in basic science research in various disciplines. From 2012 to 2015, I worked with Professor Ben Ovryn at the Albert Einstein College of Medicine, where I used advanced interferometry/microscopy techniques to visualize primary cilia in 3-D space within cellular matrices. Through this project, I learned structural biology, optics and mathematical programming to conduct the project and perform data analysis, and I gained experience in writing abstracts and presenting my research at conferences. In the summer of 2016, I worked with Professor Robert Griffin at the Massachusetts Institute of Technology, where I grew amyloid beta protein fibrils from bacterial samples and then analyzed the protein structures using advanced nuclear magnetic resonance spectroscopy techniques. Finally, from 2017 to 2019, I worked with Professor Timothy Jamison at MIT, where I developed novel organic chemistry syntheses through continuous-flow devices for pharmaceutical molecules such as Atorvastatin. I was granted considerable autonomy in the lab and I was able to plan my own sets of experiments, carry them out, analyze the data and present my research orally to the group and PI at the end of every month. In addition to learning advanced organic chemistry and chemical engineering techniques, I gained experience in manuscript writing and I helped write a publication about a novel quantitative chromatography method I helped develop, which is currently pending review in the American Chemical Society's Journal of Chemical Education. In conclusion, I am very familiar with the process behind productive research and I hope to use my experience in research writing and presentation to translate to an incredibly productive and engaging summer research opportunity.

Career goals: I am highly interested in pursuing a future career in surgery, as I find the pathologies, methodologies of treatment and the immediacy of impact to be incredibly interesting and highly satisfying. Orthopedic Surgery is a specialty with an interesting breadth of cases ranging from hands/upper-extremities to back/spine cases, and I want to use this summer as an opportunity to both conduct productive surgical research and gain exposure to Orthopedic Surgery. Furthermore, I greatly enjoyed learning about the anatomy of the hands and the various surgeries that can be performed to restore the function of injured hands. As this project will involve assessing patient satisfaction in hand/upper-extremity surgery, I will definitely be engaged and use this opportunity to learn more about the sub-specialty. Therefore, I hope to use my experiences this summer not only to further gauge my interest in Orthopedic Surgery but also to contribute to the field and provide meaningful research that would further enhance the existing compendium of clinical knowledge in the field.

Description: General Background:
Differences in clinical outcomes between surgical and non-surgical patients have previously been evaluated in hand/upper-extremity patient populations. Measurements such as radiographic results, treatment complications, pain levels and mechanistic factors such as grip strength and range of motion have been used by various groups evaluating outcome differences between surgical and non-surgical patients affected by conditions such as distal radius fractures, Dupuytren's contracture, and mallet fingers [1-6].
While such measurements are valuable in better understanding the effectiveness and success of various treatments, patient satisfaction is just as valuable as a quantitative marker. In measuring this, the use of patient-reported outcome measures (PROMs) can be extremely powerful. PROMs are measurements of health status reported directly from patients without a clinician's interpretation, and have been instrumental in advancing patient-centric practices, promoting patient autonomy, and encouraging shared decision-making [7-8]. Many studies comparing the clinical outcomes of surgical and non-surgical patients with upper-extremity conditions have actually utilized PROMs to capture the relationship between physicians' and patients' perception of treatment success and satisfaction [1-6]. The Disabilities of the Arm, Shoulder, and Hand (DASH) [9], the Patient-Rated Wrist Evaluation (PRWE) [10], the Boston Carpal Tunnel Questionnaire (BCTQ) [11], and the Carpal Tunnel Syndrome Assessment Questionnaire (CTSAQ) [12], have been commonly used in patient populations with upper extremity conditions. Still, the impact of prior surgical treatment on present hand care has not been effectively examined by such measures.
Such established PROMs are capable of integrating the patient's perspective into clinical assessments of surgical and non-surgical treatments; however, their brief and generalized nature pose a limit in their ability to effectively capture the patient's full perception of their treatment. The introduction of the comprehensive Hand Questionnaire (HAND-Q) into this group of upper extremity PROMs will be crucial in accurately capturing the potential impact that surgical history may have on patients' progress with their current hand conditions [13]. HAND-Q is a questionnaire generalized to patients experiencing various upper-extremity conditions, and assesses hand functionality satisfaction, symptom severity, emotional dissatisfaction, sexual dissatisfaction, hand appearance satisfaction, and overall treatment satisfaction.
Specific Aims and Research Plan:
In this study, HAND-Q is administered to a large cohort of patients presenting with a wide array of upper-extremity conditions at non-specific points in their treatment to document differences between surgical and non-surgical patients' responses. We believe that the extensive nature of HAND-Q will greatly aid in measuring any significant effects that prior surgical treatment may have on patient satisfaction and care, and thereby provide a novel approach to assess the patient experience during their surgical care.
The study will be retrospective as patients undergoing upper-extremity surgery between September 2018 and August 2019 have already been given the option to complete HAND-Q survey. Thus, the focus for the project this summer will be to analyze and compare the collected results of the HAND-Q for patients who have had previous surgical history versus patients who have not.
Methods and Statistical Analysis:
Patients presenting to a single, board-certified and hand/microsurgery fellowship-trained orthopaedic surgeon at an outpatient hand clinic from September 2018 to August 2019 were given the option to complete the Hand Questionnaire (HAND-Q) while waiting to be seen by medical staff. The HAND-Q survey is a Patient Reported Outcome Measure (PROM) undergoing Phase II validation worldwide, which was developed using internationally accepted patient reported outcome and quality of life measurements [14]. Consenting patients were consecutively enrolled in this international validation study, which was approved by our institutional review board.
Here, we will report our institution's collected data. Consenting patients with valid responses to the following question types will be included: Hand Functionality Satisfaction, Symptom Severity, Hand Appearance Satisfaction, Emotional Dissatisfaction, and Treatment Satisfaction. Patients under the age of 18 are excluded from this study. Composite scores (CS) will be created for each individual section by collating scores from individual questions. The CS for each section will be calculated by summing all recorded patient answers, ranging from 1-4, for each question in the section, dividing this sum by the maximum score attainable for each section, then multiplying by 100. This established a generalizable CS scale (0-100). In order to be included in the CS analysis, patients are required to have answered, at minimum, all but one question in the section. Within each individual section (Hand Functionality, Symptom Severity, Hand Appearance Satisfaction, Emotional Dissatisfaction, and Treatment Satisfaction), two CS will be created for each section, those with a previous surgery and those without.
Interpretation of CS varies for each individual section: hand functionality (range, 0 [not at all difficult] to 100 [extremely difficult]), symptom severity (range, 0 [none] to 100 [severe]), hand appearance satisfaction (range, 0 [very dissatisfied] to 100 [very satisfied]), emotional dissatisfaction (range, 0 [never] to 100 [always]), and treatment satisfaction (range, 0 [definitely disagree] to 100 [definitely agree]). T-test analysis will be used to compare CS for those with a previous surgery versus those without, within each HAND-Q category. Following this analysis, individual questions will be compared within each HAND-Q category to compare

the effects of previous surgery. Dichotomous variables will be compared with a Chi-Square test. All analyses will be performed using SPSS version 26 (IBM Corp., Armonk, NY, USA), and a p-value <0.05 will be set as the threshold for statistical significance.

References:

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Make ups:

Jonathan Amaro-Barron
Email: jonathan.amaro-barron@downstate.edu
Phone: 7864731445
Title: Transgenerational transmission of behavioral phenotype in rats exposed to folate receptor antibody
Sponsor: Dr. Edward Quadros
Cell Biology
Co-Advisor:
Location: BSB 7-15, SUNY Downstate Medical Center

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: 18-10539
Dates: 03/07/2018
Title: Transgenerational transmission of behavioral phenotype in rats exposed to folate receptor antibody
Site: SUNY Downstate Health Sciences University
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: My experience with research began when I participated in the Howard Hughes Medical Institute High School Scholars Research Program at the University of Miami in 2013. While there, I worked in a stem cell lab and was exposed to wet-lab techniques and instruments such as cell culturing, micropipettes, real-time PCR, and electrophoresis. During my sophomore year at Vanderbilt University, I was chosen to participate in a special curricular biology lab where I gained exposure to laboratory techniques involved in live animal testing by developing and carrying out a study using the model organism Caenorhabditis elegans. I gained larger-scale research experience at the Undiagnosed Diseases Network where I was employed as a Research Assistant in 2017. There, I developed my administrative skills by communicating with participants and organizing their medical records as part of a nation-wide, multi-center research project.
In the fall of 2016, I was selected to become a Research Assistant in Dr. Mark Wallace's Multisensory Integration Neuroscience Lab. I worked at this lab through the spring of 2018 (including the summer of 2017) for about 12 hours per week on average. When I first joined the Wallace Lab, my MSTP student mentor, David, taught me how to properly compose a literature review. I had submitted an independent project proposal by December of 2016, and I was awarded funding to carry out my independent study on the effects of noise on signal processing. My volunteer work with the Autism Spectrum Disorder (ASD) population in high school inspired me to study how the sensory system processes signals in noisy environments, a task many individuals with Autism struggle with. I hope to continue my investigation of ASD through my work at Dr. Quadros' lab.

Throughout my time at the Wallace Lab, there were many successes and many failures, but I did my best to learn from each experience. I completed four experiments which resulted in various significant findings. David and the rest of my cohort will follow up on these findings in the coming years. Throughout this process, I learned a variety of lab techniques such as EEG data acquisition and processing as well as coding tasks and statistical analyses in MATLAB. Furthermore, I learned to work in a team with brilliant scientists, and to serve as a leader in a scientific setting.

Career goals: My interests in the healthcare field are diverse. They stem from consistently exciting and engaging experiences I have had working with different aspects of healthcare. My father is a nurse, and watching him act as a healing touch for people in their time of need was inspiring. Shadowing physicians in college reinforced my desire to have a career in which I can directly interact with the people I am helping. I discovered my love for basic science research by conducting my own research at Mark

Wallace's neuroscience lab. Lastly, I discovered my interest in public health by participating in a service-learning program that was designed to bring free fresh produce to the patients of Vanderbilt University's student-run clinic.
My career goal is to not only become a superior clinician in order to heal and advocate for the individuals in my community, but also to contribute to several facets of medical advancement including research, public health, and medical education. The idea of academic medicine is very appealing to me because it would not only fulfill my varied passions, but also provide an interdisciplinary synergy that would allow me to maximally contribute to the health of my community.

Description: General Background:
Folates are a group of organic compounds also known as vitamin B9 that play an essential role in a variety of fundamental biochemical processes. Sources of dietary folate include dark green leafy vegetables and fruits.[9] Folates in food come in various forms. After absorption into cells, folate is reduced to THF, its biologically active form.[10] THF then enters the folate cycle and is biochemically transformed into single-carbon unit donors such as 5-methytetrahydrofolate (5MTHF), 5,10-methylene-THF, and 10-formyl-THF.
The various forms of folate are involved in many biological processes. In the form of 5,10-methylene-THF, folate serves as a single-carbon unit donor for de novo purine synthesis. This form of folate also converts deoxyuridine 5'-phosphate to deoxythymidine 5'-phosphate for pyrimidine synthesis.[4] 5MTHF is an important cofactor in the reaction that converts the amino acid homocysteine to methionine. This reaction not only metabolizes homocysteine, but also allows for the production of S-adenosyl methionine (SAM), a molecule that plays an essential role in the methylation of histones and DNA for gene expression control and genetic stability.[5] This folate-dependent regulation of homocysteine is also linked to the metabolism of glutathione (GSH), a tripeptide with many biological roles including scavenging free radicals for the maintenance of intracellular redox potential.[6] Finally, folate is essential for neurotransmitter synthesis because the folate cycle is linked to the production of GTP. GTP is required for the production of tetrahydrobiopterin (BH4), an important cofactor in the synthesis of neurotransmitters such as serotonin and dopamine.[7]
Deficiencies in folate uptake and utilization can have various detrimental effects on the body. One such effect is demonstrated by folate's complex relationship with Autism Spectrum Disorder (ASD), a developmental disorder that presents in early childhood and is characterized by deficits in social interaction and communication, repetitive or stereotyped behaviors, cognitive deficits, and sensory abnormalities.[1] The connection between folate and ASD can be studied in the context of folate receptor alpha (FRα), a receptor that mediates folate uptake in cells, folate transfer across the placenta, and folate uptake into the CNS.2
There is evidence that autoantibodies directed against FRα are linked to several neurodevelopmental disruptions including ASD. The biological processes associated with folate are particularly important during early neural development. Therefore, researchers hypothesize that these disruptions may be due to a FRα antibody(FrαAb)-mediated effect on inflammation and folate uptake. Dr. Quadros' lab has studied this hypothesis in a rat model, and has shown that exposure to FRαAb during gestation causes folate deficiency and subsequent development of a behavioral phenotype comparable to human ASD.[8] The lab has also demonstrated that this phenotype can be prevented with administration of folinic acid and dexamethasone during gestational FRαAb exposure.[3]
A preliminary observation in this animal model suggests that the abnormal phenotype of rats that were directly exposed to FRαAb may also be observed in subsequent generations. I hypothesize that the ASD-like phenotype associated with gestational exposure to FRαAb can be transferred across generations and that treatment with folinic acid will prevent the transgenerational transmission of this phenotype. The goal of this project is to test this hypothesis.
Specific aims and research plan:
Specific aim 1: Identify the abnormal behavioral phenotype associated with gestational FRαAb exposure. Pregnant dams (P) will be randomly assigned to one of three groups containing at least three dams each: saline, pooled pre-immune normal rabbit (NR)-IgG, and rabbit IgG specific to FRα (FRαAb). Their offspring (F1) will be evaluated using a series of established behavioral tests to identify their behavioral phenotype. These tests evaluate animal model systems that parallel the core systems affected in human ASD. I hypothesize that F1 animals exposed to FRαAb during gestation will display an ASD-like behavioral phenotype.
Specific aim 2: Determine whether the abnormal behavioral phenotype is transferred across generations. The F1 animals that display the ASD-like behavioral phenotype will be bred to produce an F2 generation. This and subsequent generations will be bred up to generation F4. The animals in generations F2-F4 will perform the same battery of tests administered to F1 animals to evaluate their behavioral deficits (if any). I hypothesize that the ASD-like behavioral phenotype of rats that were exposed to FRαAb will be transferred across the F2-4 generations in their lineage.

Specific aim 3: Determine whether pharmacologic treatment with folinic acid prevents the generational transmission of the behavioral phenotype. Several F1 animals that display the ASD-like phenotype will be randomly selected to be part of the treatment group. During pregnancy, the dams will be given folinic acid. The offspring will perform the same battery of tests administered to F1 animals. I hypothesize that treatment with folinic acid will prevent transmission of the ASD-like phenotype to subsequent generations.

Methods and statistical analysis:

Experimental protocols will be approved by the Animal Care and Use Committee of the State University of New York, Downstate Medical Center. Pregnant dams will be injected intraperitoneally with one of three solutions depending on which group they have been randomly assigned to. The first group will receive 2 mL of saline. The second group will receive 4 µg NR-IgG per embryo plus 1 mL of normal rat serum. The third group will receive 4 µg FRαAb per embryo plus 1 mL of normal rat serum. All offspring will be fed a normal diet containing 2 mg of folic acid per kg chow. Between PND4 and PND70, F1 rats will undergo behavioral testing. After behavioral testing, several of the F1 rats that display the ASD-like phenotype will be randomly selected to be part of the folinic acid treatment group. Pregnant dams carrying offspring of treatment group rats will receive an intraperitoneal folinic acid injection (4mg/kg) between GD7 and GD12 while control group dams will receive 1mL of saline. F2 rats will be tested using the same battery of tests used for F1 rats. Breeding and behavioral testing will continue as previously described through F4. Statistical analysis for the behavioral studies will be performed using one-way analysis of variance (ANOVA) with subsequent Student's t-tests if ANOVA shows statistical significance.

Behavioral Studies

Communication deficit testing: Pups will be separated from the mother, and their ultrasonic vocalizations over a 3-minute period will be recorded and analyzed.

Sociability study/partition test: Male rats will be placed in standard cage divided in half by a partition through which he can see, hear, and smell a typically developed male rat in the other half of the cage. The amount of time the rat spends at the partition over a 5-minute period will be recorded and analyzed.

Place avoidance tasks: Three place avoidance tests will be conducted for each rat over three consecutive days. The tests consist of passive, active, and conflict place avoidance tasks (PPA, APA, and CPA). Each test consists of 4-6 trials of a rat exploring a circular arena for 10 minutes with 10 minute breaks between trials. During PPA, an area of the floor of the arena is prohibited and will administer a mild shock if entered. In the APA and CPA tests, visual cues outside of the arena can help the animal identify the position of the prohibited area. During APA, the arena slowly rotates, and rats must learn to use the visual cues to avoid the prohibited area and complete the task. During CPA, the relationship between the prohibited area and the visual cue is reversed, and rats must ignore what they previously learned to avoid the prohibited area and complete the task. A number of parameters will be recorded by an automated data acquisition system.

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Make ups:

Lon Yin Chan
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Title: Understanding the Widening Gender Disparity in Living Donor Kidney Transplants
Sponsor: Dr. Angelika Gruessner
Department of Medicine/Nephrology
Co-Advisor:
Location: SUNY Downstate

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: During my last two years of college, I was part of Dr. Gabriela Chiosis' lab at MSKCC. My project was to work on developing a fluorescence polarization (FP) assay as a potential diagnostic tool. At the culmination of my time there, I ended up one, establishing the specificity of the FP assay in detecting tumor-associated epichaperome networks, and two, elucidating the binding mechanism of epichaperome-selective inhibitor PU-H71 to epichaperomes.
The epichaperome is a term introduced by the lab in 2016 to refer to highly integrated networks of chaperomes, chaperones, co-factors etc., that are functionally and thermodynamically different from its constituent proteins. Epichpaeromes facilitate the survival of tumor cells, which made them good biomarkers for tumor cells. The lab also previously established that certain small-molecule HSP90 inhibitors such as PU-H71 selectively bind to HSP90 in the oncogenic form, which means it selectively targets malignant cells. Its binding to the ATP pocket of HSP-90 in the epichaperome formation led to the collapse of the network, thereby killing tumor cells.
First, I established that the FP assay could be used to show biological interactions as well as chemical interactions. Previously, it was only used to elucidate chemical structures and binding affinity. However, it turns out that, by using PU-FITC2 a derivative of PU-H71 with a fluorescent probe, the levels of epichaperomes in samples shown by FP assays correlated with levels shown by biochemical analyses in the same samples.
Next, using the FP assay, I elucidated the binding mechanism of the inhibitor to the epichaperome complex. There were initially two hypotheses for the mechanism: the binding inhibited the function of the complex, or the binding led to collapse of the complex, both pathways ending in cell death. While it was established in an earlier paper that PU-H71 effectively induced epichaperome collapse, the apparent increase in epichaperome levels shown by biochemical analyses was puzzling. With data from the FP assay, I showed, interestingly, that neither hypotheses were entirely correct. In fact, the binding of the inhibitor led to an initial trapping and stabilization of the epichaperome complex, followed by a subsequent collapse. The time-dependent regulation by the inhibitor helped link the apparent discrepancy that biochemical analyses showed.
During my senior year, I presented my work at two national undergraduate conferences, ABRCMS 2018 and ERN 2019.
Additionally, I was recognized as a contributor to the paper "The epichaperome is a mediator of toxic hippocampal stress and leads to protein connectivity-based dysfunction" which was published in Nature Communications in January 2020.
Prior to the Chiosis' lab, I was also at the lab of Elaine Fuchs at Rockefeller University for a semester, where I assisted in a project on asymmetric cell polarization in epithelial stem cells and learned most of my biological laboratory techniques.

Career goals: My two greatest passions are medicine and teaching. Though I am unsure about what field to pursue yet, I am leaning towards pediatrics, obstetrics/gynecology, or emergency medicine. I would like to work in a capacity that allows me to work with patients on a personal level, and relay what I've learned to people who are interested in similar topics. I realize that in order to understand the clinical aspect, it is important to appreciate the science behind or the factors that promote clinical presentations. Even if I may not end up conducting research at the bench side, I see myself eventually analyzing large quantities of data in my career. Patterns and questions are going to show up in any setting that I work in. I know that when that happens, I will inevitably be drawn to trying to explain them because in the end it will help me become a better healthcare practitioner. Ultimately, I would like to become a physician in medical academia, which will allow me to teach, heal, and influence medical care even at a small level. Finally, I see myself working at a place that has great diversity in patients and in students.

Description: Background:
According to the USRDS report, there is a growing number of patients with end stage renal disease. Those patients require renal replacement therapy which is either dialysis or kidney transplantation. The option of a renal transplantation offers patients independence of dialysis, higher life expectancy and improved quality of life. The kidney graft can come from a deceased or a living donor while the graft function is significantly better from a living donor kidney.
There has been an upward trend in renal transplantation over the past few decades, a gender gap between male and female recipients has persisted and continue to widen along certain factors. The ratio between male and female recipients of deceased donors has remained relatively constant over time, however the disparity rate increased in living kidney donor (LKD) transplantations. Markell et al. analyzed 105,729 primary adult living donor kidney transplants reported to UNOS/OPTN from 1998 to 2018 noting the widening gender gap. In addition to the gender gap, Markell et al. noted several other interesting analyses. While the recipient's age for either men or women increased, the likelihood of a wo men receiving a transplant at increasing age declined as did that of women on dialysis. On a more biological note, sensitized women had greater chances to receive a transplant than those who weren't sensitized. Women were also less likely to receive a non-biological kidney transplant than men—as many non-biological kidney transplants seemed to be from wife to husband. One final point that their analysis mentioned was that it seemed as though black women were more likelihood to receive a living kidney transplant than white women. In this preliminary analysis, we can already see that the trajectory of living kidney donations seem to align certain sociocultural and biological factors.[2]
In a subsequent preliminary analysis Gruessner et al. analyzed all 106,260 primary adult living donor kidney transplants performed in the US and reported to UNOS/OPTN from 1998 to 2018 noting the widening gender gap. The disparity could be noted in all UNOS/OPT transplant regions and declined from 41.94% in 1998/2000 to 36.68% in 2016/18. In this analysis, especially age and PRA levels could be identified as influential factors receiving a transplant.[1]
Specific aims and research plan of your proposed project
Given the interesting trends shown by Gruessner et al., there seems to be both biological and sociocultural factors that may impact donation and transplantation in women with end stage renal disease.[1] In this project, we intend to investigate what possible factors and patterns may have an influence on living donor kidney transplantation for women. In order to do so, we will analyze all primary living donor kidney transplants performed in the US on an expanded set of characteristics in addition to factors like race, dialysis treatment, and age.
By understanding the underlying factors that promote the current trends, we may eventually be able to tailor more customized guidelines in treating patients who may benefit living donor kidney transplantation, or to bring effective policy that may increase living donor kidney transplantations that would be suitable for more patients. The results of this study may be used to narrow the gender disparity that currently exists in living donor kidney transplantation, which will allow us to increase the quality of life for more patients.
Methods and statistical analysis
All 106,260 primary adult living donor kidney transplants reported to UNOS/OPTN from 1998 to 2018 will be analyzed according to donor, recipient clinical and socio-economic, transplant related factors. Multivariate models will be developed to explain why the disparity between male and female living donor kidney recipients exists Ultimately we hope to understand the underlying forces that drive the disparities in order to eventually improve LKD transplantation rates for women in the US and provide them with an improved life expectancy and better quality of life. To answer those questions, we will use the statistical program SAS9.4 Studio to for analysis, which will allow me to develop analysis skills on a high level. This study should help us to understand problems in analyzing large data sets and to understand the resulting answers.
Additional data sets, such as the United States Renal Data System (USRDS), may be used further down the line in the study.

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Make ups: N/A

Claire Sunha Choi
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Sara Abu-Ghanem
Claire Sunha Choi A Simple Assessment Tool for Screening Dysphagia and Aspiration Prevention in Inpatient Setting
Department: Department of Otolaryngology
SUNY Downstate Medical Center
Does the proposed project involve any of the following: human subjects or tissues, fluids, or other material from human subjects; animal experimentation; work with a biohazardous substance? Yes
Not yet submitted
Summarize your research experience
My research experience began through a summer research program after freshman year at The Miami Project to Cure Paralysis. I was assigned to a lab that studied the protective role of microglial Tumor Necrosis Factor Receptor 2 (TNFR2) signaling in multiple sclerosis (MS). Fascinated by how our own immune cells attack oligodendrocytes, cells that insulate neurons, during MS, I became actively involved in research from design to discussion. My project was to quantify and compare the level of different stages of oligodendrocyte populations between control and microglial TNFR2 knockout mice. When my results deviated from the hypothesis, I went back to re-evaluate data, read countless papers, and consistently discussed the findings with my mentor to come up with a valid explanation. I loved every minute of this intellectual struggle and the excitement to explore the unexplored kept me going. As much as I was interested in MS, I was also frustrated to learn that the available MS drugs – immunosuppressants – only serve to delay the disease progression. Curious to see if there could be better alternatives, I continued to perform MS research at Columbia, and I studied other pioneering approaches in treating MS, such as by targeting the blood-brain barrier (BBB) to halt inflammation, using stem cells to restore neuronal damage or applying focused ultrasound to enhance delivery of MS drugs. In recognition of my work in MS research during college, I have been awarded several research fellowships one of which was from The National Multiple Sclerosis Society and published in three well-known journals. After spending years in bench research, I wanted to learn more about how the disease affects patients and their quality of life. Following graduation in May 2018, I transitioned to clinical research at Dr. Charvet's team at NYU Langone Multiple Sclerosis Comprehensive Care Center where we studied neuromodulation therapy such as transcranial direct current stimulation (tDCS) for managing MS patients' daily symptoms including fatigue. At first, I familiarized myself with aspects of clinical research which involved performing data entry, guiding patient visits and preparing IRB submissions. After having acquired these skills, I further expanded my knowledge and applied my engineering background to help identify metabolic and neuronal changes in brain during tDCS. This project became to represent the first research in this area and is expected to significantly advance our understanding of mechanisms underlying the rehabilitative effects of tDCS. Notably, as the first author, I was selected for a platform presentation from this work "Transcranial Direct Current Stimulation (tDCS) Induces Acute Changes in Brain Metabolism" at the 2019 American Academy of Neurology. I hope to continue to engage in clinical and translational research and make innovative contributions at Downstate and in the field of medicine.
Describe your career goals: Otolaryngology was a field that I've always been interested in. Yearning to learn more about the field, I shadowed an ENT surgeon last year and observed her do surgeries such as a tracheotomy on a NICU baby to facilitate her breathing, and ear canal reconstruction to restore hearing loss in a car accident victim. It was amazing to see how someone could bring such an immediate and lasting positive impact on another person's quality of life, and this experience allowed me to want to further explore the field. I am also attracted to otolaryngology due to its interesting research venues, many of which are tied to biomedical engineering that I have a background in. With a strong interest in

research, I aspire to pursue a career in academic medicine. From my years of experience in multiple fields of MS research, I learned that complex human disease is usually not a single pathology, but rather a series of multiple mechanisms set by multiple factors. I hope to continue to bring this multidisciplinary view to discover links between seemingly separate fields, and make medical discoveries that impact human health. The road from research to patient side will be challenging, but what motivates me is the faith that my work, even the failed experiments, would contribute to advancing medical knowledge and at some point, benefit patients. Should I be given the alumni fellowship, I will use this opportunity to the fullest to grow into a better physician, surgeon, and investigator.

Background: Dysphagia or impaired swallowing, is a highly prevalent condition affecting 3.0% of all adult US inpatients 45 years of age or older [1]. The affected dysphagic patients are more likely to suffer from reduced quality of life, malnutrition, dehydration and health complications including aspiration pneumonia, which is the second leading cause of death in elderly patients [2]. While dysphagia has been primarily evaluated in patients with stroke, a recent systematic review found a significant economic and survival burden of dysphagia regardless of etiology, contributing to higher overall healthcare cost by 40.36% and increased hospital length of stay for 2 – 8 days [3]. Patients with dysphagia were more likely to be transferred to post-acute care facility (adjusted OR 2.8; 95% CI 2.73–2.81, $P < 0.001$) and 1.7 times more likely to die in the hospital (95% CI 1.67–1.74) [1]. In an attempt for early identification and effective clinical management, many dysphagia screening protocols and approaches have been introduced in recent years. These include dysphagia/aspiration clinical screening by nurses (i.e., 3-ounce water challenge protocol [4]), instrumental assessment by speech language pathologists when indicated (Fiberoptic Endoscopic Evaluation of Swallowing (FEES) or Modified Barium Swallow Study (MBSS) [5, 6]), and a self-administered questionnaire (10-item Eating Assessment Tool (EAT-10) [7]). Yet, although validated tools exist these are not routinely implemented. Moreover, there is no accepted hospitalized inpatient based-assessment tool, as the EAT-10 questionnaire is more suited to assessing outpatient population. Given that dysphagia in inpatient settings is associated with greater hospital expenditure, length of stay and higher mortality, there is a need for an easy and reliable clinical screening tool to quickly identify high-risk patients for dysphagia/aspiration and refer them to a more extensive swallowing assessment by speech language pathologists (SLP). To address this void in care, our project aims to develop a modified Eating Assessment Tool designed for inpatient population, “inpatient Eating Assessment Tool (inEAT)”, which will help nurses assess the clinical severity and dysphagia/aspiration risk of adult hospitalized patients at the initial stage of the screening process.

Specific Aim: We will develop, and test the reliability and validity of inpatient Eating Assessment Tool (inEAT) questionnaire in screening dysphagia and aspiration risk by comparing the dysphagic patient’s overall inEAT score to current clinical standards of swallowing assessment: (1) 3-ounce water challenge protocol (2) clinical bedside SLP evaluation (3) SLP-performed FEES or MBSS. Our specific hypothesis is that inEAT questionnaire will predict clinical severity and risk for dysphagia and aspiration that would necessitate further evaluation by SLP.

Methods: This study will be conducted on adult inpatients with diverse etiologies of dysphagia at multiple institutions including Kings County Hospital Center, SUNY Downstate, Methodist Presbyterian Hospital, Stanford Healthcare, and Maimonides Medical Center. This questionnaire will be tested in different inpatient subgroups including neurological patients, head and neck cancer patients, elderly and others. My main role in this project will be to perform statistical analyses on the collected data to refine and test the validity and reliability of inEAT questionnaire. Claire Sunha Choi Downstate COM 2023 After the preliminary inEAT questionnaire has been developed, we will test the internal consistency by administering the questionnaire to selected inpatients upon their admission and again within 24 hours.

The internal consistency of inEAT questionnaire will be assessed with the Cronbach alpha and test-retest reliability will be evaluated with the Pearson product moment correlation coefficient. Inter-item correlations will be utilized to remove redundant and poorly reliable questionnaire items to derive a finalized inEAT questionnaire. For evaluating the discriminating ability and validity of inEAT to detect dysphagia and aspiration risk, we will compare the outcomes of inEAT questionnaire to the clinical and instrumental swallowing assessments done by nurses and SLPs: (1) 3-ounce water challenge protocol (2) clinical bedside speech language pathologist (SLP) evaluation (3) SLPperformed FEES or MBSS. Specifically, we will generate receiver operating characteristic (ROC) curve to determine sensitivity and specific values for inEAT questionnaire, and apply Mann-Whitney nonparametric test to evaluate correlations between inEAT and FEES or MBSS. Finally, to assess whether inEAT scores could predict dysphagia and aspiration outcome, we will use a logistic regression model (dichotomous variable: aspiration present/absent) and evaluate performance by ROC and area under the curve.
Implications: Early identification of dysphagia and aspiration risk is important in prevention and management of complications. Our project will provide evidence for a quick, reliable, validated and easy-to-use screening tool – inEAT questionnaire – that could help nurses determine inpatients at high risk for dysphagia and aspiration, and direct them to more exhaustive instrumental evaluation. When successfully incorporated into clinical use in inpatient setting, inEAT questionnaire will help ensure comprehensive care of dysphagia, improved quality of life in dysphagic patients, and reduced economic and survival burden associated with dysphagia.

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Kevin Chao
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Title: Comparison of Foot Function Between Baseline and 1 Year Follow-Up in USMA Cadets
Sponsor: Dr. Howard Hillstrom
Leon Root Motion Analysis Laboratory at the Hospital for Special Surgery (New York, NY)
Co-Advisor:
Location: Leon Root Motion Analysis Laboratory at the Hospital for Special Surgery

Fellowship period: Yes
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: I have conducted biomechanics research at the Leon Root Motion Analysis Laboratory at the Hospital for Special Surgery during my junior and senior years of high school. I worked on two projects regarding knee osteoarthritis and baseball pitching. In “The Effects of Osteoarthritis Knee Bracing with E-Tibia Prosthesis on Joint Mechanics During Stair Descent,” I tested the different efficiencies among five brace conditions (Brace 1-Brace 4 and Unbraced) during stairs-descent. Motion analysis cameras recorded 3D data for inverse dynamics, while an electronic knee prosthesis (e-tibia) measured internal forces directly. Data was processed through Visual3D, Cortex, and Matlab. Results showed that e-tibia forces were about 2417N (peak 2) greater than inverse dynamic forces, suggesting the e-tibia a better indicator of knee kinetics. Brace 4, a Brace 1 with 4° valgus, produced the lowest medial load, suggesting that greater valgus angles decrease medial loading by shifting the load to lateral direction. This research project was accepted as an abstract and at poster presentations for various journals (ORS, GCMAS). In “The Fatigability of the Shoulder in Adolescent Baseball Pitchers,” the data acquired on eight male high school baseball pitchers was captured throughout a simulated game to study the effect of fatigue on the kinematics (angular rotations) of the shoulder during the pitch. The premise of this study was that ‘consistency’ of humero- and scapula-thoracic motions would be reduced later in the game and present as reduced reliability. Reliability was measured using the intraclass correlation coefficient (ICC) between pitches 26 – 30 (fresh state) and 86 – 90 (fatigued state). Results demonstrated that ball speed and internal and external rotational strength were significantly reduced by the later pitches. Reliability, however, was not reduced for many phases of the baseball pitch for pitches 86 – 90. At Dartmouth College, I conducted biochemistry research at the Geisel School of Medicine as a Presidential Scholar. I worked on a project titled, “Identification of factor(s) that stimulate acyl-CoA:cholesterol acyltransferase 1 in vitro” with the primary objective of inducing the overproduction of cholesterol in astrocyte cells by introducing ACAT1 inhibitors and an adeno-associated virus, which carries a gene that triggers the overproduction of cholesterol, and analyzing whether increased cholesterol levels affects the biosynthesis and lipidation of ApoE4.

Career goals: I am particularly drawn to the field of orthopedics. Ever since I was young, I loved to be active and developed a genuine passion for sports. I participated in a variety of team sports, which exposed me to the severity of injuries and how they hinder the body from working properly. My fascination with science and the inner workings of the human body influenced my decision to conduct biomechanics research at the Hospital for Special Surgery regarding knee osteoarthritis and shoulder fatigue

from baseball pitching. This experience was very eye opening and showed me the intricacies of ostensibly simple motions of the human body and how we can immediately benefit patients with targeted therapies that alleviate stress on a certain body part. As I wanted to learn more about hospital life and the physician's duties, I sought out shadowing positions, specifically in the rehabilitation medicine department at NYU Langone. Shadowing a physiatrist elucidated the goal to restore the functional abilities of those with physical impairments. I carefully watched my preceptor and other physical therapists analyze the impaired area of a patient and then proceed to offer insight that improved the patient's physical capabilities. I noticed how this field differs from other specialties in that you can witness firsthand the recovery process of a patient. I really appreciated how in orthopedics, patients can get right back on their feet and the impacted area can become fully functioning again.

Description: I. General Background

Foot type can be used to depict the anatomic complexities of the foot and is comprised of 3 overarching dimensions, including 1) structure, which is further subdivided into rectus (normal alignment), planus (low arched), and cavus (high arched), 2) function, which is further subdivided into neutral, over-pronating, and over-supinating, and 3) flexibility, which is sub-categorized as moderate, low, and high [1]. Foot types differ between individuals with regards to structure, function and flexibility, which results in inherent variations of biomechanical function [2,3]. Previous studies have investigated the differences in foot type amongst United States Military Academy (USMA) cadets at West Point across sex, race, and injury incidence [4]. It has been shown that African Americans have a significantly more planus foot structure than other racial groups, Asians display much more overpronation, and women have significantly more flexible feet than men [4]. During the first 8 weeks prior to officially enrolling in the US Military, these cadets must undergo rigorous training. In their first year of basic training, approximately one-third of cadets develop a musculoskeletal (MSK) injury, but there is yet a clear explanation as to why this trend occurs.

II. Specific Aims and Research Plan

The purpose of this research project is to determine the effect of the intensive 8 week training regimen on foot function in young, active USMA cadets at West Point. The baseline group of 1090 (18-30 years of age) male and female USMA cadets at West Point class of 2017 who are all free of any MSK injury was asked to complete a 3-4 minute obstacle course. From this baseline group, a subset of cadets participated in a 1 year follow-up. Foot function data was determined for each foot using a plantar pressure measuring device. Center of pressure (COP) is the spatial average of all the pressures measured underneath the foot at any given instant in time. During an individual's gait cycle, the COP moves in a concave pattern throughout stance phase from heel strike to toe off. Foot function was assessed by the center of pressure excursion index (CPEI) which is a measure of the degree of COP concavity, peak plantar pressure (PP [N/cm^2]), maximum force (MF [N]), pressure-time-integral (PTI [Ns/cm^2]), force-time-integral (FTI [Ns]) and contact area (A [cm^2]) in 12 different regions underneath the foot (hallux, toe 2, toes 3-5, sub metatarsal head 1, sub metatarsal head 2, sub metatarsal head 3, sub metatarsal head 4, sub metatarsal head 5, medial arch, lateral arch, medial heel, and lateral heel). A 12-segment scalable geometrically based template or mask was developed to allow standardized calculations of plantar loading for specifically defined anatomical structures of the plantar foot. In a radiographic-based validation study, each region of the 12-segment mask was confirmed to appropriately represent its corresponding anatomical region of the foot [5]. Five trials for each foot were recorded and the calculated means of all five trials will be used in data analysis. It is hypothesized that the USMA cadets will experience longitudinal changes in foot function (CPEI, PP, MF, PTI, FTI, Area).

III. Methods and Statistical Analysis

Using the data collected at baseline and at the 1 year follow-up, a generalized estimation equation (GEE) model with an identify link function will be used to compare the means of the various parameters, while simultaneously accounting for potential dependence in bilateral data using SPSS software. The means of CPEI, PP, MF, PTI, FTI and area will be compared between baseline and 1 year follow-up. Significant changes (>10%) for any of the parameters in either foot is detected will signify a change in foot type, while non-significant changes (<10%) will signify no change in foot type. A manuscript will be completed and will be submitted to scientific journals for review.

IV. References

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Make ups:

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Phone: 6465302457
Title: Impact of oxygen exposure during obstructive apnea in SUDEP
Sponsor: Dr. Richard Kollmar
Department of Otolaryngology, Downstate
Co-Advisor:
Location: Downstate

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: #15-10473
Dates: 11/19/2018 - 11/18/2021
Title: Seizure-induced laryngospasm in mice
Site: SUNY Downstate
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: My research experience began the summer after freshman year of college through a summer research program at The Miami Project to Cure Paralysis. I was assigned to a lab that studied the protective role of microglial Tumor Necrosis Factor Receptor 2 (TNFR2) signaling in multiple sclerosis (MS). Fascinated by how our own immune cells attack oligodendrocytes, cells that insulate neurons, during MS, I became actively involved in research from design to discussion. My project was to quantify and compare the level of different stages of oligodendrocyte populations between MS-induced control and microglial TNFR2 knockout mice. When my results deviated from the hypothesis, I went back to re-evaluate data, read countless papers, and consistently discussed the findings with my mentor to come up with a valid explanation. I loved every minute of this intellectual struggle and the excitement to explore the unexplored kept me going. In the end, I inferred two possible roles of microglial TNFR2 signaling in MS, which resulted in a publication.
As much as I was interested in MS, I was also frustrated to learn that the available MS drugs – immunosuppressants – do not cure but only serve to delay the disease progression. Curious to see if there could be better alternatives, I continued to engage in MS research at Columbia and explored other pioneering approaches in understanding and treating MS, such as by targeting the blood-brain barrier (BBB) to halt inflammation in MS, using stem cells to restore the inflicted neuronal damage or applying focused ultrasound to enhance delivery of MS drugs.
Wanting to learn more about how the disease affects patients instead of cells, following graduation in May 2018, I transitioned to clinical research at Dr. Charvet's team at NYU Langone Multiple Sclerosis Comprehensive Care Center where we studied neuromodulation therapy such as transcranial direct current stimulation (tDCS) for managing MS patients' daily symptoms including pain and fatigue. With my engineering background, I investigated the neuronal mechanism underlying tDCS using real-time MRI and helped identify the changes in cerebral metabolic rate of oxygen and resting-state functional MRI during tDCS. With that, I proposed to further analyze a correlation between MRI measures and behavioral outcome to tDCS therapy to explore their use as predictors of clinical response to tDCS, which would help customize the tDCS treatment at an individual level to better address the unmet needs of MS patients. As the first author, I was given the opportunity to give a platform presentation on this work "Transcranial Direct Current Stimulation (tDCS) Induces Acute Changes in Brain Metabolism" at the 2019 American Academy of Neurology.

Career goals: Otolaryngology was a field that I've always been interested in. Yearning to learn more about the field, I shadowed an ENT surgeon last year and observed her do surgeries such as a tracheotomy on a NICU baby to facilitate her breathing, and ear canal reconstruction to restore hearing loss in a car accident victim. It was amazing to see how someone could bring such an immediate and lasting positive impact on another person's quality of life, and this experience allowed me to want to further explore the field. I am also attracted to otolaryngology due to its interesting research venues, many of which are tied to biomedical engineering that I have a background in.

With a strong interest in research, I aspire to pursue a career in academic medicine. From my years of experience in multiple fields of MS research, I learned that complex human disease is usually not a single pathology, but rather a series of multiple mechanisms set by multiple factors. I hope to continue to bring this multidisciplinary view to discover links between seemingly separate fields, and make medical discoveries that impact human health. The road from research to patient side will be challenging, but what motivates me is the faith that my work, even the failed experiments, would contribute to advancing medical knowledge and at some point, benefit patients. Should I be given the alumni fellowship, I will use this opportunity to the fullest to grow into a better physician, surgeon, and investigator.

Description: Impact of oxygen exposure during obstructive apnea in SUDEP

Background:

Sudden unexpected death in epilepsy (SUDEP) is the leading cause of death among people with epilepsy, and yet no preventative intervention has been developed. SUDEP is estimated to cause 1-2 deaths per 10000 people with epilepsy per year and the numbers are increased to 6.3 – 9.3 cases per 1000 in high-risk populations such as in patients after epilepsy surgery [1].

While SUDEP was largely assumed to be due to cardiac arrythmia, recent studies including our own [2, 3] and clinical data suggest that respiratory depression and subsequent oxygen desaturation could be the primary cause of death [2-5]. 59% patients undergoing seizures developed apnea [4], and oxygen desaturation (SaO_2) were observed to be below 90% in 33.2%, 80% in 10.2% and 70% in 3.6% of seizures respectively [5]. Despite the increasing documentation of SUDEP cases, the exact etiology still remains largely unresolved in large part due to the challenges of gathering data at the time of death in SUDEP patients.

In research settings, SUDEP can be modeled in DBA/2J mice which are susceptible to audiogenic (sound-induced) seizures, manifested as progressive phases of running, clonic seizure activity, tonic seizure activity and recovery or death. Using rats and DBA/2J mice, our lab has demonstrated that during SUDEP, laryngospasm due to seizure spread into respiratory brainstem regions causes severe obstructive apnea resulting in respiratory arrest and cardiac asystole, and that airway preservation with open tracheal tube alone significantly increases survival rates [2, 3]. Progressive oxygen desaturation following obstructive apnea has been shown to contribute to seizure termination [2, 3, 6] which suggests that SUDEP deaths may be prevented if airway obstruction resolves before respiratory arrest occurs. In a previous study with DBA/2J mice, oxygenation completely prevented sudden deaths in mice undergoing seizures [7]. With these findings, we propose oxygenation as an early preventative intervention in obstructive apnea and hypothesize that introduction of an oxygen-rich environment may protect DBA/2J mice from seizure-induced death.

Specific Aim:

We will investigate the effectiveness of oxygenation as a preventative intervention in SUDEP by comparing survival rates between mice exposed to pure oxygen vs. mice exposed to only air (vehicle) during different phases of audiogenic seizures. Our specific hypothesis is that exposure to pure oxygen after the start of a seizure, but before the start of obstructive apnea, will protect against death.

Methods:

We will be using seizure-prone DBA/2J mice and randomly assign them to four groups: (1) exposure to pure oxygen from seizure onset until onset of the tonic phase when the airway closes, i.e., before obstructive apnea; (2) same gas delivery method and time frame as for (1), but exposure to air only instead of pure oxygen; (3) exposure to pure oxygen from the onset of the tonic phase until the end of the seizure or respiratory arrest, i.e., during obstructive apnea; and (4) same gas delivery method and time frame as for (3), but exposure to air only instead of pure oxygen.

Audiogenic seizures will be induced by exposure to loud high-frequency sounds, and the progression along seizure phases will be monitored by behavioral markers: freezing followed by wild running as seizure onset, rigid fore- and hindlimb extension as onset of tonic phase, and relaxation of the pinnae as end of seizure or respiratory arrest. At appropriate moments, the atmosphere surrounding the seizing animal will be switched by rapid transfer between containers filled with air or pure oxygen. (This atmosphere switching has been tested in pilot experiments and works very reliably.) Seizure outcome will be scored as a binary variable with the values death or survival. Video recordings will also be taken during each experiment to determine the duration of each seizure phase and the actual time points of atmosphere switching relative to the seizure phases.

To evaluate the statistical significance of these experiments, we will apply Fisher's exact tests to 2x2 contingency tables of seizure outcome (death/survival) vs. atmospheric treatment (air/oxygen) for groups 1 & 2 or 3 & 4, respectively. Power analysis suggests that 16 mice per group (64 total) are required for a power β of 0.95 and a significance level α of ≤ 0.05, assuming 50% survival in air and 100% survival in oxygen.

Implications:

Determining the exact mechanism underlying SUDEP is critical in order to develop effective preventative strategies for people with epilepsy. While oxygenation is not currently required as standard-of-care, it is often supplied during postictal care. Our results will provide evidence for treatment with oxygen as a preventative measure to reduce the rate of oxygen desaturation and decrease the mortality associated with SUDEP. Our data will inform practical preventative protocols, in particular, the optimal timepoint during a seizure to apply oxygenation as a method for protection from death. Furthermore, the physiological data collected may serve as useful biomarkers for detecting the time of obstructive apnea and respiratory arrest, which we could apply to explore other prevention and resuscitation interventions.

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Make ups:

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Title: A Simple Protocol and Assessment Tool for Aspiration Prevention and Dysphagia Screening in Adult Hospitalized Patients: A Multicenter Study

Sara Abu-Ghanem

Department of Otolaryngology

SUNY Downstate Medical Center

Does the proposed project involve any of the following: human subjects or tissues, fluids, or other material from human subjects; animal experimentation; work with a biohazardous substance? Yes

If not yet approved by the appropriate institutional review boards, when were the applications/proposed submitted? Not yet submitted

Summarize your research experience: Previously I was a research assistant in Dr. Natalie Kacinik's cognitive neuroscience lab at Brooklyn College. This lab was concerned with the Theory of Embodied Cognition— that sensorimotor systems influence an individual's real-time understanding of a concept. That said, our experimental investigations focused on the effect of various perceptual experiences and manipulations on conceptual representations. Specifically, we examined the role of size and color on word processing, and in adherence to embodied cognition accounts, we hypothesized that variations in representation of size and color would impact (semantic and lexical) processing and memory. My responsibilities were to run participants in ongoing studies, assist in data preparation and entry, perform literature searches, summarize peer-reviewed articles, and train other research assistants in the lab. Additionally, I wrote a research paper at the end of each semester, totaling four papers over two-half years. My interest in language and how the brain processes language compelled me to be involved in this particular research lab.

Describe your career goals: As a future pediatric otolaryngologist, I aspire to work with kids in both outpatient and inpatient settings while also conducting research with the goal of improving patient outcomes and quality of care. I envision having a position in academic medicine where I can support the next generation of physicians. I also hope to use my clinical expertise to contribute to health equity efforts in under-served communities.

General Background Dysphagia or impaired swallowing is a widespread issue amongst hospitalized individuals, affecting 3.0% of all adult U.S. inpatients 45 years of age or older [1]. This may even be an underestimation considering inpatients may have dysphagia that is either not severe enough to be recognized by a clinician or not immediately relevant enough to the primary purpose of hospitalization. Not only are dysphagic patients particularly prone to dehydration and malnutrition, but they also have an increased risk of aspiration and its subsequent complications [2]. Moreover, some studies have found that dysphagia, regardless of etiology, can lead to significant economic and survival burden [1,3]. One systematic review focused on the impact of oropharyngeal dysphagia on healthcare costs and patient length of stay (LOS), and found that overall costs increased by 40.36% in dysphagic patients compared to their non-dysphagic counterparts, and that the presence of oropharyngeal dysphagia increased hospital

LOS by 2 to 8 days regardless of the reason for admission, the study design utilized, or the region in which the study was conducted [3].

The inpatient burden of dysphagia has primarily been investigated in patients post-stroke [4,5], however a wide range of other risk factors were found to be associated with dysphagia. These risk factors include patients who are frail and elderly, those with high-risk comorbidities [6], as well as those with dehydration, malnutrition, need for rehabilitation, neurodegenerative disease, pneumonia, and cardiac disease [7,8]. Other studies have found that patients with head and neck cancer [9,10], patients following cervical spine surgery [11,12] or cardiothoracic surgery, and patients following extubation [13] are also at increased risk of dysphagia.

Screening protocols are driven in part by the concept that early identification results in more effective clinical management and reduced complications. In recent years, numerous screening approaches and protocols to address oropharyngeal dysphagia have been introduced for the use of nurses and/or speech language pathologists (SLPs). One approach uses a direct clinical assessment, specifically a 3-ounce water challenge protocol executed by nurses [14]. Another approach also uses a direct clinical assessment, specifically a Fiberoptic Endoscopic Evaluation of Swallowing (FEES) or a Modified Barium Swallow Study (MBSS) executed by SLPs in patients with indications for further clinical assessment [15,16].

All of this is to say, we believe there is a need for a large, multicenter study that tests a protocol (for aspiration prevention and dysphagia screening) in all inpatients regardless of dysphagia and aspiration etiology. If proven effective, this protocol could then be used as a universally acceptable protocol for aspiration prevention and dysphagia screening. Even more, although the Eating Assessment Tool (Eat-10) is a reliable and validated self-report tool for dysphagia in outpatient populations, we believe there is a need for a reliable and valid questionnaire to assist in dysphagia and aspiration screening specifically for adult inpatient populations [17].

Specific Aims and Research Plan The goal of the present study is to develop, and subsequently test the reliability and validity of a dysphagia/aspiration protocol and assessment questionnaire for aspiration prevention and dysphagia screening in adult inpatient populations.

The aims of the project are as follows:

Aim 1. Develop a valid and reliable inpatient Eating Assessment Tool (inEAT) questionnaire to assess the severity of dysphagia in adult hospitalized patients.

Aim 2. Develop a “STOP-ASPIRATION” checklist tool for use by nurses to assess for known risk factors associated with aspiration in adult inpatients.

Aim 3. Test the feasibility, safety, and implantation of multidisciplinary dysphagia screening and aspiration prevention protocol.

Methods and Statistical Analysis This multi-center study will be conducted at multiple sites including SUNY Downstate Medical Center, Kings County Hospital, Methodist Presbyterian Hospital, Maimonides Medical Center, and Stanford Health Care. Specific designated medicine/neurology departments and ICU units will be serving as pilot departments at each site. At each site, the staff and specifically the nursing staff will be instructed how to follow the protocol for all admitted inpatients to improve the quality of care with dysphagia screening and aspiration prevention protocol.

The specifics of the protocol are as follows: Upon admission and again after 24 hours, all selected inpatients will receive the inEAT questionnaire to assess for symptoms of dysphagia. After, nurses will complete the STOP-ASPIRATION checklist tool for all inpatients to assess for known risk factors associated with dysphagia and aspiration. Patients found to be positive for dysphagia and aspiration risk factors will undergo further clinical assessment using the validated Yale Swallow Protocol in which nurses evaluate patients for signs and symptoms of aspiration using a brief cognitive screening test, an oral mechanism examination, and drinking of 3 ounces of water under observation [18]. Patients found to be negative for signs of aspiration will be reassessed after 24 hours and will be cleared for oral diet. Patients found to be positive for signs of aspiration will be designated NPO, considered for NPO medication, and formally evaluated by an SLP (including a FEES or MBSS examination).

The internal consistency of the inEAT questionnaire will be assessed using Cronbach's alpha. The test-retest reliability of the inEAT questionnaire will be assessed using the Pearson product moment correlation coefficient. Inter-item correlations will be used to remove redundant and poorly reliable items from the questionnaire, consequently making a final inEAT questionnaire. The outcomes of the inEAT questionnaire and STOP-ASPIRATION checklist will be compared to the established clinical and instrumental assessments previously detailed to assess for validity and reliability.

During this project, I will be responsible for the implementation of the protocol at different sites. I will contribute to the finalization of the protocol, IRB submission, grant submission, presentation of the protocol to pilot departments at each site, follow-up in regard to the adherence of the protocol, and gathering of data. After statistical analysis, I will play a role in paper writing and submission.

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Title: Glucocorticoid Receptor Dependence of Steroid-Induced PLAT Transcription Repression.
Sponsor: Dr. John Danias
Ophthalmology
Co-Advisor:
Location: SUNY Downstate

Fellowship period: Yes
Involve any? Yes

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where: Study is IRB exempt.

Research Experience: Master's Student Thesis Research Project - Imperial College London, Center for Neuroinflammation and Neurodegeneration, Gene Therapy. March – September 2016
Goal of research was to study the tropism of a unique Chikungunya envelope glycoprotein pseudotyped lentiviral vector for use in the treatment of neurodegenerative ailments such as Parkinson's and Huntington's diseases. Lentiviral vector production and characterization were carried out to determine the scalability and scope of the vector for therapeutic use. The vector transduction patterns were examined both in vitro in primary cell culture and in vivo in the brains of adult rats. The transduction pattern was shown to heavily favor astrocytes, which would benefit our strategy to produce neuro-protective environments and halt disease progression.
An additional project was carried out with novel lentiviral vector containing the IGF-1 gene. The vector was tested in animal models of ALS (SOD1 defective mice). The vector was introduced into peripheral muscle where it was transported to the spinal cord through retrograde transport to enhance motor neuron survival. Motor neurons were counted and it was determined that the vector decreased neuronal death. The treatment also increased survival by 50% when compared to controls.

Undergraduate Student Research – University of Rochester. Jan 2014-Aug 2015
Goal of the research was to examine HIV-1 latency in various cell lines and conduct independently driven experiments to study protein interactions in the host/virus relationship. Focus was placed on host proteins associated with the immune response (interferon inducible genes) and those governing reactivation of transcription within infected cells. Additional research carried out pertaining to KSHV and HTLV latency and similar host and virus components.

Career goals: My career goals include extensive involvement in academic medicine. My previous work with translational research was very interesting and drew me into the intersection between laboratory research and clinical therapeutics. Having the opportunity to help develop additional strategies to hopefully alter the course of detrimental diseases was very profound. During my time in medical school this interest has continued to grow as we have learned about evolving therapies for diseases ranging from very rare to widely prevalent in the population.

This interest in research and academic medicine has continued to grow so much so that I am currently applying to the Downstate MD/PhD program. This combined program will provide me the skills necessary to develop meaningful experiments, manage aspects of a medical research laboratory, and be a well-rounded clinician.
Since I am early in my medical education I do not have a specific specialty or area of research set. Based on my previous areas of research however, I have found an interest in neuroscience and I plan to continue this interest in the study of neuronal damage in a different organ, namely the optic nerve of the eye.

Description: General background:
Steroid-induced ocular hypertension is a frequent complication of chronic treatment with corticosteroids [1]. If the rise in the intraocular pressure (IOP) is of sufficient magnitude and for a long enough duration, progressive changes to the optic nerve head, retina, or both may occur leading to visual field loss and often blindness [2]. Steroids are among the most commonly prescribed drugs to combat various autoimmune and inflammatory conditions. Steroid-induced glaucoma can occur after steroid use in susceptible individuals and is most commonly seen following topical, periocular, or intraocular administration [3]. This marked rise in intraocular pressure usually can be observed 3 to 6 weeks following topical steroid use, while corticosteroid injections may cause a rise in IOP after several months [3]. Discontinuation of the use of the steroid is the first line of management and in a majority of acute cases the IOP decreases to normal levels within days, while more chronic cases may take 1 to 4 weeks [4]. There are numerous risk factors that have been considered to increase the risk of steroid induced glaucoma, with the most significant being patients with primary open angle glaucoma (POAG) [4]. In testing with a 4-week topical course of dexamethasone 0.1%, roughly 30% of glaucoma suspects and 90% of patients with POAG may develop elevated intraocular hypertension [5].
The role of tissue plasminogen activator (tPA) in the pathogenesis of steroid induced ocular hypertension and general open-angle glaucoma is complex and initiates several signaling pathways including matrix metalloproteases (MMPs). The MMP controlled remodeling of the extracellular matrix and its dysregulation can lead to decreased outflow and increased intraocular pressure [6]. Increased understanding of the steroid signaling pathway and downstream effectors, including tPA, will provide information relating to the development of steroid-induced IOP and other open angle types of glaucoma.
Specific aims and research plan of the proposed project:
The goal is to determine if the changes in the transcription profile of PLAT (the gene that encodes for tPA) is glucocorticoid receptor (GR) mediated.
Methods and statistical analysis:
tPA expression will be measured in human trabecular meshwork (HTM) primary cell cultures.
HTM cells from multiple donors (N>3) will be seeded into 12-well plates and will be exposed to prednisolone acetate (200uM – a concentration that provides a robust PLAT expression change). In addition to the steroid addition, cells will be exposed to one of several inhibitory components that targets the signaling pathway to isolate whether the increase of PLAT expression is GR mediated. These inhibitors include mifepristone (a cytosolic GR blocking agent)(10µM), SP600125 (AP-1 inhibitor), caffeic acid phenethyl ester (CAPE) (NF-KB inhibitor) (50µM) or vehicle. An additional set of HTM cells will receive treatment with siRNA to GR, AP-1, and NF-KB or multiple control siRNAs (2 for each target).
Cells and culture media will be collected at various timepoints (0 minutes, 6 hours, and 24 hours) following the addition of the steroid and the inhibitory agents. The harvested cells will undergo RNA extraction and conversion into cDNA and subsequent RT-PCR to determine the amounts of PLAT mRNA compared to an internal control mRNA expression. The calculated mRNA amounts will be compared between cultures exposed to steroid and those exposed to vehicle in the presence and absence of mifipristone, SP600125 and CAPE as well as the presence and absence of siRNA against GR, AP-1, and NF-KB using t-tests.
It is expected that the mifepristone and GR siRNA treatment will at least partially reverse the steroid-induced decrease of tPA in the HTM cells. The absence of a reversal in the other inhibitory setting will demonstrate that the steroid effect is through the GR rather than the other pathways and transcription factors.
References to prior publications:
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Make ups:

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Title: Adult Single Ectopic Ureteral Abnormalities
Sponsor: Dr. Jeffrey Weiss
Urology
Co-Advisor:
Location: Veterans' Affairs New York Harbor Healthcare System, SUNY Downstate

Fellowship period: Yes
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience:
I have worked both with clinical research and basic science research. My clinical research experience was done at the University of Chicago, my alma mater. I worked at the Social Cognitive Neuroscience lab, which focuses on the intersection between clinical psychology, neuroscience, and behavioral economics to assess the development of neural pathways in children. The study I worked on used fMRI testing on children aged 3-12 to determine how their empathy and fairness pathways develop. My role as a research assistant, involved scheduling appointments with potential subjects of the study and ensuring that the children were taken care of while waiting for their session. In addition, I also learned how to conduct fMRI scans on the children being studied.
My basic science research was conducted at the Neonatal Perinatal U54 lab at SUNY Downstate. The Neonatal-Perinatal U54 lab seeks to study the clinical pharmacology of retinopathy of prematurity. In my independent project, I studied the effects of intravitreally administered Avastin on the neurogenesis and angiogenesis of neonatal rats; the study compared the effects of the drug under normal atmospheric conditions, hypoxic conditions, and intermittently hypoxic conditions. I also assisted in over four other neonatal projects with bench laboratory work, utilizing techniques such as ELISA, polymerase chain reaction, and immunofluorescent staining. I presented the results of my independent research as a platform presentation at the 2016 Pediatric Academic Societies (PAS) conference.

Career goals: Throughout my career, I hope to experience the duality of the term "physician-science". I would like to balance my medical career between substantial clinical time with pediatric populations and research that forwards the field I eventually choose. Urology, with its wide array of procedures and intriguing anatomy, is a major interest of mine. I hope to focus my career on forwarding our understanding of the embryological roots of congenital malformations through research, while also helping treat young patients' genitourinary pathologies in the clinic.

Description: General Background
We intend to conduct a case control study that looks at five different examples of a rare urological pathology, single ectopic ureters. Single ectopic ureters are extremely rare embryological malformations in which an abnormally placed ureter drains a single kidney [1]. Children with this condition present with wetness/dampness even after training, and often present with systemic malformations; their kidneys are asymmetrical both in presentation and function, and in women, the ureteral orifice is

pathologically found in the vagina. When diagnosed properly, treatment has been established and patients usually experience an immediate and lasting fix to their symptoms.

Specific Aims and Plans for our Proposed Project

For this study, we will be using the cases of five patients that Dr. Weiss has treated over his career of 35 years. Four of the patients are male, under an age range of 17-85, and one is female, aged 53. All have exhibited single ectopic ureter, though their pathologies vary in terms of severity and anatomical positioning. The anatomical comparisons will be made by the use of x-ray, CT, MRI and urodynamic images. We hope to tie in the anatomic presentation to our understanding of the embryologic basis for such anomalies, a topic that Dr. Weiss has written about extensively [2]. Because single ectopic ureteral anomalies are quite rare, we were hoping to extend the literature on such cases and make the condition easier to identify and differentiate for future clinicians. In addition, we will review the treatment options, both chosen and considered, and outcomes for these patients.

Methods and Statistical Analysis

As seen in a previous study done by Dr. Weiss early in his career [3], this study will first focus on each case, looking at medical history, diagnostics, quality of renal tissue, imaging presentation, imaging analysis, and treatment. Finally, we will try to come to some conclusions regarding the embryology and how it connects to the varied presentations of each patient.

References to prior publications

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Make ups: N/A

Alana Engelbrecht
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Phone: 9143306458
Title: Chlamydia trachomatis seroepidemiology in NY
Sponsor: Dr. Stephan Kohlhoff
Pediatric Infectious Disease
Co-Advisor:
Location: SUNY Downstate Medical Center

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: 1573197-1
Dates: 3/1/2020-3/1/2021
Title: Chlamydia trachomatis seroepidemiology in NY
Site: SUNY Downstate Medical Center
Type:

Additional Study:
Dates:
Title:
Site:

When/Where: 3/1/2020

Research Experience: The summer before my third undergraduate year, I contributed to ongoing Huntington's disease (HD) research at an on-campus laboratory. The project investigated the biochemical mechanism of HD in transgenic Drosophila. I contributed to development and trouble-shooting of a Drosophila larval crawling assay that attempted to measure the cytotoxic effects of different poly-Q repeats. I also used fluorescence immunohistochemistry (IHC) to visualize GFP-labeled protein aggregates in the transgenic adult flies. We then utilized a software program to count the aggregates to correlate increasing poly-Q repeats and number of aggregates. My biology major required completing at least four upper-level labs in two semesters. Each lab was a research project in which we would utilize current literature to develop a hypothesis and later create a poster to present. These labs entailed maintenance and experimentation with stem cells, C. elegans, and Drosophila. My undergraduate thesis studied the evolution of two genes in the embryonic development of Drosophila melanogaster and Anopheles gambiae. The genes studied, t48 and mist, have specific functions in Drosophila gastrulation. Because Anopheles is an evolutionarily earlier species, elucidating the role of these genes in A. gambiae gastrulation would inform the potential evolution of these genes. This yearlong project entailed removing the shell from A. gambiae embryos, maintaining Drosophila lines and harvesting gastrulating eggs, optimization of and performing a colorimetric IHC protocol assessing t48 and mist gene expression in gastrulating embryos, as well as performing scanning electron microscopy to compare their ventral furrow morphology. My thesis paper addressed the technical difficulty of these protocols and provided literature-supported fluorescent IHC assays for future research. The summer before my senior year, I facilitated clinical research at the Cooper University Hospital Emergency Department. This entailed screening for eligible patients, obtaining their consent, ensuring completion of appropriate surveys, and entering responses into the database. I also interned at the Stephen Klein Wellness Center and was able to improve, carry out, and analyze a quality improvement survey for ~200 clinic patients. After graduation, I worked as a clinical research coordinator (CRC) for one year at Mt. Sinai Hospital. I was appointed lead coordinator of a pharmaceutical-initiated research study, and was involved with the protocol and consent development, patient screening and recruitment, patient visits, and data reporting. I then worked as a CRC at NYU Langone for a year, carrying out NIH-funded translational research as well as investigator-initiated studies including chart reviews. My role involved consenting patients, maintaining a large patient database, collecting appropriate biological specimens, and data analysis.

Career goals: My current interests are in Emergency Medicine, Pediatrics, and Infectious Disease, with intersections among these. Not only are these fields clinically stimulating and personally rewarding, but they also provide essential opportunities for public health and basic science research. The research experiences I have had thus far have motivated me to integrate research into whichever medical field I end up in. The research project I am proposing for this summer demonstrates the crucial intersection of public health and basic science research that I plan to pursue as a clinician. While I could envision myself undertaking either basic science or clinical research, the ultimate goal of my research would be to elucidate the interactions between disease mechanism and public health to facilitate high quality evidence-based medicine and policy change.

Description: General Background

The most frequently reported sexually transmitted infection (STI) in the United States is infection with the bacterium Chlamydia trachomatis [1]. This infection tends to be asymptomatic in about 70-85% of women and more than 50% of men [2], and might be attributed to the bacteria's ability to evade host immune response [3]. The asymptotic nature of most C. trachomatis infections contributes to its clinical complications that have profound consequences for women's health. Complications resulting from lack of treatment in women can include cervicitis, urethritis, infertility, chronic pelvic pain, tubal pregnancy, and pelvic inflammatory disease (PID) in up to 40% of cases [2]. Despite these consequences, few studies have elucidated the prevalence of C. trachomatis infection in general US populations. The nucleotide acid amplification test (NAAT) typically is performed in sexually active individuals and only indicates the presence of active C. trachomatis infection. Alternatively, serological assays allow the unique opportunity to study the lifetime prevalence (LTP) of infection in the general population.

Few studies have utilized serological C. trachomatis assays in a non-selective population, both internationally and domestically. One study in Washington State found that non-Hispanic (NH) black women have five times the incidence by age 34 than NH white women [4]. Both international and domestic studies have also found that a higher proportion of women than men were seropositive [5]. A national study performed in England utilized the serum of individuals 16-44 years old and developed a pgp3 ELISA [6]. It was shown that age, poverty, condom use in past 4 weeks, self-reported chlamydia, and sexual partner number were factors associated with seropositivity. The higher prevalence of C. trachomatis infection associated with increased age and females parallel national trends, further strengthening the relevance and reliability of this assay.

The LTP of C. trachomatis in the adult NYC population has never before been studied. This project aims to utilize epidemiological data and blood samples from the NYC Health And Nutrition Examination Survey (NYC HANES) repository to assess the seroprevalence of C. trachomatis in adults. The data will then be correlated with potential risk factors including age, socioeconomic status (SES), race (NH black and NH white), and past year condom use. This will facilitate a more comprehensive understanding of high-risk populations and racial disparities such that more effective prevention, screening, and treatment methods can be developed. The World Health Organization has listed C. trachomatis as one of the top five priorities for vaccine development for the eventual eradication of STIs [7]. Regional and national monitoring of the LTP of C. trachomatis prevalence also provides quantitative evidence informing continued vaccine development efforts. Future studies can also monitor the seroprevalence of infection over time to evaluate the effectiveness of public health interventions in preventing or detecting C. trachomatis infection.

It has also been established that inflammatory markers are present and involved in active C. trachomatis infection. However, the role of inflammatory markers in seropositive individuals indicative of a chronic inflammatory process has yet to be studied in a representative general population. Studies of IL6 or CRP have been conducted in the setting of C. trachomatis associations with PID [8], tubal factor subfertility [9], and heart disease [10]. This study has the unique approach of measuring inflammatory markers in a general population to better understand the clinical implications of C. trachomatis seropositivity.

Once these assays are completed, we will be able to estimate the burden of C. trachomatis in the general NYC population. The presence of inflammatory markers in seropositive individuals would inform investigation of a potential hyper-inflammatory state that can have various clinical implications. This information will help direct public health measures that address prevention, screening, and treatment of C. trachomatis infection.

Aim 1: Measure Chlamydia trachomatis seropositivity as a marker of lifetime prevalence (LTP) from a representative sample of New Yorkers, then correlate results with age, SES, and past year condom use.

This is a clinical, observational, and retrospective study to assess the seropositivity of C. trachomatis in the general NYC adult population in 2013. Based on previous serological studies, we predict that C. trachomatis IgG prevalence will be higher in females than males, will increase with age, with lack of condom use in past year, and with NH black women compared to NH whites. As such, these trends are likely to parallel national infection trends.

Aim 2: Evaluate serum levels of CRP and IL6 in C. trachomatis seropositive individuals to assess the clinical effects of infection.

Seropositive individuals revealed in Aim 1 will be further analyzed for CRP and IL6 markers of inflammation, which are known to advance disease progression in those with chronic health conditions. Confounding variables such as inflammatory illnesses will be controlled for. A different member of the lab team will work on carrying out this specific aim.

Methods – Aim 1

Blood samples from the NYC HANES 2013 repository will be acquired along with participants' corresponding epidemiological data. An enzyme immunoassay (EIA) protocol will be used to detect anti– C. trachomatis IgG antibody against the major outer membrane surface protein (MOMP) (Labsystems Diagnostics Oy, Finland) (Labsystems C. trachomatis-EIA). The MOMP is also the main candidate antigen for vaccine development [11]. The enzyme immunoassay (EIA) kits will be stored at 4°C and brought to room temperature before testing. The assay will be performed according to the manufacturer's instructions with no protocol deviations. Serum samples will be diluted in assay buffer and loaded in duplicate along with calibrator, positive and negative controls onto an antigen-coated 96 well plate. Following a wash step horseradish peroxidase-conjugated IgG will be added to the well and incubated. After further washing a chromogenic substrate will be added and incubated for 15 minutes. The reaction will be stopped and the presence of IgG as well as average calculations will be determined using absorbance readings at optical density (450/620 nm).

Over the course of 8 weeks, 1210 subjects' blood samples will be assayed. Two EIA plates will be run each day, and each plate will contain 24 subjects' samples. Therefore, about three weeks of assays will yield results from 1210 subjects. The 1st week will be spent setting up the samples, materials, and protocol requirements. I will perform the EIA's during the 2nd, 3rd, and 4th weeks. The 5th week will allow time for troubleshooting and repeating any assays as needed. In the 6th week, I will work with Dr. Rosenbaum of the School of Public Health to analyzing the serological data acquired and its correlations with NYC HANES epidemiological data using descriptive statistical methods and Statistical Analysis Software (SAS). The samples will be divided into ages 20-39, 31-42, 43-57, and 58+ in analyzing the data. The prevalence of seropositivity will be assessed by age, race, past year condom use. The 7th week will entail potential collaboration with a lab member on Aim 2. The 8th week will be dedicated to data organization as well as abstract and poster development.

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5. Banniettis N, Thumu S, Weedon J, Chotikanatis K, Szigeti A, Hammerschlag MR, Kohlhoff SA. Seroprevalence of Chlamydia trachomatis in Inner-City Children and Adolescents-Implications for Vaccine Development. Sex Transm Dis. 2017 Jul 19

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8. Park, S., Lee, S., Kim, M. et al. Clinical characteristics of genital chlamydia infection in pelvic inflammatory disease. BMC Women's Health 17, 5 (2017). https://doi.org/10.1186/s12905-016-0356-9

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11. Stagg AJ, Elsley WA, Pickett MA, Ward ME, Knight SC. Primary human T-cell responses to the major outer membrane protein of Chlamydia trachomatis. Immunology, 79, 1–9 (1993).

Make ups: Currently I have no pending make-up work or exams for the summer.

Kyra Gassmann
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Title: Molecular Profiling Analysis of Type I and Type II Endometrial Cancers in an Inner City Population
Sponsor: Dr. Yi-Chun Lee
Obstetrics and Gynecology
Co-Advisor:
Location: University Hospital of Brooklyn

Fellowship period: Yes
Involve any? Yes

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience:

Career goals:

Description:

Make ups:

Fradah Gold
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Title: Evaluation of Ophthalmology Follow-Up on Retinopathy Disease Outcomes
Sponsor: Dr. Ilya Leskov
Ophthalmology
Co-Advisor:
Location: King's County Ophthalmology Clinic

Fellowship period: Yes
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: Beginning in May 2018, I was a researcher in Dr. Deborah J Walder's Neurodevelopment Lab at CUNY Brooklyn College. As part of a year-long honors thesis project, we worked on the first, to our knowledge, comprehensive meta-analytic review examining sex differences in neurocognition and social cognition among individuals at clinical high-risk for psychosis. Since level of functioning prior to illness onset may impact illness progression, the primary aim of the current study has been to gather cognitive performance data by sex from authors of nationally and internationally peer-reviewed studies, and then meta-analyze these data to elucidate potential sex differences among at-risk individuals. Findings have been aimed to be utilized in the development of tailored early detection techniques and higher efficacy intervention or treatment plans. Additionally, in 2017, as part of a study abroad program at Vrije Universiteit Amsterdam, I worked with research leaders and peers from international universities to develop ideas for future neurodegenerative disease therapy. Utilizing confocal and live-cell imaging microscopies in the laboratories of the Centre for Neurogenomics and Cognitive Research, I studied the molecular mechanisms responsible for the diseases of brain function. Further, in 2017, I was a HRTP (Health Research Training Program) Intern at NYC DOHMH, Bureau of Early Intervention: Data and Analysis Unit, led by Allan Uribe. Specifically, I administered the Early Intervention Cultural Competence research survey via phone, contacting families in English and Russian to increase health equity. After collecting data into Access, I performed data tracking, cleaning, and quantitative analysis. Moreover, I conducted outreach, data planning, and descriptive analyses, presenting at weekly team meetings and a final HRTP presentation. In 2015, I participated in a study aimed to use statistical analyses to improve the accuracy of IMRT/ VMAT-IGRT Radiotherapy Treatments, as part of the Radiation Oncology Department at New York Presbyterian-Brooklyn Methodist Hospital under the guidance of Dr. Ashamalla. Specifically, after retrieving numerical data from visual scans, I compiled analytical summaries to determine how to reduce differences between initial couch and final online matched positions. As an undergraduate student, I also worked in Dr. Ryan Murelli's Organic Chemistry Lab at CUNY Brooklyn College. In this wet-lab, we used multiple alkynes to synthesize hydroxytropolones through oxidopyrlylium cycloadditions in an effort to develop a medicinal target for HIV and HBV. Techniques performed include column and TLC chromatography, as well as analysis of samples using NMR spectroscopy. Lastly, as a high school student, I conducted research on the polymer Polycarbonate as part of the Cooper Union Research Internship Program led by Professor Benjamin Davis, Chemical Engineering Department, discovering possible applications based on chemical properties.

Career goals: Following my medical education at SUNY Downstate, I aim to become a physician, clinical researcher, and health educator. Particularly, I am in interested in the field of ophthalmology, as many systemic conditions may manifest in the eye and significantly impact an individual's quality of life. Therefore, as a medical student, I am interested to research not only the interplay of multiple pathophysiological mechanisms underlying eye function, but also understand barriers in access to care and consequent outcomes in visual health. Further, I hope to utilize the skills I gained as a Public Health HRTP intern at the NYC DOHMH as well as current Secretary of Downstate's AMA/MSSNY (focuses on medical advocacy) to provide access to evidence-based resources and heighten awareness/health literacy about proper eye health in the local community. Moreover, as a student of the Medical Educator Pathway, I aim to take part in academic medicine as a physician, remodeling medical curricula to incorporate key principles of ophthalmology throughout foundational and clinical years. Moreover, I would like to apply the techniques I have obtained as a tutor and current near-peer educator to teach students. As a future physician, I hope to enact changes across multiple platforms, fostering shared decision-making with patients in a clinical setting, applying research findings to update guidelines, teaching students in group sessions, and educating community members through outreach programs.

Description: General Background

Diabetic retinopathy (DR), a microangiopathy that may develop in the background of diabetes mellitus, serves as a leading cause of vision-loss and preventable blindness globally. Further, the Salisbury Eye evaluation noted that African Americans had at least a two-times greater risk of developing visual impairment and loss compared to non-Hispanic white patients (Munoz et al., 2000). Given varied trajectories of the disease, including degree of severity and type of the retinopathy, the American Academy of Ophthalmology recommends follow-ups ranging from 1-12 months. As demonstrated in LALES (Los Angeles Latino Eye Study), though, individuals with inadequate access to healthcare are less likely to be screened or progress along an appropriate treatment course (Barsegian et al., 2017). Further, even in studies where financial barriers to care were minimized, a limited access to eye health literacy continued to impede on follow-up adherence (Keenum et al., 2016). Consequently, despite established goals, intervals between follow-up appointments often fail to meet the aforementioned recommended guidelines. Given the rising incidence and great prevalence of diabetes mellitus, especially afflicting lower socioeconomic, diverse communities as East Flatbush, it is critical to elucidate which key factors hinder ophthalmologic follow-up. In turn, results can be aimed for the development of a targeted approach for preventing DR-associated blindness, specifically in the East Flatbush community.

Specific aims and research plan

Given the preventability of blindness in patients with diabetes and patterns presented in studies likewise conducted in urban settings, the objective of this retrospective, quantitative clinical study will be to discern which elements may occlude patient follow-up in the East Flatbush community. Factors that may reduce retinopathy follow-up outcomes include referral services, communication methods (i.e. telephone), appointment reminders, housing situation, and availability of transportation choices. In turn, specific initiatives may be established, such as modified outreach programs and eye health education, to alter the trajectory of diabetic retinopathy and work to prolong/improve patients' quality of life.

Methods and statistical analysis

The retrospective clinical study will examine which factors impact the frequency of adherence to recommended follow-up eye care of patients with diabetic retinopathy. Patients will include individuals who seek care at King's County Ophthalmology clinic, one that serves many uninsured minority groups in an urban setting. Further inclusion criteria include approximately 500 patients older than 65 years who have a visual impairment (worse than 20/40 and better than 20/200) as well as Type II diabetes mellitus (criteria developed based on previous studies, like that of Munoz et al. 2000, to foster consistency and replicability). Exclusion criteria include patients who have legal blindness or have had life-long visual impairments, such as due to prior trauma, to be able to isolate retinopathy due to Type II diabetes mellitus. While initial data to be collected will include patients who have other comorbidities, this factor may serve as a modifying variable during analyses. Data is planned to be accessed from King's County Ophthalmology Clinic medical records, specifically concerning the frequency of patient follow-up, availability of referral services, type of communication methods patients use, insurance status, patients' housing situation, and availability of transportation choice. Statistical approach is planned to involve the chi-squared test to examine the relationship between patients who did and did not have a follow-up visit within the recommended period with respect to the factors mentioned above. Further, regression analyses may be completed to evaluate the associations between the features aforementioned and follow-up adherence. Since data to be analyzed will already be collected by the start of the study (retrospective design), the study will span June – August 2020 (my roles throughout the summer -first phase: retrieval and formatting of data, second phase: analyses).

References to prior publications

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Make ups:

Michael Goldberg
Email: michael.goldberg@downstate.edu
Phone: 9175260301
Title: Association of Dietary Patterns and Self Reported Exercise Habits with Distribution of Body Fat and Skeletal Muscle Mass and Other Markers of Health in Kidney Transplant Patients and Patients with CKD
Sponsor: Dr. Mariana Markell
Department of Nephrology
Co-Advisor:
Location: Most of the work will be conducted at the SUNY Downstate chronic kidney disease clinic and dialysis clinic. Depending on other factors, work may also be conducted in conjunction with King's County and their associated kidney and dialysis clinics.

Fellowship period: Yes
Involve any? Yes

Review Board Type: IRB
Study#: 763663-14
Dates: 12/19/2019 and approved 01/09/2020
Title: Comparison of Factors Affecting Nutrient Intake in Kidney Transplant Comparison of Factors Affecting Nutrient Intake in Kidney Transplant Recipients, Patients with CKD or ESKD and Local Controls: Relationship of Blood Levels of Phosphorous, Calcium, Vitamin D and Hgb and Body Composition Analysis by InBody S10 Bioimpedance Machine. A Cross-sectional StudyRecipients, Patients with CKD or ESKD and Local Controls: Relationship of Blood Levels of Phosphorous, Calcium, Vitamin D and Hgb and Body Composition Analysis by InBody S10 Bioimpedance Machine. A Cross-sectional Study
Site: SUNY downstate medical center suite C.
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: I have worked mostly in basic science labs throughout undergrad. I spent 3 non-consecutive Summers working with the National Oceanic and Atmospheric Administration lab in Miami, Florida on Key Biscayne under Chris Sinigaliano. I worked in a number of different capacities, mostly working as a lab tech to handle processing of environmental samples with RT-PCR and microarray analyses, amongst other techniques.
I worked a summer at Memorial Sloan Kettering as a research assistant with Dr Deng, working to develop novel bacteriophage strains that would be useful in the treatment of cancer. I used many of the same skills as above, with the addition of specific skills such as maintenance of cell cultures, viral specific isolation techniques, and ultra high speed centrifuge usage.
I spent my gap year working as a clinical research assistant at Mount Sinai's Institute of Critical Care under Dr Oropello. I worked on a number of different studies there, mainly focusing on the VICTAS study regarding novel treatments for sepsis, as well as another study regarding telomere length correlations to sepsis outcomes. I mostly spent my time using EPIC and REDCAP to organize and pull information and help consent patients for the study.

Career goals: I think it is a little difficult to describe my full career goals, as I havent finished narrowing down what speciality I am most interested in at the moment. That being said, I would say that I am most interested in working at an academic hospital in NYC where I have the opportunity to both teach and practice medicine. My exposure to research thus far has primarily been in the context of basic science research, so I am particularly keen on working this summer with Dr Markell to better understand how to both develop good research as well as how to leverage my research experiences into becoming a good clinician.

Description: Background

It is well established that fruits and vegetables are an integral part of a healthy and balanced diet. In particular, plant-based diets and diets high in vegetable intake have been shown to have significant health benefits. The preponderance of evidence gathered by epidemiological and interventional studies have supported that plant based diets lower mortality rates across the board, but particularly in areas such as type 2 diabetes incidence rate, cardiovascular health, and obesity.(1,2,3) In particular, plant based diets have been shown to reduce inflammation, along with increasing insulin sensitivity and lowering blood glucose levels.(4,5) Exercise has also been shown to have significant effects in preventing type 2 diabetes, through both burning calories and increasing GLUT 4 receptor expression, among other notable health benefits.(6) This makes both exercise and plant based diets potentially integral in long term care of patients who have undergone kidney transplant surgery.

In order to prevent acute kidney rejection in a recent transplant patient, standard drug regimens often include calcineurin inhibitors and glucocorticoids. Chronic glucocorticoid usage is associated with a number of adverse side effects, including iatrogenic Cushing disease, central adiposity, skeletal muscle proteolysis, osteoporosis, as well as insulin resistance and other diabetogenic effects.(7) Calcineurin inhibitors are similarly associated with hypertension, abnormal glucose control and hyperlipidemia.(8) These side effects are prompting physicians to conduct research into developing regimens that can mitigate these side effects or replace these drugs altogether. Whether a relationship between immunosuppression, dietary patterns and body composition exists has not been studied in kidney transplant or chronic kidney disease patients.

The InBody Body Composition Analyzer has been demonstrated to be as an effective tool to study body composition. One study found that the tool was effective at accurately measuring lean mass in both normal and overweight populations as confirmed by DEXA scans.(9) Other studies found that InBody accurately measured body fat and water as confirmed by DEXA.(10,11)

Goals of the Project

Plant-Based Eating and other diets have been major talking points in the public discourse surrounding general health for years. While the overall benefits in regards to prevention of morbidities such as stroke, heart attack and general mortality are well studied, there are still many questions surrounding specific health benefits of plant-based diets. Considering the numerous side effects of common post kidney transplant medication regimens, we hypothesize that patients who eat more plant-based may have better body composition when compared to those who eat a higher fat, animal-based diet.. We will also seek to understand how self -reported exercise may be associated with these measures and whether there is a relationship between immunosuppression exposure and body composition.

To that end, we will use the InBody Body Composition Analyzer to look at measures of body fat, body water and its distributions between extra and intracellular compartments, as well as differential skeletal muscle mass in the extremities and trunk. The literature surrounding the InBody Body Composition Analyzer support its use in measuring body compartment fat, muscle and water, and thus developing a set of clinical guidelines for its use in monitoring kidney patients may be a valuable asset in personalizing care. Our aim of identifying specific ranges of body composition may also yield more targeted dietary recommendations and interventions, and may allow us to further understand the long-term effects of post kidney transplant medication regimens.

Methods and Analyses

40-50 patients will be recruited from the Chronic Kidney Disease (20) and Transplant clinics (20-30). Patients who have been hospitalized for more than one week in the past month and those who will be started on dialysis within the next 4 weeks will not be enrolled because of confounding effects of illness and uremia on body composition.

A face-to-face survey will be administered which will include a 24 hour diet recall, food frequency questionnaire including daily vegetable and meat servings, and a questionnaire regarding frequency, type and duration of exercise per week.

During the course of their regularly scheduled appointment, we will perform the In Body Composition analysis as follows: patients are asked to assume a seated position for 5 minutes, following which time, plastic electrodes are attached to the middle fingers, and placed below the ankle. The test takes approximately two minutes. Patients will also be asked to take a hand grip ergonometer test after the analysis is performed.

Chart review will examine demographics, immunosuppression dose and level, type and age of transplant, kidney function, hemoglobin, albumin, cholesterol and other values.

Statistical Analysis

These results will be compiled into a spreadsheet and analyzed using SPSS. Descriptive statistics will include means and standard error. Relationships between variables will be assessed using Pearson r or Spearman rho as appropriate. Between group comparisons will be made using t-test or Chi square analysis. An n of 20 should give a significance value of $p<0.05$ for moderate sized effect.

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Make ups: N/A

Bana Hadid
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Title: Postoperative Lumbar Spine MRI Protocol
Sponsor: Dr. Afshin Razi
Maimonides Medical Center Orthopaedics Department
Co-Advisor:
Location: Maimonides Medical Center Orthopaedics Department

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: I spent about two and a half years working in a hematology/oncology laboratory at Lifespan Hospital in Providence, RI during my undergraduate years. The lab focused on using a mouse model to study the mechanisms responsible for the anti-cancer responses observed when haploidentical, or half-matched, donor peripheral blood cells were infused into cancer patients' blood streams. I was awarded the Karen T. Romer Undergraduate Teaching and Research Award to help fund my studies. I obtained spleens from mice and set up assays of immune function, which included using low dose irradiation, antibodies, and immunogenic chemotherapy. After inputting data and analyzing results, I created graphs and charts to portray trends we observed. I attended two poster presentations, where I organized, delivered, and defended my scientific findings.
I was the only intern in the lab and had to rapidly learn how to run the experiments, prepare specimens, read and interpret primary literature, and analyze and prepare data for presentation. Doing much of this work independently helped me improve my time management and organizational skills to balance the time spent in lab with my other responsibilities. Importantly, I also gained insight into the intricate relationship between bench work and clinical medicine and that the work done in the lab is critical for progress in the clinic. I learned the importance of rigorous documentation so that a foundation for troubleshooting is set and the experiment can be replicated. Whenever an experiment failed, my PI and I would assess what went wrong and devise an alternate approach; sometimes our revisions did not work, and we would have to start again until we got it right. Without careful notes, this success would not have been possible. Moreover, my poster presentations and honors thesis helped me gain skills to describe my work to a variety of academic backgrounds. I needed to use different language when speaking to a history student than a biology professor. I valued my time in this lab and plan on using the experiences I gained to help me excel in medical and research settings during my SUNY Downstate career.

Career goals: I am aware of the importance of individuals who have the right training and the willingness to step up to improve their neighbors' health. At Downstate, I am taking advantage of the opportunities available to get the training I need to be such a leader.
While I aim to get a firm grounding in primary care, I am considering specializing. During earlier clinical experiences, I worked with many specialties, including orthopaedics. I valued the combination of clinical work and surgeries they offer. We were able to make a difference by diagnosing problems and developing treatment plans both in the clinic and in the OR. Thus, I aspire to be in an

area of medicine where I can provide immediate help to patients when possible and where there are multiple aspects to the practice, including surgery.
I also have a passion for teaching and hope to work in academic medicine to take part in education and scholarly pursuits. I would like to engage in the clinical trials of new treatments and surgical techniques. I believe that I can best serve my patients by being involved in both patient care and academic inquiry.
Finally, I am interested in global health and expect to continue to be involved through both clinical missions and research.
I am confident that Downstate COM will prepare me for my future. By engaging in the academic, clinical, and research opportunities at Downstate and its affiliates, I believe that I can thrive and acquire the skills I need to be an outstanding physician.

Description: Title
Does postoperative lumbar spine MRI accurately predict clinical infection?
General background
Magnetic Resonance Imaging (MRI) is used following posterior lumbar spine surgery to detect postsurgical site infection (2), and it has been shown to have high sensitivity in this detection (1). Compared to Computed tomography (CT) scans or plain radiographic imaging, MRI can readily detect abnormalities such as hyperemic changes and edema in the vertebral bone marrow in addition to subtle erosive changes of the vertebral endplates at a much earlier stage of infection. This is imperative to clinicians since postsurgical discitis infection often may not present with fever and elevated white blood count.
The interpretation of the images is mainly directed towards the findings of discitis with changes in the spinal disc, vertebra, and adjacent paraspinal tissue. Nonetheless, infection may also exist in the subcutaneous tissues and muscles. Yet these may be difficult to differentiate from normal postsurgical changes on MRI (4). Seroma and non-infectious edema are frequently present following posterior lumbar surgery without any underlying infection (2), especially if bone morthogenic protein is used, and distinguishing them from an abscess has proven to be difficult since they both produce enhancement of peripheral soft tissue (3, 5).
Studies regarding the use of MRI to determine noninfectious seroma versus normal inflammatory change in soft tissue are scarce. Thus, this investigation aims to identify the patterns of language used by radiologists to describe postoperative lumbar spine MRI imaging for cases suspected of clinical infection compared to cases not suspected of clinical infection. The language identified to be used in cases suspected of clinical infection will then be correlated with instances of definitive clinical infection. This data will then be used to determine potential specific patterns of clinical value. These patterns can aid surgeons in their interpretations of postoperative MRIs in addition to potentially assisting radiologists in understanding the clinical consequences of the way abnormalities in images may be described.
Specific aims and research plan of proposed project
The aims of this investigation are to establish the pattern of interpretation of postoperative imaging with MRI following posterior lumbar surgery; the study then aims to find correlations between specific language on the postoperative posterior lumbar MRI reports that raise suspicion for infection and the actual presence of clinical infection.
The hypothesis of this study is that in the absence of discitis, the specificity of MRI in distinguishing between noninfectious postoperative seroma/soft tissue inflammation and true surgical site infection is diminished.
Experimental design of the study: This will be a retrospective chart review of patients who have undergone posterior lumbar spine surgery at Maimonides Medical Center.
Study population: All patients who have undergone posterior lumbar spine surgery at Maimonides Medical Center from 1/1/2010 to 7/1/2018.
Inclusion criteria: Of the aforementioned patients, those included in the study will be any patient who has received an MRI of the lumbar spine for any clinical reason within 10 weeks of their surgery. Of this subset, those with infection of the disks, vertebra, or spinal canal will be excluded from further study.
Study Samples: The remaining patients will be divided into 2 groups: 1) Those who were determined to have definitive clinical infection and 2) Those without definitive clinical infection. Imaging reports of the postoperative MRI will then be analyzed for language describing infection and the relative incidence of such language will be compared between the 2 groups.
Study outcomes: The study is interested in the language of the MRI reports and their relation, if any, to the presence of actual postoperative clinical infection.
Methods and statistical analysis
Subject selection procedures: All patients who have undergone posterior lumbar spine surgery at Maimonides Medical Center from 1/1/2010 to 7/1/2018 will initially have their charts reviewed.

Inclusion criteria: Any of these patients who received an MRI of the lumbar spine for any clinical reason within 10 weeks of their surgery. Of this subset of patients, those with infection of the disks, vertebra, or spinal canal will be excluded from further study.
Randomization procedures: N/A
Methods: The MRIs of the included patients will have the language of their radiology reports analyzed with respect to suspected infection. The charts of these included patients will be examined with regards to their blood cultures, findings from re-operation, etc. in order to determine if there was an actual clinical presence of infection. The language from the MRI reads will then be compared to the actual clinical presence of infection to determine if any patterns in the reports correlate with presence of infection.
Safety Monitoring Plan: No harm is anticipated to study participants, as this is entirely a retrospective review of existing data that will be de-identified upon collection.
Data will be destroyed following completion of data analysis. The file with de-identified patient information will be permanently deleted from the computer on which it resides, as well as from any hospital shared drives. No copies of this information will be kept beyond completion of the study.
Analysis: The incidence of specific language describing infection will be compared between the 2 groups by the non-parametric Mann–Whitney U test. Odds ratios, sensitivities, and specificities will be calculated as well.
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Make ups: Unit 3 Summative Exams begin March 16, 2020 until March 20, 2020. Grades do not come out until at least 2 weeks after that time. I anticipate passing my Unit 3 exams.

Stefan Hamaway
Email: stefan.hamaway@downstate.edu
Phone: 516-521-9252
Title: Male Sexual Health in Patients with Chronic Kidney Disease, Dialysis Patients and Patients with Kidney Transplants
Sponsor: Dr. Mariana Markell
Nephrology
Co-Advisor:
Location: Chronic Kidney Disease, Transplant, Family Medicine clinics, as well as the Parkside Dialysis Unit at Downstate

Fellowship period: Yes
Involve any? Yes

Review Board Type: IRB
Study#: 763663-14
Dates: 01/09/2020
Title: Comparison of Factors Affecting Nutrient Intake in Kidney Transplant Recipients, Patients with CKD or ESKD and Local Controls: Relationship of Blood Levels of Phosphorous, Calcium, Vitamin D and Hgb and Body Composition Analysis by InBody S10 Bioimpedance Machine. A Cross-sectional Study.
Site: SUNY downstate medical center suite C
Type:

Additional Study:
Dates:
Title:
Site:

When/Where: IRB approved last year, to be amended by expedited amendment in April

Research Experience: My research experience began at Union College working in a bioinorganic chemistry lab where I completed an honors thesis. I synthesized Copper (II) complexes and characterized their antibacterial and nuclease activity by minimum inhibitory concentration, zone of inhibition, and by performing gel electrophoresis assays. The initial goal of these studies was to find more targeted alternatives to current platinum based chemotherapy. I also developed a new student laboratory procedure to determine antibacterial properties of test compounds. The work was presented at the national ASBMB conference and was published in the Journal of Inorganic Biochemistry. I also worked as a Clinical Research Associate to manage patients on Phase I clinical trials at MSK. I managed sponsored and institutional Phase I and Phase II targeted cancer therapy studies and acted as a liaison between investigators, patients, pharmaceutical companies, and research and clinical staff. I analyzed patient responses to treatment while maintaining data integrity for retrospective and prospective databases. In addition, I worked with the Early Drug Development Service and performed chart reviews to look at drug induced liver injuries for patients on clinical trials. A manuscript for this work has been submitted to Hepatology.

Career goals: Currently, I am interested in pursuing a career in academic medicine. After working in a large academic center and volunteering and shadowing in suburban hospitals and private clinics, I feel that I would be a good fit working in an academic setting so that I can continue clinical research projects while being able to provide patients with novel therapies that can potentially have a profound impact on their lives. The field of medicine is continually being expanded upon by the research endeavors and I envision my career working at the forefront. I would like to continue exploring potential fields but am particularly interested in a surgery specialty, particularly urology and transplant surgery. My work over the summer will be able to increase my exposure to both fields as I will be able to work with patients and faculty in these clinics. I am also considering nephrology and internal medicine so the additional exposure can help solidify my career aspirations.

Description: Background
The CDC estimates 37 million US adults have chronic kidney disease (CKD)[1]. The percentage of adults with CKD is highest among non-Hispanic blacks (16%), as well as in adults aged 45-64 (13%) and over 65 years old (38%)[1]. Because of the high prevalence in

men of reproductive age, it is important to consider the quality of life and potential sexual health complications in men with CKD. Erectile dysfunction (ED) is a common condition in male CKD patients with a prevalence ranging from 50 - 80% among these patients[2]. A pilot study in Europe indicated support that sexual disability correlates with depression, anxiety and serious impact on quality of life in dialyzed CKD patients[3]. There is a complex relationship between sexual ability and quality of life, and it is important to consider how CKD affects our unique patient population in Brooklyn. ED in the CKD population is multifactorial and involves abnormalities in the hypothalamic-pituitary-gonadal axis, autonomic nervous system disturbances, peripheral neuropathy, endothelial dysfunction, anemia, secondary hyperparathyroidism, and medication effects[2, 4]. In addition, CKD patients are at an increased risk of several psychosocial factors such as depression, anxiety which can be an independent factor to further increase the risk of sexual dysfunction among male dialysis patients[5, 6]. A lower incidence of hypogonadism among dialyzed and transplant patients was observed suggesting that renal transplant might have a protect male sexual capabilities among CKD patients[7]. Treatment of ED is comparable in CKD and non-CKD patients. Treatments modalities include PDE5 inhibitors, vacuum erectile devices, intracavernosal injections, and penile prostheses but renal transplant has been shown to improve the contributing comorbid conditions that lead to ED in CKD patients[4]. The treatment of CKD can have a substantial impact on quality of life by addressing the underlying abnormality that resulted in ED. The improvement was sufficient for a subset of patients to father children naturally or with assisted following transplant[8]. While rates of ED are improved post-transplant, some patients remain with persistent ED after renal transplant[4]. It is not well-known which factors contributed to this observation.

Goals of the Project

Erectile dysfunction can have a profound effect on quality of life but remains an understudied aspect in CKD patients. Previous studies focused on patient populations in several ethnic communities worldwide, but little research was performed that can translate to the predominantly Afro-Caribbean patient population in Central Brooklyn. The incidence of ED and other sexual dysfunction in our CKD patient population remains to be explored and can have treatment implications to improve their quality of life. The primary aim of the study will be to determine the prevalence of sexual dysfunction and association with quality of life in the population served by Downstate. We will also explore relative rates among dialysis and renal transplant patients to investigate if transplant patients have improved quality of life and less sexual dysfunction. Prior studies in other populations showed mixed results in restoration of sexual function following renal transplant but incidence may change in our patient population. This can help with patient family planning and better their understanding of their disease course.

Methods and Analyses

A random convenience sample of 60 patients will be recruited from the Chronic Kidney Disease (20), Transplant (20) and Family Medicine clinics (20), as well as the Parkside Dialysis Unit (20) at Downstate. All male patients who agree will be screened. A survey will be administered to quantify erectile function and quality of life using the following validated questionnaires: the International Index of Erectile Function (IIEF)-5, the Erection Hardness Score (EHS), the Self-Esteem and Relationship (SEAR), and Schedule for the Evaluation of Individual Quality of Life-Direct Weighting (SEIQOL-DW). Questions will assess erectile function and hardness, self-esteem in sexual relationships, as well as quality of life in each cohort on a numeric scale, and timing as well of history of sexual dysfunction. Other questionnaires that will be administered include the BIM (Beliefs in Medicine) Questionnaire, the PSS (Perceived Stress Scale) and the SSS (Social Support Scale). Chart review will be performed to assess kidney function, degree of hyperparathyroidism, anemia, history or diabetes or cardiovascular disease, antihypertensive medications and immunosuppression. We will analyze the data to determine the prevalence of ED among the treatment modalities as well as association with factors mentioned above. Associations will be made using Pearson r or Spearman rho as appropriate. Between group comparisons will be made using t-test or Chi-square analysis. For a moderate sized effect, an “n” of 20 should give a p value of <0.05. Data analysis will be performed using SPSS.

References

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Make ups:

Sharif Hosein
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Title: Race-Based Disparities in the Management and Treatment of Prostate Cancer
Sponsor: Dr. Quoc-Dien Trinh
Department of Surgery, Harvard University
Co-Advisor:
Location: Brigham and Women's Hospital - Boston, Massachusetts

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where: 2/1/2020

Research Experience: Since enrolling at Downstate, I have quickly developed a relationship with Dr. Andrew Winer from the Kings County Department of Urology. I am working on a project that identifies urologic patients treated surgically or conservatively in trauma settings. The purpose of the study is to determine if there are better outcomes associated with conservative care and if the standard of treatment should be altered. I am responsible for:
•Surveying databases for patients who can be included in the study and categorizing them based on the severity of their injuries and several parameters indicative of recovery outcomes
As a community health worker and researcher for a cervical cancer screening program at the University of Miami, I helped identify vulnerable participants from the Hialeah and Little Haiti communities. I quickly learned the communication skills necessary to deliver culturally competent care, and established rapport with patients while discussing sensitive matters like sexual health and cancer prognoses. While there I:
•Identified subjects who met inclusion criteria and informed them of procedures and contingencies of the study
•Developed surveys, upheld IRB protocols, maintained patient confidentiality and performed statistical analysis
During my graduate studies at the University of Florida, I rotated through labs with interdisciplinary focuses and contributed to projects at various stages including protocol development, troubleshooting, and data mining and analysis. I weighed in on department journal clubs and presented findings to my cohort at the culmination of each rotation.
My first 4-month rotation was in an environmental microbiology lab. The focus of our projects was designing and implementing synthetic biology tools for genome editing and transcriptional control in bacteria. My key responsibilities included:
•Optimizing media for sulfur-metabolizing organisms by analyzing literature and data on phylogenetically and metabolically similar specimen in order to obtain more robust cultures better suited for genetic manipulation
•Investigating methods to incorporate CRISPR-Cas9 technology into prokaryotes in order to study the function of select genes in isolation
While in the transcriptomics lab rotation, our objective was to understand the functional aspects of gene expression at the genome-wide level and across different organisms. We integrated these platforms to understand the progression of complex diseases and study how transcriptional complexity is shaped by annotating the functional consequences of alternative splicing. My key responsibilities were:

•To use a new pipeline to assess whether alternative splicing plays a role in neurological degenerative diseases in mice with the goal of identifying a model for the study of Alzheimer's disease
•Engaging in weekly journal club discussions of cutting-edge genomic research and insights in the field

Career goals: Combatting health disparities became my raison d'etre early in the pursuit of my medical career. Ultimately, I aim to practice in a field that will provide me with a platform to impact people of color and disadvantaged communities like those of Miami and Flatbush. Although I am in the exploratory phase of medical school, conversing with my esteemed mentor Dr. Andrew Winer, along with the possibility of providing equitable care to future patients have made me excited for the prospect of a career in urology. Participating in summer research at a prestigious institution like Harvard will open many doors for me, regardless of the medical field I end up pursuing.

Description: Background
Cancer is the leading cause of death in nearly half of the US states (1), and prostate cancer (CaP) is now the most common cancer of men, with an estimated 180,000 diagnoses in 2016. While CaP management has been dramatically shaped by the advent of active surveillance and emerging technologies there are still significant disparities in mortality as a function of race & ethnicity for several common malignancies. (2,3) For example, the CDC reports that Black men are more likely to develop CaP and twice as likely to die from it when compared to Whites. Blacks also tend to develop CaP earlier and are found to have higher grade disease compared to others.
In addition to likely genetic variability in disease, the Institute of Medicine documented multiple instances in which minorities received different treatments than matched Whites for multiple disease types, including CaP. For example, Blacks were less likely to receive indicated lymph node dissection for locally advanced disease during prostatectomy. (4) This is particularly problematic as many providers remain unaware that such disparities exist in their own practices. (5) Part of our effort will be spent identifying the factors contributing to differing treatment patterns such that biases and prejudices can be identified and rectified at the provider level.
However, this problem can also be demonstrated more broadly at the hospital level. A significant proportion of minorities receive their care at facilities in which the total patient volume is comprised of as many as 90% minorities; these are termed Minority-Serving Hospitals (MSHs). The MSHs identified in this study also rank in the top quintile of hospitals with respect to the total volume of Black patients discharged with one of the four major cancers (breast, colon, lung, and prostate). MSHs provide a critical array of services to this population, but many are under-resourced and have poor performance outcomes compared to non-MSHs in terms of common medical conditions and post-surgical outcomes, including high rates of readmission. (6,7) While differences in surgical mortality between Blacks and Whites have improved, MSHs were less likely to demonstrate these improvements. (8) Part of this can be attributed to the fact that MSH leaders lack similar expertise as their non-MSH counterparts when it comes to quality of care. (9) And, despite these documented trends by race and ethnicity, little is known about the outcomes following cancer diagnosis at the MSH level.
In addition to race-based disparities attributable to the patient make-up, there are demonstrated factors at the provider, leadership, and hospital level. This project will focus on systemic barriers. Much of the existing disparities research has concentrated on the biased care provided by individuals, rather than on the attributes of organizations and processes influencing individual outcomes and treatments. Moreover, it is no longer about whether MSHs provide less than optimal quality on average, but rather recognizing that there is considerable variation amongst MSHs (with a nearly two-fold difference in quality scores between the best and worst MSHs). (10,11) The factors driving these differences remain unknown, and improving quality at all MSHs may significantly help improve CaP outcomes for Blacks. Therefore, the overarching goal of this study is to understand how to optimize the quality of CaP care at MSHs.
Specific aims:
Specific Aim 1: Analyze the quality of cancer care for Medicare beneficiaries with localized and metastatic CaP treated at MSHs and non-MSHs.
Hypothesis 1: After controlling for patient-level clinical characteristics (e.g. comorbidities, stage of cancer, socioeconomic status), quality of CaP care for patients at MSHs will be lower than at non MSHs.
Hypothesis 2: The quality of CaP care within MSHs will vary substantially.
Specific Aim 2: Identify associated structural factors that may facilitate disparities in care.

Hypothesis 3: With respect to patient-level clinical characteristics, better access and outcomes are associated with services provided by the hospital itself (e.g. having a recognized cancer program, being a high-volume center, having access to high-technology oncology equipment, having a fully implemented EMR system, being a member of a hospital system, having community health partnerships, being designated as an NCI Cancer Center); the magnitude of this effect will differ between MSHs and non-MSHs.

Methods and statistical analysis:

To accomplish aims 1 and 2, we will utilize Medicare enrollment and claims data as well as a national tumor registry to survey access measures (receipt of therapy, time to therapy) and outcomes (30-day perioperative complications), with control for individual patient characteristics. We will subsequently use a comparative case study approach to identify factors, processes, programs, and practices at high- and low-performing MSHs. This project is innovative for multiple reasons. Much of the existing disparities research is “first-generation” research that documents outcomes and utilization differences. (12) This research project will advance “second-generation” research that explores the underlying mechanisms of inequities. This project will identify actionable targets to further optimize care for minorities. To this end, improving care at MSHs is essential.

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Make ups: None.

Talia Jubas
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Title: Serum Levels of CRP and IL6 in C. trachomatis seropositive adults
Sponsor: Dr. Stephan Kohlhoff
Pediatric Infectious Disease
Co-Advisor: Rosenbaum, Janet, School of Public Health Department of Epidemiology and Biostatistics
Location: Chlamydia Research Laboratory at SUNY Downstate

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: 1573197-1
Dates: 03/2020-03/2021
Title: Chlamydia trachomatis seroepidemiology in NYC
Site: SUNY Downstate
Type:

Additional Study:
Dates:
Title:
Site:

When/Where: 3/10/2020

Research Experience: While I was a post-baccalaureate student, I worked as a research assistant at the NYU Perlmutter Cancer Center in the department of Breast Surgical Oncology. In this capacity, I reviewed medical records as well as pathology and imaging reports to cull data for NYU's institutional breast cancer database. I used this data to identify appropriate study subjects and determine the characteristics of their disease for multiple retrospective studies. I also collected data on individuals with genetic risk factors, family history of breast or ovarian cancer, or a history of non-cancerous breast disease for our high risk breast cancer consortium.

Career goals: I did not decide to pursue a career in medicine until my senior year of college, but I have long known that I wanted to be in a “helping profession.” Volunteer experiences and speaking with professionals who work in the healthcare space in other capacities led me to understand that I wanted a clinical career: to interact directly and in a personal way with patients. Due to my own personal experiences and those of friends and family, I am drawn to women’s health and adolescent medicine, and hope to work in these areas. However, as I am only a first year, I am open to different specialties, and as we move through the curriculum, I make sure to note what I am drawn to (hematology, oncology, and infectious disease stand out from the first three units). While clinical medicine will be at the core of my professional future, I remain passionate about health equity and the many issues plaguing the American healthcare system. For this reason, I am concurrently pursuing my MPH and hope to incorporate policy work into my career as well. During my post-baccalaureate, I had the opportunity to work as a clinical research assistant. That was my first exposure to research, and I realized that, as someone who wants to help progress American medicine forward, gathering and interpreting evidence (i.e. research) must be an important part of my career, as well.

Description: Summer 2020 Alumni Research Fellowship
Applicant: Talia Jubas, COM/SPH 2023
Working with Alana Engelbrecht, COM 2023 (fellow applicant)
Faculty sponsor: Dr. Stephan Kohlhoff (College of Medicine)
Faculty co-sponsor: Dr. Janet Rosenbaum (School of Public Health)
General Background

The most frequently reported sexually transmitted infection (STI) in the United States is infection with the bacterium Chlamydia trachomatis [1]. Infection is commonly asymptomatic, particularly in women [2], which hinders diagnosis and treatment and increases the potential for complications, such as pelvic inflammatory disease (PID), ectopic pregnancy, and tubal factor subfertility [3]. In 2017, New York City ranked among the top 12 cities with highest numbers of reported cases of Chlamydia in the Untied States [4]. Because infection is often asymptomatic, these numbers are likely an underreporting. Despite the risks and consequences, few studies have analyzed the prevalence of C. trachomatis infection in the general US populations or the association between prevalence and certain risk factors. The nucleotide acid amplification test (NAAT), which is typically used to diagnose C. trachomatis in sexually active individuals, indicates only the presence of active infection at the time of testing. Alternatively, performing serological assays enables the study of lifetime prevalence of infection in the general population.
The lifetime prevalence of C. trachomatis in the adult NYC population has never been studied. Moreover, despite ongoing global efforts to control chlamydia, a decrease in infection rates has not been observed [5]. This project will utilize epidemiological data and blood samples from the NYC Health And Nutrition Examination Survey (NYC HANES) repository to assess the seroprevalence of C. trachomatis in adults. The data will then be correlated with potential risk factors including age, socioeconomic status, race, and sexual behaviors (e.g. past-year condom use). This will facilitate a more comprehensive understanding of high-risk populations such that public health interventions can be targeted for more effective primary and secondary prevention of C. trachomatis infection.
It has also been established that inflammatory markers are present and involved in active C. trachomatis infection. According to the cellular paradigm of chlamydial pathogenesis, the clinical manifestations of infection are thought to be due to the epithelial inflammatory response. This process involves secretion of chemokines and recruitment of leukocytes, which mediate local inflammation and can cause damage to surrounding tissue [5]. Studies of interleukin-6 (IL-6) or C-reactive protein (CRP), both documented markers of inflammation, have been conducted in the setting of C. trachomatis associations with PID [6], tubal factor subfertility [7], heart disease [8], preterm delivery [9], and in reproductive epithelial cultures [10]. This study will measure inflammatory markers in a representative general population to better understand the clinical implications of C. trachomatis seropositivity. The presence of inflammatory markers in seropositive individuals would inform investigation of a potential hyper-inflammatory state that can have various clinical implications. Furthermore, the identification of noninvasive biomarkers associated with a higher risk of clinical complications would be extremely beneficial for guiding the allocation of resources in public health initiatives [5].
Aim 1: Measure Chlamydia trachomatis seropositivity as a marker of lifetime prevalence (LTP) from a non-specific NYC 2013 cohort, then correlate results with age, SES, and past year condom use.
This is a clinical, observational, and retrospective study to assess the seropositivity of C. trachomatis in the general NYC adult population in 2013. A different member of the lab team will work on carrying out this specific aim.

Aim 2: Evaluate serum levels of CRP and IL6 in C. trachomatis seropositive individuals to assess the clinical effects of infection.
Serum samples from the NYC HANES respository will be analyzed for CRP and IL-6. These markers of inflammation are known to advance disease progression in those with chronic health conditions. Confounding variables such as smoking status or other inflammatory illnesses will be controlled for.
Methods – Aim 2
CRP and IL-6 are commonly measured markers of systemic inflammation and were selected for this study based on their relevance for a mucosal infection as well as markers of chronic diseases that could be associated with C. trachomatis infection. Higher levels of these proteins may indicate chronic low-level systemic inflammation and predict increased risk for cardiovascular events, certain cancers as well as all-cause mortality. These biomarkers will be determined by ELISA assays according to the manufacturer's recommendation (Invitrogen, Carlsbad CA).
Over the course of 8 weeks, 1207 subjects' blood samples will be assayed. The first week will be spent setting up the samples, materials, and protocol requirements. During the second and third weeks, a fellow lab team member will perform the EIA's on the samples to detect antibodies, while I conduct ELISA assays to look for CRP and IL-6.
In the fifth week, I will conduct statistical analysis using standard survey-weighting techniques under the guidance of Dr. Rosenbaum. We will analyze racial, gender, and age disparities in chlamydia using survey-weighted regression models. Our model for analysis of inflammatory markers depends on their prevalence: if common, we will use the same methodology as with chlamydia, but if rare, we will use survey-adjusted logistic regression. After analysis has been completed, in week six or seven, I will work on organizing the data and developing an abstract and poster for submission to a reputable journal.
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Make ups:

Gabriel Kabarriti
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Phone: 3475643738
Title: Lower Extremity Amputation Rates in African Americans Exceed Those in Caucasian. A Performance Improvement Study To Detect And Eliminate Those Differences.
Sponsor: Dr. Robert DiRaimo
Vascular Department
Co-Advisor:
Location: The research will be performed at SUNY Downstate Medical Center in the Division of Vascular Surgery.

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: In high-school, I shadowed at Beth Israel Medical Center in NYC. I noticed many patients were readmitted after discharge and sought to change that. I joined Dr. Rizk to investigate methods that would improve doctor-patient communication to reduce readmission. We identified that patients with serious diseases, such as AIDS, were often readmitted. We sought to prevent readmission by implementing family meetings, and facilitating more frequent check-ins with doctors and family members to ease a patient's transition out of hospital.
During college, I developed an interest for organic chemistry and joined a drug discovery lab. The lab's goal was to develop therapeutic inhibitors for glutamate, as excess glutamate contributes to neurological disorders. Some of the difficulties with such drugs is that they can deplete the entire body's supply of glutamate. By identifying enzymes specific to certain regions, I synthesized two glutamate carboxypeptidases as potential therapeutic agents that passed through the blood-brain barrier and target the brain. Our manuscript, "Structural and Computational Basis for Potent Inhibitions of Glutamate Carboxypeptidase II by carbamate-based inhibition," was published in Journal of Bioorganic and Medicinal Chemistry.
I carried the lessons forward to a project that identified the effects of mergers and acquisitions in the pharmaceutical industry on drug prices. Using data I gathered on pharmaceutical firms and drug prices between 1992 and 2017 for generic medications such as doxycycline, we found that mergers almost always led to an increase in drug prices regardless of the number of firms producing drugs and number of available alternatives. We presented this data to policymakers in the hope of proposing legislation for the Federal Trade Commission, whose approval is needed for mergers, to not only take into account the number of competing firms for a drug after a merger but to also focus on possible collusion in price settings and other non-competitive behavior at the firm level post mergers.
One of the projects during my gap year focused on identifying and eliminating gaps in the transition of care for patients suffering from opioid addiction at Johns Hopkins Hospital. Many patients with substance use disorder have behavioral health needs that are important to treat, and many services existed at the hospital to address those needs. However, the services worked in siloes and were not integrated in such a way to provide accessibility across the institution. To address the gaps, we established a Substance Use Disorder Consult team to help manage and work towards comprehensive, integrative care of patients.

I learned from these experiences the impact research has. Research gave me opportunities to do something novel and have wide-ranging impacts on patients. My efforts will continue to make long-lasting impact, something I hope to do in my career as a physician where I will be at the forefront of creating progress.

Career goals: I see my future medical career in academic medicine where I can practice in an area that allows for long-term care of patients as well as the opportunity to pursue clinical research. While shadowing at hospitals as an undergraduate, I have repeatedly seen the importance of the physician-patient relationship in understanding and overcoming obstacles faced by patients. I have participated in multiple projects to address obstacles such as a high readmission rate and medication noncompliance due to cost. Through these research projects, I have learned the importance of individualized treatment by addressing each patient's unique circumstances and how clinical research is most successful when doctors have a full understanding of their patients. Practicing in academic medicine in an area with long-term continuity of care will not only allow me to remove barriers directly affecting my patients but also implement and enhance programs through research with wide-ranging impacts beyond my patients.

Description: BACKGROUND:
A recent study in JACS (1) by Lillemoe et al. entitled "Variation in Amputation Risk for Black patients: Uncovering Potential Source of Bias and Opportunities for Intervention" may have profound clinical implications for our patient population. The study, which was based on NYS SPARCS data, concluded that disparities, because of which African Americans are more likely than white patients to have a primary amputation of an ischemic lower limb as opposed to vascular surgical reconstruction, indeed exist in New York State. The disparities exist throughout New York State and range from an average of 10.1% in counties in Central New York State, to 18.5% in New York City, exceeded only by 0.3% in the urban countries just north of the city. Within New York City, the highest rate of disparity in any county in the state, with black patients having the higher primary amputation rates, is in Kings County, where it is 23.3%.1
Four of the fifteen hospitals in Brooklyn have surgery departments staffed by the SUNY Downstate Medical Center Department of Surgery. Our study will evaluate whether the racial disparities are present at our institution. Our findings may call PDCA action plan to eliminate these racial disparity. The prerequisite to formulating a PDCA action plan to eliminate racial disparities is to determine first of all whether they exist here. It will also be important to determine the antecedents of the disparity. With this knowledge we will devise plans and measures to reverse those trends if they exist. To reverse these trends is to evaluate the quality of care offered by Downstate Medical Center will enable us to better to fulfill the Downstate mission statement: "SUNY Downstate will be nationally recognized for improving people's lives by providing excellent education for healthcare professionals, advancing research in biomedical science, health care and public health, and delivering the highest quality, patient-centered care." An unexplained and possibly the invidious difference in primary lower extremity amputation rates between Caucasian and African American patients, if present, vitiates the meaning of the mission statement and runs counter to the ethical foundations of medicine under the oath all physicians take.
In the past decade there have been many studies addressing such racial disparity issues. There is no evidence that genetic factors drive the racial outcome differences.2 Insurance status may affect access to treatment but is under control of the political process. Other factors include healthcare industry attitudes, institutional policies and practices, and the actions of the surgeons here concerned. Additionally, lack of cultural competence among providers, racial bias, deeply ingrained distrust for healthcare institutions in the minority population, including elite academic medical centers all impinge on this problem. These latter factors are modifiable, provided we can identify them and devise action plans to address them. Selby & Zhang state "African American do not appear to be at increased risk for diabetes-related amputation when access to medical care is comparable."3 However, these results were obtained in a large dedicated HMO. Whether these results apply to non-diabetic peripheral vascular disease patients or to those in less structured setting is still open. The problem of racial disparity in amputation rates is potentially soluble.
PLAN:
A retrospective study reviewing medical records will be performed to collect data. Medical records will be reviewed of patients who received amputations performed by the staff vascular surgeons at DMC. Charts will be reviewed to determine whether or not prior revascularization was performed or considered by either bypass, grafting with angioplasty with or without stenting. Charts from a five-year period, 2015-2019, will be chosen to assure a significant sample size. The MGH study used SPARCS data, an administrative data base which can give very granular information, including types of operation done, timing, location of surgery, and names of individual practitioners. However, it is not a clinical data base, and it will be a clinical factor only which will enable us to discern the reasons why racial disparities exist in surgical decision making.

Clinical factors:
We will evaluate the treatment dichotomy in patients with distal lower extremity ischemia, between those undergoing vascular reconstructive surgery versus primary amputation either below or above knee, tarsometatarsal, and toe amputation. The question is, at our institution, whether there is a racial distinction such that black patients have a higher primary amputations rate and lower vascular surgery rate, compared with whites.
DO
Charts will be examined for the following factors: race; co-morbid cardiovascular disease and disease complication codes; ASA classification which will affect operability; where available information on smoking, exercise, and obesity; NIDDM and IDDM and Hgb A1c levels; mode of presentation; mode of presentation (emergent with dry or wet gangrene or pre-gangrene versus elective); and zip code. The latter two factors are surrogates for living in a segregated and therefore highly stressful neighborhood. Individual surgical decision making be examined. These parameters will be arranged on a spreadsheet to determine what demographic and co-morbid factors correlate with it.
Data Protection: Data collected will be completely de-identified, making the information anonymous. It will be stored on one computer that is password protected. A lock screen will be activated every 5-minutes of idleness.
Analysis: We will use STATA, a statistical software, to develop a regression model that evaluates the effects of race on receiving an amputation and revascularization opportunities. In our model, we will control for variables that may impact the care they receive. The neighborhood a patient lives in will be captured by their zip code. Smoking, obesity, exercise, diabetes, presentation of symptom and demographic variables will be controlled through dummy variables in the model.
CHECK
Checking will consist of tallying the correlations of increased primary amputation rates, reduced vascular surgery rates in African American patient population, and comparing these to the etiologic factors listed above. If the number of white patients is too small to permit of the drawing of valid statistical comparisons with results in African American patients, comparisons will be made with national data bases such as Medicare, used as historical controls.
ACT
Assuming no racial disparities appear at DMC vascular cases in the years from 2015-2019, the parameters listed above as well as individual questionnaires will be pursued to discern why we have avoided such a widespread problem. Assuming that racial disparities in amputation versus vascular reconstruction are present, the mandate would be to eliminate those differences.
A possible solution in an allied field may derive from a study of the same issue as addressed in ERAS (Enhanced Recovery After Surgery) in colorectal surgery. This article states that a pre ERAS greater LOS in black patients at UAB Department of Surgery was totally eliminated by adopting ERAS practices.4 What is relevant in this study, as translated from colorectal surgery to vascular or acute emergency surgery patients with ischemic limbs, is the ERAS protocol. While the steps for such a protocol in patients with threatened limbs would be different from those applying to colorectal surgery patients, the underlying symmetry rests in the adoption of an exhaustive itemized menu, requiring minute tenacious attention to detail to produce enhanced results. The ERAS protocol outlined in this article is approximately 50 steps in length, and draws in personnel at the very least from surgery, anesthesia, and nursing. By requiring careful attention to the inventory of practices in all professions dealing with the patients, in carrying each patient through protocol, any personal difference in interactions, practices or attitude on a racial basis are diluted out by the diligence required by observance of each step of a minutely demanding program. While the authors themselves are unsure of the mechanism of their advance, they observe that “future research will likely require qualitative, non-administrative based approached to understand these mechanisms”. If these disparities exist at DMC, we will devise a point by point multi-disciplinary program by which to evaluate patients with ischemic limbs. This program requires close adherence to the enumerated steps by all professions concerned. As with ERAS LOS study, there will be no room for racially differentiated treatment.
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Make ups:

Nikhil Kasarla
Email: nikhil.kasarla@downstate.edu
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Title: Phenotyping Nocturia in hypertensives according to 24 hour urine composition, free water clearance, and volume status in a racially diverse primary care population.
Sponsor: Dr. Jefferey Weiss
Department of Urology, SUNY Downstate
Co-Advisor:
Location: University Hospital of Brooklyn Family Medicine Clinic

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: 1471991-3
Dates: 1/23/2020-11/04/2022
Title: Phenotyping Nocturia in hypertensives according to 24-hour urine composition, free water clearance, and volume status in a racially diverse primary care population
Site: University Hospital of Brooklyn Family Medicine Clinic
Type: IBC

Additional Study: 19-297
Dates: 1/07/2020-1/7/2021
Title: Phenotyping Nocturia in hypertensives according to 24-hour urine composition, free water clearance, and volume status in a racially diverse primary care population
Site: B6-326

When/Where:

Research Experience: Clinical Research Assistant III with Dr. Robert Chapman (June 2017-June 2018)
•Researching the onset of Alzheimer's disease, focusing on changing EEG activity in elderly subjects. Monitoring and collecting data via individuals evoked response potentials (ERP) utilizing data software and excel
•Worked with PI and staff scientists to assist in writing journal publications and grant applications. Responsible for data management.
•Coordinate incoming elderly subjects and administer lengthy cognitive and neuropsychological testing
Independent Study of Circadian Rhythms with Dr. Michael Sellix (Fall 2016-Spring 2017)
•My research focused on examining the impact of aging and chronodisruption on the physiological response to influenza infection in mice
•Developed skills in small animal handling, infection technique, behavioral analysis, PCR, and sacrificing of animals and tissue harvesting for RNA extraction
•Presented findings and scientific journal articles in weekly lab meetings to PI and fellow peers
Lab Intern for Dr. Sanjay Maggiwar HIV Laboratory (Summer 2015)
•Interacting with PI, doctoral candidates, post-graduates, and staff scientists to utilize laboratory instruments to run experiments
•The purpose of my summer research was to determine the biological pathway in the platelet activation model of MLK3 when induced with the drug minocycline
•Utilized techniques such as ELISA, western blotting, platelet isolation, and application of drug treatments groups
•Observed fixation of rodents, harvesting of blood samples, and isolation techniques. Utilized layers of platelets in order to run experiments
Independent Study of Lysosomal Disruption in the brain with Dr. Mark Noble (Spring 2015)
•Interacting with PI, doctoral candidates, lab technicians and fellow peers in order to learn and apply new laboratory techniques

•The goal of my Independent Study is to characterize the effect of lysosomal disruption on subcellular localization of protein s involved in lysosomal biogenesis, autophagy, and cell survival, division, differentiation, and apoptosis in primary human and rodent cell cultures
•Utilized techniques such as immunohistochemistry and microscopy
Clinical Research Assistant II for Dr. Supriya Mohile (Summer 2014)
•Coordinated with PI, clinical researcher, as well as fellow peers in order to assess patients and organize data through Excel, eRecord, as well as RedCap
•Dr. Mohile's research focused on assessing and treating Geriatric patients suffering from cancer based on data retrieved from surveys and interviews with patients
•Interviewed patients along with Clinical Researcher for data collection during clinic hours
•Ability to perform data entry and organization of confidential documentation, clinical protocols, and group focused projects

Career goals: As a first-year medical student interested in urology, I still have a lot to learn. However, I have an idea as to how I would like to practice medicine. Firstly, I know I love working with patients and having the opportunity to develop meaningful relationships with those patients. Secondly, I know I love procedures, surgery in particularly. The best way for me to learn more about the field is to engage in research projects and gauge my interest. I have been working on this project with Dr. Weiss and his students for the past 2 months and already I feel like I have found a like-minded community. Conversations ranging from the breadth of the practice, favorable patient outcomes as well as the faith, trust and mutual respect that urologists have with their patients have all pushed me towards the field. Working with patients on an intimate level requires urologist to develop meaningful relationships with their patients, an aspect of the practice I am very much looking forward to.
As an MPH student with a focus in epidemiology, urology presents a unique opportunity in the development of new technologies and the pervasiveness of pathologies. I can use my skills in SPSS to run large analysis of data in order to develop the best algorithms of care for patients and to evaluate novel surgical techniques and tools. Urologic pathologies are pervasive in our society and I can have a large impact on describing those populations, assessing risk and looking for trends in risk reduction.

Description: Background:
Nocturnal Polyuria (NP) is characterized by increased nocturnal urine output over the course of a 24-hour period. The pathophysiology may have multiple etiologies; however it has become apparent that it is not simply an increase in overnight urine production (Goessaert, 2014). Instead it is a condition with underlying mechanisms involved in water and/or solute diuresis (Monaghan, 2018). Water diuresis is represented by high free water clearance and decreased osmolality whereas solute diuresis is characterized by increased sodium clearance during the night. This study is critical for evaluating the effects of hypertension (HTN) on NP, as HTN is one of the most prevalent and morbid chronic conditions. Previous studies have indicated the need for larger case-control studies to specify the effects of comorbidities on increased nocturnal sodium and water diuresis.
Aims:
This study will be a prospective cross-sectional analysis designed to track the frequency, amount, and concentrations of electrolytes present in the urine samples of HTN patients with NP.
Methods:
All patients >18 years of age, with a recent creatinine from within the past year, with a history of primary HTN (130/80) will be considered eligible candidates and screened for enrollment. Exclusion criteria include Age < 18 years of age, severe dementia or intellectual disability, para/quadriplegic patients, hx of previous bladder/urethral surgery, neurogenic bladder, and CKD Stage III (GFR<59).
Patient Instruction:
A detailed questionnaire specifying medical history and medication use will be completed to separate the effect of confounding variables. The patient will then be given 3 labelled urinals and instructed on maintaining 24-hour voiding diaries. The first urinal will be allocated for first nighttime void after falling asleep. The second container will be allocated for the remainder of the volunteer's nighttime voids as well as their first void upon waking. The third container will be for the remainder of the volunteer's voids during the daytime over a full 24-hour period.
Urinalysis Procedure:

We will be preforming chemical analysis on the collected specimens to assess the concentrations of Na+, K+, urea, sulfate, creatinine, ammonium, and the osmolarity of the urine specimens provided by the volunteers. Equipment provided and analyzed by SUNY Downstate Department of Nephrology, at no charge to the patients.

Statistical Analysis and Variables:

We will be controlling for abroad spectrum of variables in order to eliminate confounding variables and specify the association between hypertension and nocturia. These variables include: Age, gender, hypertensive medication class, osmolar makeup of urine produced at night vs during the day, volume of urinary output during the day and night (via collection and 24-hour voiding diary), osmolar makeup of urine, and volume of urine produced in the first nightly void vs subsequent nighttime voids, baseline number of daily and nightly voids, baseline etiology of nocturia. In addition, participant medical records will be abstracted for laboratory test results, demographic information, vital signs, results of cardiovascular and genitourinary tests and procedures, current medications, and comorbid diagnoses.

We will utilize statistical analysis software and methodology including regression models in order to analyze the significance of our findings. In addition, participants' medical records will be examined for previous laboratory test results, demographic information, vital signs, results of cardiovascular and genitourinary results and procedures, current medications and comorbid diagnosis in order to account for confounders.

Make ups: N/A

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Phone: 9142278003
Title: Machine Learning for the Prediction of Acute Ischemic Stroke
Sponsor: Dr. Steven Levine
Neurology
Co-Advisor:
Location: SUNY Downstate

Fellowship period: Yes
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: As an undergraduate at the University of Southern California, I was involved in a biophysics research lab, the El-Naggar laboratory, which studied the bacteria Shewanella oneidensis and its unique electron transport mechanisms through its projections of the periplasmic space known as “nanowires”. One of the main projects I undertook was to determine whether these nanowires had any ability to transfer bulk material such as protein from one cell to another. It was unclear whether the nanowires served a purpose to the bacteria aside from their ability to transfer electrons to external surfaces for its metabolism. The project involved first electroporation and transformation to uptake a plasmid into S. oneidensis, thus creating a new strain that contained genes for a green fluorescent protein that would be exclusively expressed in the periplasm. With this new strain and another strain that expressed cytoplasmic red fluorescent protein, I observed a mixture of them under fluorescent microscopy to determine whether or not we would see an event such that green periplasmic fluorescent protein would transfer to another bacteria with red cytoplasmic fluorescence. As it turns out this event never occurred, but it was confirmed that the green fluorescent protein is expressed in both the periplasm and the projections of the periplasm known as nanowires.
Another main project that I worked on in this lab involved a computational approach to the study the same nanowires. This involved creating a Matlab simulation of the nanowire itself, such that changing different parameters of the simulated nanowire, such as intrinsic membrane characteristics, length, diameter, etc. would change the most stable conformation or shape based on the energetics. The purpose of this simulation was to address the question of why the nanowires took on the shape that was observed in electron microscopy, since the nanowires has a peculiar “beads on a string” appearance. The simulations had similar findings to previously established findings in the field of differential geometry and confirmed that intrinsic attributes of a membrane surface lead to changes in the most stable conformation of the shape of the membrane structure. The intrinsic attributes of the membrane are thought to be influenced by the types of phospholipids and other molecules interspersed, including the transmembrane proteins.

Career goals: As of right now, I am most interested in the field of neurology. This is a very academic field and research plays an important role in informing the medical knowledge and practice. I wish to continue to develop my understanding and ability to participate in the research that informs this field. I have joined the Evidence Based Medicine Club here at Downstate and hope to join the Clinical Neurosciences Pathway in my second year.

Description: Title of Project: Machine Learning for the prediction of Acute Ischemic Stroke

General Background:

Stroke is a major cause of death and disability. More than 800,000 strokes occur every year in the United States, leading to more than 200,000 deaths (1). For those who survive, it is the most common cause of adult disability in the modern world, requiring expensive long-term rehabilitation care (1). The ability to predict acute ischemic stroke (AIS) using both demographics and clinical characteristics may be valuable in identifying high risk patients in order to guide treatment options. A previous paper (2) used statistical analysis of multiple logistic regression in large-scale hospitalization data sets, such as the SPARCS- data set (Statewide Planning and Research Cooperative System) (3), to determine factors influencing AIS risk in a specific subset of patients presenting to the ER with complaints of dizziness, imbalance or vertigo. Multiple independent positive and negative predictive variables were identified for this subset of patients presenting with dizziness, imbalance or vertigo, such as history of hypertension (OR 1.60, 95% CI 1.49-1.72, $p<0.001$), admission presentation of vertigo (OR 0.56, 95% CI 0.41-0.75) and several more (2). Although logistic regression models may allow for the identification of predictive variables such as these, machine learning algorithms offer an alternative, especially for the purpose of large-scale data, with the advantage of easily incorporating new data to improve prediction performance (1). Furthermore, there is also the question of which specific machine learning techniques would be the best to apply to this problem of predicting stroke. While one paper found that the technique of support vector machines had the best performance in predicting stroke outcomes(1), another found that there was only significant improvement with the technique of deep neural network (4).

Specific aims and research plan:

My question is to determine if machine learning methods can accurately predict acute ischemic stroke, using a large retrospective data set of prior hospitalizations, and if so, which specific methods are the best for this purpose.

Methods and Statistical Analysis:

My plan is to train, validate and test several different machine learning algorithms on the SPARCS data set to determine if there is the ability to accurately predict acute ischemic stroke based on information such as demographics, medical conditions and presenting complaint. Methods for machine learning can generally be divided into two main forms: supervised and unsupervised. The supervised forms of machine learning refer to the condition where one has a data set where the predicted outputs are known and can be used to train the model. Supervised forms of machine learning include linear regression, logistic regression, neural networks and support vector analysis. In the case of this research proposal, only supervised machine learning techniques would apply, since the predicted output of presence of acute ischemic stroke ($y=1$) or absence of acute ischemic stroke ($y=0$) is known. In brief, neural networks act as a way of sending a large number of independent variables through several layers of mathematical functions, with each layer creating a temporary set of independent variables, and then sending each of those temporary independent variables to the next function of the “neural net”. The final layer of the neural net can converge to predict either one or several dependent variables “y”. For example, in this project, I would plan to have the neural net act to predict the presence of acute ischemic stroke as the dependent variable, where $y=1$ would be the presence of acute ischemic stroke and $y=0$ would be the absence of acute ischemic stroke, after sending several independent variables, such as demographics and medical characteristics, through the neural network.

The remarkable strength of this type of computation is that it can create a model that is very good at predicting non-linear hypotheses, especially in the case that there are many initial independent variables to begin with. This ability to predict a non-linear hypothesis is also what gives this type of algorithm an advantage over the more traditional logistic regression, since a non-linear logistic regression analysis would require many polynomial terms and would be computationally expensive, especially if there are a lot of independent variables. I imagine this is exactly why the paper by Heo et al (4), was able to use a deep learning network to predict modified Rankin score for stroke patients several months in advance, with better area-under the curve than the MD-CALC score, ASTRAL – Acute Stroke Registry and Analysis of Lausanne Score.

On the other hand, support vector machines are a very different type of machine learning algorithm. These are more similar to the traditional logistic regression model, however use a different formula for the cost function. In short, the advantage of this cost function is to create a more of a distinct and clear separation between positive and negative examples. This can lead to greater accuracy in the ability to classify the output variable and is likely the reason why this type of algorithm showed some promise according to Asadi et al (1).

I do plan to use several forms of supervised machine learning algorithms, including but not limited to a support vector machine and artificial neural network to evaluate the ability of the algorithms to predict AIS. I would then compare the receiving operating

characteristics of the different methods of data analysis. Once again, the reason for testing several different supervised machine learning algorithms is that it is unclear which type of algorithm might be best (1,4).

I anticipate that there will be much time devoted to “cleaning” and extracting the data from the SPARCS data set for its use in data analysis. The remainder of the time will be spent applying pre-existing machine learning packages to the data set (5). I anticipate that applying these packages to the data-set could require some fine-tuning and debugging, thus requiring another significant portion of time. For example, this would mean that I would need to spend the time matching the independent variables of interest within the SPARCS data to the inputs of the machine learning packages.

Another important step in the process would be to evaluate performance of the algorithm, and this will also require a significant amount of time. Specifically, one needs to be cognizant of the two main pitfalls that could affect performance of machine learning algorithms, which are namely over-fitting and under-fitting. Over-fitting is the tendency for the algorithm to fit the training data very well, but is inaccurate when presented with novel test data. The other main pitfall is under-fitting to the data, in which case the algorithm doesn’t even match up to the training data. The main strategy to ensure that one does not fall into either of these pitfalls involves two steps; the first step is to divide the data into 3 sections. The first section of data would be the training data subset, the second would be cross-validation data subset and the third would be the test data subset. The second step is that one then plots the error function “J” as a function of the number of examples for both the training data and the cross-validation data. Based on the characteristic of these overlaid graphs, one can then determine if the algorithm is suffering either from over-fitting or under-fitting. I anticipate that it will take a significant amount of time to monitor and plot these error vs training set size curves and subsequently make alterations to the overall strategy of the algorithm, such as changing the learning rate “alpha”, or changing the number of initial variables, etc.

By testing several of the machine learning algorithms on these data sets we hypothesize that the results will be positive - namely indicating that there is a good ability for the independent variables such as demographics or clinical characteristics to predict acute ischemic stroke. I will devote the last phase of my research project and experience towards writing up the results and submitting an abstract and manuscript to a peer-reviewed meeting and journal (such as Stroke or Neurology).

A major limitation for this form of research is that the data to be analyzed has been collected retrospectively. Although we may anticipate finding statistically significant results and trends, the data collection did not occur in an ideal setting of a randomized control trial, or even a prospective cohort trial, which are considered to be studies of higher quality evidence. Furthermore, another limitation is that the algorithms may be seen as non-intuitive or too much of a “black box” phenomenon.

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Make ups: None

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Title: Dubousset Functional Test (DFT): The First Application on Spine Patients and Asymptomatic Volunteers
Sponsor: Dr. Carl Paulino
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Co-Advisor:
Location: BSB 3-7

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: 1111613-7
Dates: effective 1/29/20
Title: A Prospective Evaluation for Building a Registry of Kinematic and Temporal-Spatial Aspects of Gait in Upper and Lower Extremity Musculoskeletal Injuries and Pathologies or Spine and Stress Pathologies
Site: SUNY Downstate Medical Center
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: My first research experience began during my sophomore year at Hunter College when I started volunteering in Dr. Pereira's lab. Dr. Pereira's research focused on the ubiquitin/proteasome pathway and inflammation in neurodegeneration allowing me to better understand Alzheimer's and Parkinson's disease. There, I was introduced to basic lab research techniques such as western blotting, animal work, immunohistochemistry, and daily lab responsibilities.
That summer, I started my next research experience as a volunteer in Dr. Mulholland's lab at the Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai. Initially, I worked under the supervision of Dr. Edwards whose research focused on neuroendocrine prostate cancer, a sub-type of advanced prostate cancer. Unfortunately, Dr. Edwards left the lab before any significant progress could be made. Nevertheless, I continued to expand my research skills by learning how to handle and set up cell cultures, perform and analyze qPCR, resect tissues from mice, and manage mouse colonies in the vivarium.
The following year I was promoted to a paid part-time trainee position in the same lab. Working with Dr. Wang, we were able to publish an abstract, which turned into a poster presentation at the 2018 American Association of Cancer Researchers (AACR) Annual Conference in Chicago. There, I presented research about the impacts of World Trade Center (WTC) dust exposure on cancer. Epidemiological studies showed increased incidence of prostate cancer in first responders versus the general population. The mechanism for this phenomenon is poorly understood and thus my lab used mouse models to try to gain a better understanding of the underlying pathophysiology.
For my gap year, I was promoted to a full-time associate researcher position. I continued to work on the WTC project as well as a new project investigating how to improve the efficacy of immune checkpoint blockade (ICB) therapies in prostate cancer. Successful clinical trials have led to FDA approval of anti-PD-1/PD-L1 and anti-CTLA-4 ICB in various solid cancers. In prostate cancer, ICB has largely been ineffective and thus we started testing novel combinatorial strategies with agents such as CDK4/6 inhibitors. At the end of my gap year, I was proficient in FACS analysis, single cell sorting, subcloning, genotyping, implanting tumors, and conducting drug treatment studies using mouse cohorts.
Now in medical school, I am involved in research with the Department of Orthopaedics. Switching gears to clinical research, I learned how to use national databases such as National Inpatient Sample (NIS) and Kids' Inpatient Database (KID) as well as how to analyze data with SPSS software. My work thus far has resulted in the submission of abstracts to multiple Orthopaedic journals

as well as a poster to SUNY Downstate's 2020 Research Day. My project looked into categorizing fracture patterns in blunt trauma patients with Adolescent Idiopathic Scoliosis.

Career goals: My career goal is to become an orthopaedic surgeon. Coming into medical school, I was very interested in orthopaedics as a specialty and in my few months here, that interest has only grown. Having spoken to orthopaedic surgeons here at Downstate, I have heard repeatedly that the best part of their job is seeing instant improvement in patients after surgeries. In my gap year, I was fortunate enough to work with several urologists who have also pointed to surgeries as the best part of their profession. Surgeries provide life saving and oftentimes immediate relief to patients. Improving the quality of life of a patient, getting them back to a normal life, and feeling the tangible sense of gratification that comes afterwards are qualities of the profession that draw me orthopaedic surgery.

Since becoming involved during my undergraduate years, I have witnessed the impact research has on medicine. Any new technology, treatment, or discovery is aided by the efforts of researchers worldwide. Research in Orthopaedics is an extremely diverse and highly active field that strives for continual improvement of patient outcomes. Whether it's biomechanics, oncology, pediatrics, or prosthetics, one can get involved with research in many different ways by choosing a career in orthopaedics. By dedicating my summer to research with the orthopaedics department, I hope to gain greater exposure to the field and ultimately make a meaningful contribution to existing medical knowledge.

Description: General background
Spinal deformity is becoming more common as adults 55–64 years of age are the fastest growing proportion of the U.S. population [1]. Spinal deformities in adults have complex etiologies but can be associated with overall deterioration of the muscles of the spine, pelvis, or lower limbs, as well as with overall body-balance compromise [2]. Currently, the functional status of patients undergoing spine surgery is assessed with quality-of-life questionnaires. Standardized patient-reported outcome measures (PROMs) and radiographic parameters have advanced our ability to assess patients, but radiographs are static, and PROMs are limited by quantifying the patient's perception of disability [3]. A more objective and quantifiable assessment method is lacking.
Recently, Dr. Jean Dubousset proposed a practical four-component global functional assessment test called the Dubousset Functional Test (DFT) [4-5]. The DFT includes the following components: getting up from a chair that does not have arms and walking 5 meters forward and 5 meters backward, climbing steps, sitting down on the floor from a standing position, and a dual-tasking test. The baseline for completing the DFT has already been assessed in asymptomatic volunteers [2]. Assessing the performance on the DFT in patients with spinal pathologies as compared to asymptomatic controls is needed.
Specific Aims
Aim #1: Recruit patients with spinal deformities and asymptomatic volunteers to participate in the study.
Aim #2: Assess performance (time to completion) on the various components of the DFT in spinal deformity patients and asymptomatic volunteers.
Aim #3: Ensure participants of the study complete various standardized PROMs (EQ5D, ODI, SF12), and Montreal Cognitive Assessment (MoCA).
Aim #4: Organize, analyze, and interpret data collected from the first three aims. Specifically for analysis, describe the differences between spinal deformity patients and asymptomatic volunteers.
Aim #5: Help draft final manuscript that will be submitted for publication.
Research Plan
We believe that the DFT will be a useful clinical tool in stratifying risk of deformities in adult patients, tracking surgical outcomes, and possibly predicting complications from surgeries. We expect performance on DFT to correlate with PROMS and will be assessing this in spinal deformity patients as compared to asymptomatic volunteers.
Methods
This will be a prospective, single center, 2-arm study that will include asymptomatic volunteers and primary patients presenting to the spine service for evaluation of lumbar degenerative disease and spinal deformity. DFT is a test which assesses functional status via 4 components: (1) the Up and Walking Test (UWT): participants are asked to rise without assistance from a seated position in a chair that does not have arms, walk 5 meters (500 cm) forward before stopping, walk backwards 5 meters, and sit back down without assistance; (2) the Steps Test (ST): from a starting position 50 cm away, participants are asked to climb three stairs, turn around on the third step (top), and walk down the three steps; (3) Down and Sitting Test (DST): from a standing position, participants are asked to sit on the ground and stand back up, using assistance as needed; (4) Dual-Tasking Test (DTT):

participants are asked to walk 5 meters forward, turn around, and walk 5 meters back to the starting position while performing a working memory test (counting down from 50 by intervals of 2). Each test will be timed and performance will be scored by time (in seconds) required to finish the test. Patients will complete PROMs (EQ5D, ODI, SF12), and Montreal Cognitive Assessment (MoCA). DFT will be compared between populations and correlated to PROMs.

Statistical Analysis

Statistical and descriptive analyses will be conducted using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). A univariate analysis will include descriptive means, SDs, 95% CIs, and the median and range for the time it took for participants to perform each component of the DFT. A t-test will be used to compare DFT performance between asymptomatic volunteers and patients with spinal pathologies. Pearson's correlation analysis will be used to investigate linear correlations between PROMs, MoCA, and DFT components.

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Make ups:

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Title: Impact of Severity of Hand Conditions on HAND-Q scores.
Sponsor: Dr. Steven Koehler
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Co-Advisor:
Location: BSB 3-7

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: 1299140
Dates: 10/09/2018
Title: Developing the HAND-Q: Phase 2 Field Test
Site: SUNY Downstate
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: During undergraduate college at Stony Brook University, I worked as a research assistant at the Suffolk County Mental Health Project (SCMHP). The SCMHP is a 27-year longitudinal study investigating the long-term trajectories of patients with serious psychiatric disorders (i.e. schizophrenia and bipolar disorder. My main roles there were to perform EEG experiments on research participants and process resulting data as well as collect biometric data through phlebotomy.
As a first-year medical student, I was involved in creating a poster with the Anne Kastor Brooklyn Free Clinic (BFC) and an abstract/poster with the SUNY Downstate Department of Orthopaedic Surgery. With the BFC, I worked with a team of medical students to extract/analyze data spanning the last 2 years about prescriptions given to clinic patients and create a poster which was presented at the Annual New York Student Run Free Clinic Regional Conference 2019.
With the Orthopaedic Department, I worked with the lab to extract/analyze data from the SPARCS database concerning postoperative courses of patients with multiple sclerosis whom underwent long segment (4+ level) fusion. A propensity score-matched analysis was done, and the abstract was submitted to the North American Spine Society.

Career goals: My goal is to become a surgeon. As a current first-year medical student, I am exploring various fields in surgery such as orthopedics. I am currently working with the SUNY Downstate Orthopaedic Lab to learn more about the field of Orthopedics. I look forward to learning more about surgery as I go through medical school.

Description: General Background:
Treatment of carpal tunnel syndrome (CTS) is often tailored based on the severity of the patient's condition [3]. While both conservative and surgical approaches are used to relieve symptoms, carpal tunnel release (CTR) procedures are seen less favorably for patients with advanced CTS, due to intrinsic medial nerve damage [4]. Usage of quantitative metrics, such as nerve function and atrophy of the abductor pollicis brevis (APB) muscle, have been useful in guiding clinicians, but may not always reflect the patient's desires [2]. Several studies have used patient-reported outcome measures (PROMs), demonstrating the value of surgery for patients with advanced CTS beyond symptom relief. It is important that the patients' own motivations be considered by the physician along with quantitative measures to help promote shared decision-making and increase patient satisfaction [1].

Various PROMs specific for upper extremity patients, including the Disabilities of the Arm Shoulder, and Hand (DASH), Carpal Tunnel Syndrome Assessment Questionnaire (CTSAQ), and the Boston Carpal Tunnel Questionnaire (BCTQ), have been used to gain insight into the patient's own perspective on their treatment and recovery [5-7]. While patient-reported outcomes have been compared for patients with varying severities of illness, currently established upper extremity PROMs are brief and generalized, and thus are limited in effectively capturing the impact of hand/upper extremity disease severity on patient outcomes. The recently developed Hand Questionnaire (HAND-Q), however, is more comprehensive, assessing various factors of the patient's experience such as: hand appearance satisfaction, hand functionality satisfaction, symptom severity, emotional dissatisfaction, sexual dissatisfaction, and overall treatment satisfaction. HAND-Q, which is uniquely generalizable to patients experiencing a wide variety of upper-extremity conditions, will be essential in capturing the various ways that patients of varying disease severities are affected by their condition [8].

Specific aims and research plan of your proposed project:

HAND-Q is administered to a large cohort of patients presenting with a wide array of upper-extremity conditions at non-specific points in their treatment. This study will be retrospective, looking into patients who already underwent upper-extremity surgery and completed the HAND-Q survey between September 2018 – August 2019.

For this summer, this proposed project aims to analyze and compare the results of the HAND-Q between patients with mild conditions and patients with moderate/severe conditions. My roles in this study are to help collect and analyze the data as well as draft the manuscript.

Methods and statistical analysis:

Patients presenting to a single, board-certified and hand/microsurgery fellowship-trained orthopaedic surgeon were given the option to complete the Hand Questionnaire (HAND-Q) while waiting to be seen. HAND-Q is a Patient Reported Outcome Measure (PROM) undergoing Phase II validation worldwide, which was developed using internationally accepted patient reported outcome and quality of life measurements. Consenting patients were prospectively and consecutively enrolled for participation in this international Phase II validation study from September 2018 to August 2019.

This study aims at reporting our institution's collected data. All consenting patients with valid responses to the following sections of the HAND-Q survey will be included: Hand Appearance Satisfaction, Hand Functionality Satisfaction, Symptom Severity, and Emotional Dissatisfaction. Patients under the age of 18 are excluded from this study. Patients are prompted to report the condition they were being seen for, with available choices including: Carpal Tunnel, Dupuytren's Contracture, Trigger Finger, Osteoarthritis, Rheumatoid Arthritis, Injury (Please Describe), Fracture (Please Describe), Other Hand Problem (Please Describe), and Not Sure. Patients are also asked to report their perceived severity of their condition. Severity scores were assigned as either 1 or 2, with mild conditions assigned as 1, and moderate and severe conditions assigned as 2.

Composite scores (CS) will be created for each individual section by collating scores from individual questions. The CS for each section will be calculated by summing all recorded patient answers, ranging from 1-4, for each question in the section, dividing this by the maximum score attainable for each section, and then multiplying by 100, which established a generalizable CS scale (0-100). In order to be included in the CS analysis, patients are required to have answered, at minimum, all but one question in a section. For CS analysis, patients will be separated into two groups based on their self-reported severity of their disease: one corresponding to patients with mild conditions, and one corresponding to patients with moderate or severe conditions. Interpretation of CS varies for each individual section: hand appearance satisfaction (range, 0 [very dissatisfied] to 100 [very satisfied]), hand functionality (range, 0 [not at all difficult] to 100 [extremely difficult]), symptom severity (range, 0 [none] to 100 [severe]), and emotional dissatisfaction (range, 0 [never] to 100 [always]). T-test analysis will be used to compare CS between mild and moderate/severe patients for each HAND-Q category. Following this analysis, individual questions within each HAND-Q category will be compared to evaluate the effects of disease severity on specific outcomes. Dichotomous variables will be compared with a Chi-Square test. All analyses will be performed using SPSS version 26 (IBM Corp., Armonk, NY, USA), and a p-value <0.05 will be set as the threshold for statistical significance.

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Make ups:

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Title: Multipolar pacing and ventricular arrhythmia
Sponsor: Dr. Adam Budzikowski
Division of Cardiovascular Medicine - EP section
Co-Advisor:
Location: SUNY downstate

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: Undergraduate research:
Worked with Dr. Benoit Lacroix at Stony Brook University. The goal of our study was to identify and study genes and proteins involved in agrobacterium gene transformation. I was responsible for preparing and purifying plasmid containing the gene of interest (via E.Coli and yeast culture). And studying the effect of different genes on the transformation process via gel electrophoresis / western blot.
Under Dr. Lacroix's guidance, we were able to identify dozen of potential proteins/genes involved in the regulation of agrobacterium nuclear import machinery.

Career goals: Prior to medical school, I worked as a medical assistant in a cardiologist's clinic. There, I was exposed to the complex anatomy and pathophysiology of the human heart. I was deeply fascinated by how this intricate organ, only as large as a fist, can have such a profound impact on a patient's quality of life. Knowing that I have only touched the tip of the iceberg, my desire of learning more about the human heart has grown even more.
By working with Dr. Budzikowsk, I hope I can learn more about the human heart. Not only the heart's anatomy/pathophysiology but also the patient perspective: how a heart condition can affect their day to day life. In addition, I seek to confirm my interest and passion for cardiology through this opportunity. And possibly set a goal of becoming a cardiologist in the future.

Description: Background:
Heart failure has been singled out as an epidemic that is a staggering clinical and public health problem that affects 5.8 million people in the US and 27 million worldwide. It is associated with significant mortality, morbidity, and healthcare expenditures, Hospitalizations for HF remain very frequent and readmission rates continue to rise.(1) Cardiac resynchronization therapy (CRT)is a well-established method of treatment for people with heart failure. (2). With the advent of multipolar pacing of the left ventricle (LV), research has demonstrated that it can outdo multipolar pacing. It is associated with lower mortality rates, hospitalizations, better hemodynamic response, and overall clinical outcomes (3-6). Although all these effects may be a result of reverse remodeling, reduction in the burden of ventricular arrhythmias (VA) may be contributing to this effect. At the very fundamental level, the presence of myocardial scar and viable tissue creates milieu for ventricular arrhythmia by allowing non-homogenous spread of depolarization hence creating a reentry (7-10). At the same time, one could construe that under correct circumstances

colliding wavefronts of depolarization resulting from CRT may also extinguish the reentry. Furthermore, creating more complex waveform associated with multipolar pacing may further contribute to a reduction of ventricular arrhythmias. Additionally, further reduction in intraventricular conduction delay may contribute to lowering ventricular arrhythmia burden. In our previous study with bipolar only pacing, we demonstrated a 24.3% reduction in ventricular burden most significantly pronounced in women (11).

Therefore, we seek to determine whether the multipolar LV pacing is associated with a further reduction of VA.

Methods:

We will be seeking access to Abbott remote device monitoring database Merlin. Merlin database contains several hundred thousand of patients with implantable Abbott devices that are undergoing remoted device monitoring. Detailed data is available for each patient including the model of the LV lead pacing factors and whether multipolar pacing is turned on as well as the burden of VA. We will select patients with implanted defibrillator connected with a quadripolar left ventricular lead. Comparison will be made between the patient with only bipolar pacing turned on as compared to patients with multipolar pacing turned on. Only patients with true bipolar and multipolar pacing will be enrolled since earlier reports have suggested that extended bipolar pacing (particularly LV electrode to device) may not result in effective cardiac resynchronization.

Classification of ventricular events:

All episodes will be reviewed by 2 independent electrophysiologists. If disagreement is present, the event will be classified by a consensus. Ventricular tachycardia was identified by a rate greater than 170 bpm, regularity of rate and the following: evidence of V-A dissociation and a local electrogram morphology different from baseline. If 1:1 A:V relationship was present, V-V changes had to drive A-A changes. Ventricular fibrillation was identified by rate greater than 240 bpm and disorganized ventricular electrograms. All ventricular events will be collected, which included those that were non-sustained or that required either ATP or shock therapy.

Statistical analysis

Arrhythmic burden will be measured as the sum of ventricular episodes. All data will be checked for normalcy. Wilcoxon signed rank test will be used to compare the differences in cumulative ventricular events. SPSS software will be used for statistical analysis. A p-value of <0.05 will be considered significant. The study protocol will be reviewed and we will seek approval by the SUNY Downstate Institutional Review Board. This proposal will be also submitted for approval and access to Merlin database to Abbott.

Sample size calculation:

The purpose of this study is to determine the reduction in ventricular burden in patients received quadripolar CRT, where the ventricular burden is measured by the number of ventricular events. We have used the standard sample size calculation formula (Power = 0.8; Confidence = 0.95) to determine the number of patients we will need to study to determine these effects. In this study, we are hoping to demonstrate a 30% decrease in ventricular event in patients received quadripolar CRT.

That is,

Post-CRT VA = Pre-CRT VA * 0.7

From our previous study, the average pre-CRT ventricular event per patient was 7.4 (11). Hence, a 30% decrease in post-CRT ventricular event will be 5.6. Applying these to the standard sample size calculation formula, the sample size is calculated to be 215 patients.

With a sample size of 215 patients, data collection should take about 4 weeks. The remainder of the time will be used for data analysis and draft of the manuscript.

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Make ups:

Tai Lai Li
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Title: Neonatal Compartment Syndrome: A Case Report and Systematic Review of the Literature
Sponsor: Dr. Steven Koehler
Department of Orthopaedic Surgery and Rehabilitation Medicine
Co-Advisor:
Location: Department of Orthopaedic Surgery and Rehabilitation Medicine

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: During my time as an undergraduate student at Stony Brook University, I was the lead undergraduate research assistant in my lab, where my responsibilities included training other undergraduate students and leading projects. Two of my most successful projects revolved around the complications of chromatin remodeling protein purification, specifically SWR, a remodeling complex that incorporates H2A.Z into the nucleosome at promoters. In my first project, I developed a sequential purification method that yields more active SWR by shortening the traditional method by 12 hours. This is an effective purification procedure for isolating active SWR which could be generalized to purification of other protein complexes in yeast. In my second project, I adapted a new method that my lab has developed, which probes for intranucleosomal dynamics, to map heterotypic H2A/H2A.Z and homotypic H2A.Z/H2A.Z nucleosomes on the genome. My work in these projects have now been published in two different papers. I graduated with honors in Biochemistry after completing a research thesis on my work in the development of the sequential protein purification method. Additionally, for my thesis, I received an award for outstanding academic and research accomplishments in cell biology.
Currently, I am part of the Continuous Quality Improvement team of the student-run Brooklyn Free Clinic where I investigated prescription trends at the free clinic over a period of two years through retrospective analysis. My team and I presented our findings at the annual New York Student Run Free Clinic Regional Conference. In addition, I am involved in the Orthopedics Surgery research department of SUNY Downstate where my latest project focused on the characterization of traumatic injuries and outcomes within spinal diseases. This was performed through a retrospective analysis of nationally available inpatient care databases. My work has been submitted to two conferences as abstracts with pending review.

Career goals: In the long term, my goal is to become a competent physician who is involved in research to provide care and elicit impact on both a personal and academic level. That is why I am interested in this Alumni Summer Research Fellowship because it will afford me the opportunity to gain invaluable experience in the intriguing and multifaceted field of Orthopedic Surgery as I continue to hone my focus as a future physician.
Through my experiences, I have fallen in love with the hands-on learning and critical thinking nature of research. These same qualities are what drive me towards a surgical field such as Orthopedics. I enjoy the procedural finesse that is intertwined with inventiveness to achieve a desirable outcome that can tremendously change a patient's quality of life. By participating in research over the summer with the Department of Orthopaedic Surgery and Rehabilitation Medicine, I hope to make significant

contributions in different research projects to advance the field incrementally and improve my own research aptitude to become a better physician in the future.

Description: Background:
A surgical emergency, neonatal compartment syndrome is a scarce yet limb-threatening condition that originates from an increased pressure within a closed musculofascial space with a resulting decrease in distal capillary perfusion (1, 2). It is associated with debilitating morbidity, mainly as a result of a missed or delayed therapeutic intervention (3). Identifying and recognizing this condition remains a challenge, as it closely resembles the clinical presentation of multiple other more prevalent diseases such as osteomyelitis, cellulitis, necrotizing fasciitis, and vascular injuries (9). Delay in the diagnosis or treatment of neonatal compartment syndrome results in devastating consequences, which include limb deformities in the short-term, and Volkmann's contracture with concomitant extrinsic muscle infarction, intrinsic motor paralysis, insensate extremity, and limb growth arrest later in life (3, 6). As a result, even when traditional laboratory tests and radiographs are unable to discern an identifiable pathology, maintaining a high index of suspicion for the condition ensures a timely recognition and mitigates the devastating sequelae. Albeit early suspicion and management do not always guarantee complete function restoration, urgent decompressive fasciotomy is warranted to optimize patient prognosis and mitigate the need for ancillary reconstructive surgeries (3-8).
Aims:
In this project, we aim to present the first case of neonatal compartment syndrome seen at SUNY Downstate Medical Center to highlight the importance of an early diagnosis. In this case, our patient was diagnosed with neonatal compartment syndrome and underwent emergent decompressive fasciotomy, subsequently restoring full upper extremity functions two months postoperatively. In addition, I will perform a systematic review of the literature on neonatal compartment syndrome to review the critical operative steps that must be undertaken to ensure better outcomes in newborns with neonatal compartment syndrome. I will assist in the quantitative collection and meta-analysis of available data to analyze appropriate surgical intervention and postoperative managements in a neonatal compartment syndrome patient. I will also take part in manuscript drafting of the case report and the systematic review.
Methods:
The systematic literature retrieval will be done with the utilization of literature databases such as Embase, PubMed, Cochrane, Google Scholar, and Web of Science, with specific search criteria of "Neonatal compartment syndrome", or "Volkmann contracture", or "Volkmann syndrome". All articles will be reviewed by two independent investigators for an inclusion criterion of full text available, English and French literature that discuss compartment syndrome in the neonatal setting. Exclusion criteria will include commentary articles, manuscripts reporting a compartment syndrome in locations other than the upper/lower extremities, and those published in languages other than English or French. Information that will be collected for characterization of the literature will include age and gender of the patient, the location of neonatal compartment syndrome, the timing for surgical intervention, as well as outcomes such as function, sensation, contractures, etc.
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Make ups:

Anna Lin
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Title: Comparing Relative Value Units Among Shoulder Arthroplasty, Hemiarthroplasty, and ORIF for Proximal Humerus Fractures in the Elderly: Which is Most Worth Your Time?
Sponsor: Dr. William Urban
Department of Orthopaedic Surgery
Co-Advisor:
Location: SUNY Downstate BSB 3-7

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: In 2016, I worked with Dr. Nicole Cameron of the Behavior Neuroscience Department at SUNY Binghamton to test the effects of estrogen on allocentric-learning and egocentric-learning strategies. Another experiment was testing the effects of ethanol on locomotion. I conducted these experiments on rats and used a T-maze to test their cognitive ability for both projects. I was in charge of obtaining the data and calculating the statistics by performing T-tests, ANOVA, and Fischer's post-hoc tests. Through this experience, I became familiar with how to conduct experiments and how to write abstracts.
Since the fall of last year, I have been working with the Orthopaedics Surgery Department research lab at SUNY Downstate. With the guidance of my peers, I helped to draft and edit 15 posters that were submitted to the American Academy of Orthopaedic Surgeons 2020 annual conference. I have also worked with a team to edit abstracts. In addition, I am currently learning how to code with the SPSS statistics software to perform statistical analyses. This experience allowed me to become familiar with the type of research that was done at the Orthopaedics lab and has guided me on coming up with research project ideas.
My goal for this summer is to work in the Orthopaedics lab to conduct my own research projects and produce results that will hopefully benefit the medical field of Orthopaedics Surgery. By being fully engaged in the Orthopaedics lab in the summer, I can become more knowledgeable and skilled in the different aspects of research. With this opportunity, I can create and conduct better research, and also help guide the new students next year who wish to join the Orthopaedics research lab.

Career goals: My career goal is to become a surgeon as I wish to perform procedures where I can be hands-on. After learning about the anatomy of the human body and dissecting in anatomy lab, my interest in the surgical field grew. I also like how surgeries can have a long-term impact on a patient's life. I experienced firsthand the impact surgeons had on patients' lives when my dad broke his ankle and underwent surgery. I was amazed by the level of skill these doctors had and the complexity of the procedures.
While the surgical field of medicine is very advanced and many lives are greatly improved after surgical procedures, research can help further improve the field. For this reason, I wish to conduct Orthopaedics research in order to understand how different factors, such as demographics, surgical preparations, prior illnesses, affect the outcomes of surgery. This research will guide me on how I approach surgeries in the future, and help me provide the best patient care for my future patients.

Description: General Background:

Proximal humerus fractures make up a large portion (~6%) of all fractures in America, and it is a common injury amongst the elderly population. Different surgical management options exist, such as arthroplasty (reverse [RSA] and total [TSA]), hemi-arthroplasty (HA), and open reduction and internal fixation (ORIF), with specific economic values (in terms of relative value unit per time [RVU]) assigned to each procedure. However, the economic values of these different procedures have not been studied and compared. Since there is a continuous rise in the number of people over the age of 65 years in the population, the management of proximal humerus fractures is important.

The Centers for Medicare and Medicaid Services use the resource-based relative value scale (RBRVS). The RBRVS utilizes RVUs to give relative economic value to different Current Procedural Terminology (CPT) codes. Each CPT code has a preset number of RVUs that are calculated based on physician work (wRVU), practice expense (peRVU), and malpractice (mRVU). The physician work component, which makes up the largest portion of the total RVUs, is based on relative level of time, skill, intensity, effort, and training to provide a specific service. The practice expense component is based on practice costs such as rent, equipment, supplies, and non-physician staff costs. The malpractice component, which normally makes up the smallest portion of the total RVUs, is based on professional liability expenses. Each of these components are also multiplied by a geographic practice cost index (GPCI), which adjusts the values based on differing costs across geographic areas. Finally, a conversion factor is used to convert RVUs to dollar amounts to determine compensation. While the RVU attempts to incorporate all relevant reimbursement factors, the literature has shown that there are still discrepancies in relative time and effort spent by the surgeons versus the amount of RVUs allocated. Knowledge of potential discrepancies can lead to a better understanding of the economic worth of a physician's time. In addition, orthopedists can optimize procedural cost-effectiveness in their practices.

Specific aims and research plan:

Due to the discrepancies within the RVU calculations, we sought to explore into the assigned RVUs between different surgical options for proximal humerus fractures. We aim to compare relative value parameters in RSA/TSA, HA, and ORIF for proximal humerus fractures in the elderly to determine which surgical procedure has higher proportional reimbursements. Specifically, we aim to compare mean operative times, average RVU per minute, reimbursement rate, revenue per day, and average annual revenue differences between the different surgical procedures.

Methods & Statistical Analysis:

This study will be retrospective, and we will use the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database to identify all patients older than 65 years old who underwent RSA/TSA, HA, and ORIF for proximal humerus fractures between 2008 and 2016. The Institutional Review Board approval will be obtained for unidentified data being used. RSA/TSA, HA and ORIF procedures will be identified based on their CPT codes (23472, 23470, and 23615, respectively). Proximal humerus fractures will be identified based on the International Classification of Disease, 9th revision, Clinical Modification (ICD-9-CM) codes.

Operative times for each patient will be obtained, as well as raw wRVU values and conversion factors from the CMS and American Medical Association website. Since wRVU and conversion factors differ based on the year, the respective wRVU and conversion factors will be used based on the patient's operation year. To convert RVUs to dollars, wRVUs will be multiplied by their respective conversion factors. wRVUs will be used instead of total RVUs to maintain focus on the physician work portion of the total RVU formula in addition to preventing the effects of practice expense and malpractice on the analysis. Univariate analysis using SPSS Statistics version 26 (IBM Corporation, Armonk, NY) will be used to compare operative time as well as relative value parameters, such as RVU per minute, reimbursement rate, revenue per case, revenue per day, and the average annualized cost difference across cohorts.

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Make ups: None

Ryan Marder
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Title: Revisiting AORN Guidelines for WALANT Hand Surgery
Sponsor: Dr. Steven Koehler
Department of Orthopaedic Surgery
Co-Advisor:
Location: BSB 3-7

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: 1177375-3
Dates: 5/31/2019
Title: Opioid Restrictions for Post-Operative Analgesic Use in De Quervain's Tenosynovitis, Carpal Tunnel Syndrome, and Trigger Finger Surgical Intervention
Site: SUNY Downstate
Type: IRB

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: During my junior year of college in 2016, I worked with faculty and doctoral students at the Korey Stringer Institute within the Department of Kinesiology at the University of Connecticut. I assisted with data collection, experimental procedures, video editing and laboratory preparation on the "Halo Wearable Technologies Study". With the help of a doctoral student, I constructed a research question concerning the relationship among heat illness, hydration status, and sleep which became the main focus of my Honors Scholar Thesis. During my senior year at UConn, I completed my Honors Scholar Thesis entitled, "Effects of Ad Libitum Versus Prescribed Rehydration on Sleep Measures Following Exercise-Induced Dehydration in Males". More specifically, I examined the difference in objective and subjective sleep outcomes between euhydrated and excessively dehydrated males who had exercised in a heat-stressed environment. Currently, as a first-year medical student at SUNY Downstate, I am actively involved in the Orthopedic Research Laboratory on campus. I recently worked on a poster presentation concerning the impact of multiple sclerosis on postoperative outcomes following anterior cervical discectomy and fusion surgery that will be submitted to the annual SUNY Downstate Research Day. I plan to continue my involvement with the Orthopedic Research Laboratory during the upcoming units and summer break.

Career goals: Due to my background in athletic training, I aspire to work in the sports medicine field as an orthopedic surgeon. Based on my experiences shadowing and collaborating with orthopedic surgeons and sports medicine physicians, I believe that becoming an orthopedic surgeon will satisfy my intellectual and clinical desires. I am attracted to the hands-on approach to the clinical evaluation of musculoskeletal pathologies and the potential to work with athletes and physically active patients. Additionally, I thoroughly enjoy learning about the anatomical structure and function of the musculoskeletal system and want to incorporate my passion for anatomy into my future career. As an orthopedic surgeon, I would like to work in a collegiate setting where I can make an immediate impact on the lives of competitive athletes through surgical and non-surgical interventions. Working in a collegiate setting would also provide me with the opportunity to educate and mentor students who are interested in pursuing a career in medicine. I am grateful for the close relationships that I formed with orthopedic surgeons and sports medicine physicians during college and for this reason, I feel compelled to support and help other aspiring future physicians work toward achieving their goals.

Description: General Background:

The Guideline for Care of the Patient Receiving Local Anesthesia was approved by The Association of Perioperative Nurses (AORN) in January 2015 [1]. Current guidelines suggest at least one perioperative nurse attends any operation performed under local anesthesia and recommends additional monitoring nurse(s) presence for patients at higher risk for local anesthetic systemic toxicity. Despite these recommendations, most facilities require two nurses to be present. Periodically assessing the utility of such guidelines within the context of contemporary hand surgical care is critical to optimize workflow efficiency.

Specific Aims and Research Plan:

The purpose of this study is to assess The 2015 AORN Guideline for Care of the Patient Receiving Local Anesthesia in patients undergoing hand/upper extremity surgery via Wide-Awake Local Anesthesia No Tourniquet (WALANT) technique. To assess the utility of such guidelines, patient demographics, hospital-related parameters, and complications will be examined for each surgical case.

My goal during the summer will be to assist with data retrieval and data analysis by retrospectively reviewing all hand/upper extremity WALANT technique surgeries completed from October 1st, 2017 to August 31st, 2019 by a single, board-certified orthopaedic surgeon in the same ambulatory surgery outpatient procedure room. After the data retrieval and analysis are completed and reviewed, I will help write the manuscript to report the results of our assessment of The 2015 AORN Guideline for Care of the Patient Receiving Local Anesthesia.

Methods and Statistical Analysis:

After obtaining institutional review board approval, consent will be obtained from consecutive patients undergoing hand/upper extremity surgery via Wide-Awake Local Anesthesia No Tourniquet (WALANT) technique. All cases performed at our single institution from October 1st, 2017 to August 31st, 2019 will be retrospectively reviewed. A single, board-certified and hand/microsurgery fellowship-trained orthopaedic surgeon performed all cases in the same ambulatory surgery outpatient procedure room with minor field sterility. All, if any, complications that arose while operating were documented. Patients will be excluded from the study if they had peripheral arterial disease, Raynaud's disease, or scleroderma. Demographic information, including sex, age, race, and BMI, will be collected from patients' electronic charts, and the Charlson Comorbidity Index (CCI) will be calculated for each patient. The CCI provides weighted scores based on mortality risk of different measured medical conditions, including age, myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accident/transient ischemic attack, dementia, chronic obstructive pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, diabetes mellitus, hemiplegia, moderate/severe chronic kidney disease, solid tumor, leukemia, lymphoma, and Acquired Immune Deficiency Syndrome (AIDS).

The minor field sterility procedure is as follows: One circulating nurse and one resident assisted the surgeon for each procedure. No surgical scrub technician was present for any operation. All surgeries were performed using the WALANT technique in a minor procedure room, outside the traditional operating room setting. The room structures were not washed in between procedures, and there was no defined control of airflow within the procedure room. No preoperative prophylactic antibiotics were given for any case performed in this room. Prior to surgery, patients were taken to the holding area and consent was obtained. The incision site was prepped with betadine and 1% buffered lidocaine with epinephrine injected per WALANT technique [2]. Patients then waited at least 27 minutes before the start of surgery for epinephrine to take effect. After this waiting period, patients were brought into the procedure room. Patients were dressed in their street clothes with their shoes on and did not wear a cap or gown. In the procedure room, the hand and forearm were prepped with Chloro-Prep, and draped with four surgical towels, with one towel around the elbow and three towels under the forearm. The surgeon used an alcohol-based surgical scrub and wore 1 set of surgical gloves for each procedure. A surgical mask was worn by the surgeon, in addition to scrubs and a cloth scrub cap. On a typical operating day at this minor procedure room, the surgeon obtains consent from and injects each patient within the first 30 minutes. Patients undergoing bony procedures are injected last to ensure full anesthetization. During this time frame, the circulating nurse sets up the minor procedure room. After the last injection, the first patient is ready to be operated on. Patients are operated on in the order that they received an injection from the surgeon. There is approximately a five-minute turnover time between cases, during which the room is broken down, the existing surgical instrument tray is replaced with a sterile one, and the sterile instruments are laid out.

Except for those undergoing fracture and tendon repairs, patients were instructed to remove their own dressing after five days, at which point normal hand hygiene with soap and water could resume. Upon discharge, patients were provided with return instructions, listing signs of postoperative infection to be vigilant of. Otherwise, patients were instructed to follow up with their surgeon two weeks after their operation, except for patients with active, non-surgical infections or tendon repairs, who were instructed to return to the clinic one week after surgery. No postoperative prophylactic antibiotics were prescribed for any case, and patients were instructed to use over-the-counter non-opioid analgesics as needed for pain control. At the follow-up

appointment, the surgeon searched for potential postoperative infections and documented any signs of superficial or deep infection. Patients were directly contacted at these specified time points, and their medical records will be further surveyed at the time of data collection for any additional complications regarding their hand surgery.

Patient demographics, hospital-related parameters, and complications will be calculated as mean with 95% confidence intervals or percentages. All analyses will be performed in SPSS version 26.

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Make ups:

Joel Mathew
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Phone: (516) 589-1466
Title: Investigating Brain Cytoplasmic RNA Targeted by SLE Autoantibodies
Sponsor: Dr. Henri Tiedge
Physiology and Pharmacology, Neurology
Co-Advisor: Ginzler, Ellen (MD, MPH), Department of Medicine
Location: SUNY Downstate Health Sciences University BSB
450 Clarkson Avenue, Brooklyn, NY 11203

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: [268627-15]
Dates: Approval Date June 27, 2019
Title: Collection of Blood Samples from People with Systemic Lupus Erythematosus (SLE)
Site: SUNY Downstate HSU
Type: IACUC

Additional Study: [12-10346]
Dates: Date of Initial Protocol Approval (3-year Start Date): 12/12/2018
Title: Use of neuronal cultures to study RNA transport and translation
Site: SUNY Downstate HSU

When/Where: Not applicable

Research Experience: I volunteered as a research intern for the Institute for Bladder and Prostate Research (IBPR) under the mentorship of Dr. Jerry Blaivas, a urologist affiliated with Mount-Sinai. The IBPR provides for patients with a variety of genitourinary disorders such as urinary incontinence or overactive bladder. My primary responsibilities involved compiling clinical data concerning patient symptoms and outcomes that would be used for retrospective studies. The project that I contributed to involved assessing the efficacy of utilizing bladder diaries, which are patient-driven recordings of their urinary habits such as frequency of voiding, time of voiding, volume that was voided, etc. The goal of the bladder diaries was to provide the clinician insight into specific patient phenotypes to better diagnose and treat the voiding dysfunction. I had the fortunate opportunity to contribute to a publication in the Journal of Urology regarding patient outcomes and complications after mesh sling operations (a procedure that is performed to resolve urinary incontinence).
I was also a member of a lab group led by Dr. Alexander Greer of the Brooklyn College Department of Chemistry. Dr. Greer's work focused on the application of organic synthesis to produce photosensitive compounds for the purpose of photodynamic therapy (PDT). Photosensitizers are molecules that are able to capture energy from light (due to the presence of their large conjugated π systems) and transfer this energy to molecules such as oxygen or oxygen containing compounds to generate reactive oxygen species (ROS). In the context of PDT, photosensitizers are applied near target tissues such as neoplastic or infected cells and then irradiated with light so the produced ROS can destroy these cells. I assisted in the synthesis of fluorinated alkyl chain pterin, a photosensitizer with unique therapeutic potential due to the fluorine chain attached. Working alongside a PhD student researcher, I helped in the purification and analysis of our synthesized product. Analysis was usually done via NMR or a form of chromatography such as HPLC. Additionally, I have co-authored with Dr. Greer a highlight paper for a study regarding the use of cyanine derivatives for the photorelease of amine compounds utilizing near-infrared light. Similar to photosensitization, photorelease involves harnessing electromagnetic radiation, but in this case the energy is used to cleave and release biological compounds at their target destinations instead of producing ROS.
My previous experiences with the IBPR and Dr. Greer's lab provided me with unique skills involved with clinical research and basic science, respectively. I am looking forward to working on this translational project concerning SLE and regulatory RNAs to experience how these two worlds of academia work together.

Career goals: It is difficult to succinctly express my career goals as I am still in the process of determining what specialty I would like to pursue. Generally, I want to be a practicing clinician while simultaneously contributing to medical academia, whether it be through teaching or leading in research. I hope that my experiences in my medical Foundations years will contribute towards selecting a field that I am passionate about. That being said, this translational research project will be invaluable to my medical education regardless of the specialty I go into. I became involved with rheumatology research because of a family history of rheumatoid arthritis. I supplemented my knowledge of autoimmune disorders by engaging the instructors leading our rheumatology subunit, who eventually introduced me to the work of Dr. Tiedge. I am grateful for the support that I have received from faculty and want to take advantage of the great opportunities that Downstate has to offer. As a nascent medical professional, I hope that my curiosity will continue to guide me towards great learning opportunities and facilitate the direction I would like to take my medical career.

Description: General Background:
I have been granted the wonderful opportunity to join Drs. Tiedge and Ginzler in their research project investigating Systemic Lupus Erythematosus (SLE) autoantibodies that target brain cytoplasmic (BC) RNAs. BC RNAs are regulatory RNAs that regulate the production of proteins in neuronal cells. These proteins are involved with synaptic function; thus, BC RNAs are crucial in the proper synaptic transmission of neuronal signals. A key component for the regulatory function of BC RNAs is specific delivery to their dendritic targets, which is facilitated by the binding of the transport factor heterogeneous nuclear ribonucleoprotein A2 (hnRNP A2) to a specific 5' stem loop domain [1]. It has been shown that loss of regulatory RNA function in proteins results in neuronal hyperexcitability, which phenotypically presents with cognitive dysfunction and epilepsy [2].
Specific Aims and Research Plan:
The research project that I will be participating in is a continuation of recent efforts by Dr. Tiedge and his colleagues, where they have established that SLE autoantibodies are able to also target and bind the 5' stem loop domains of BC RNA [3]. The foundation of this study is the hypothesis that competition between hnRNP A2 and SLE auto-abs against BC RNAs, also referred to as SLE anti-BC abs, for the 5' stem loop binding site may possibly be a source of disruption for proper BC RNA function. The influence of SLE auto-abs on BC RNA activity is presumed to be a potential explanation for the neurological manifestations of Neuropsychiatric SLE, which involve cognitive dysfunction and epilepsy.
As an extension of previous work, this project will investigate groups of high-reactive SLE anti-BC abs that weren't studied in the previous experiments. The specific aims of investigating SLE anti-BC abs are to (1) further understand the molecular interactions between SLE anti-BC abs and hnRNP A2 with the BC RNA stem loop binding sites; (2) elucidate how the competition between SLE anti-BC abs and hnRNP A2 (for BC RNA binding) affects the ability of BC RNAs to effectively migrate to their dendritic targets; and (3) discern if this improper migration of BC RNA contributes to phenotypic manifestations of epilepsy and/or cognitive dysfunction seen in Neuropsychiatric SLE.
Methods and Statistical Analysis:
To further understand the molecular interactions of the SLE anti-BC abs in aim 1, we will be studying the functional analogs of rodent BC1 RNA and primate BC200 RNA. As established from previous work [2], the 5' stem loop of BC RNA features GA structural motifs formed by non-Watson-Crick (noncanonical) pairing, and it is these motifs that are recognized by the SLE anti-BC abs and hnRNP A2. To dissect the interaction at this 5' domain, we will convert the noncanonical pairs into standard Watson-Crick pairs, then examine how this change influences the binding of SLE anti-BC abs and hnRNP A2. Additionally, EMSA (Electrophoretic Mobility Shift Assay) competition analysis will be conducted to see if SLE anti-BC abs displace hnRNP A2. For this analysis, we will first ensure that BC1 RNA and BC200 RNA are capable of binding to SLE anti-BC abs (purified from sera of SLE patients with histories of seizures) and hnRNP A2. The degree of binding will be assessed via EMSA and compared to control IgGs taken from the serum of healthy subjects and patients with rheumatoid arthritis and multiple sclerosis. Previous data has shown that the autoantibodies against BC RNAs were specific to SLE patients, where the other control IgGs did not present binding to the BC RNAs [3]. In an additional experiment, BC1 RNAs or BC200 RNAs will be incubated with hnRNP A2. After 30 minutes of incubation the SLC anti-BC abs will be added and then incubated for another 30 minutes to see if the abs displaced the hnRNP A2 – this will be observed by changes in the EMSA. Previous data provided evidence that the SLE anti-BC abs displaced the hnRNP A2 after the incubation periods [3].

For aim 2, we will examine the transport and localization of BC RNAs to their targets utilizing neurons in culture and in vivo. Building from the study of antibody interactions in aim 1, this aim seeks to assess how the autoantibody prevents BC RNA from implementing its function. Previous data supports our hypothesis that BC RNA function is impeded because of its inability to be migrate to the specific dendritic targets [3]. To further test this, we will preincubate SLE anti-BC abs and other control IgGs with

radiolabeled BC RNAs and then co-inject them into sympathetic neurons in culture, a method that has been established previously [2, 3, 4]. Similarly, neuronal cultures will be incubated with bath-applied SLE anti-BC abs and healthy IgGs, where the extent of BC RNA migration in the culture will be observed in phase-contrast photomicrograph. The signal intensities associated with the different applications of IgGs will be compared. Previous application of this method utilized a one-way ANOVA, Dunnett's post-hoc analysis of results and established changes to BC RNA migration (in the presence of the SLE anti-BC abs) as significant [3]. For the in vivo studies, mouse models will be treated with lipopolysaccharide (LPS) to permeabilize the blood-brain barrier (BBB) and then injected with purified SLE anti-BC IgGs intravenously as done in prior work [3]. Signal intensities within parts of the hippocampus of the mouse subjects will then be assessed via photomicrographs to quantify levels of activity.

As part of aim 3, we will examine mouse models (treated with IV SLE anti-BC abs as described in aim 2) and their susceptibility to sound-induced audiogenic seizures (AGS). This study will provide insight into our hypothesis that disruption to BC RNA migration is associated with neurological manifestations such as seizures or cognitive dysfunction. Like the previous experiment [3], Spearman's rank-order correlation analysis will be used to quantify the link between SLE anti-BC reactivity and occurrence of neurological phenotypes. There is also a clinical component to aim 3 that consists of a longitudinal study with lupus patients from the Division of Rheumatology at the SUNY Downstate HSU. Blood will be collected from these patients every four months and any time they visit the clinic for symptomatic concerns. Patient sera will be purified and then undergo EMSA analysis to establish anti-BC reactivity. Based on current data, we expect 104 patient enrollees (out of 400) to meet the criteria of having high baseline anti-BC reactivity. The goal of this longitudinal study is to assess the hypothesis that increased SLE anti-BC antibody titers will correlate with NPSLE symptom flares, and that lower titer levels will correspond to clinical latency. Thus, SLE anti-BC ab titers may be able to be used as prognostic indicators. Statistical work will be conducted in collaboration with the Scientific/Academic Computing Center of SUNY Downstate HSU.

This study will contribute to the understanding of the enigmatic etiologies behind Neuropsychiatric SLE symptoms. To our knowledge, this is the first example of SLE autoantibodies against regulatory RNAs such as BC RNA.

References:

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Make ups: Not applicable as of 03/11/20.

Electra Nassis
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Title: Early life exposure to anesthetics and seizure development later in life
Sponsor: Dr. Ira Kass
Anesthesiology
Co-Advisor: Dela Pena, Margarita - Anesthesiology, University Hospital
Location: SUNY Downstate, 6-90B

Fellowship period: Yes
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: I have had two research experiences, both of which were during my undergraduate studies at CUNY - City College (CCNY).
The first research project I worked on was in cell biology through the biochemistry department at CCNY. The title of my project was: The Induction of the Cyclin D1 (CD1) Promoter by UVB Irradiation In Sodium-Arsenite Treated Human Keratinocytes. The goal of this project was to identify transcriptional elements within the CD1 promoter that mediate the inductive effects of arsenic and UVB on CD1 expression. I transfected immortalized cells in culture with a pGL2 vector (synthesized plasmid) containing CD1 promoter deletion mutants. The cells were either treated with 400-nM sodium-arsenite, subject to UVB radiation, or untreated. After 72 hours, cells were collected for the luciferase reporter assay which indicated the induction effect of each deletion mutant. For this study, I received training the CCNY- Memorial Sloan Kettering Cancer Center Partnership for Undergraduate Research and presented at the 2015 Annual Biomedical Research Conference for Minority Students, where I was awarded best poster presentation in cancer biology.
The second research project I worked on was in neural engineering through the biomedical engineering department at CCNY in collaboration with my professor's biotech company, Soterix Medical Inc. The title of my project was: Tolerability of an Adaptive-tDCS up to 4 mA using subject assessment and machine-learning to optimize dose. The goal of this project was to take an already FDA approved 2mA tDCS (transcranial direct current stimulation) device and test human subjects' tolerance to a higher current 4mA. tDCS is a non-invasive, painless brain stimulation treatment that uses direct electrical currents to stimulate specific parts of the brain. tDCS is used to treat depression in patients with neurological disorders and previous computer modeling has shown that an increased current from 2mA to 4mA would offer greater clinical benefits to patients. For this study, I tested the new 4mA tDCS device algorithm for quality assurance, helped draft the IRB, consent forms, and study materials, and conducted the human trials. I presented a poster at the 2017 NYC Neuromodulation Conference, and have had an abstract and two papers published on this since then.

Career goals: My career goals include applying to and being accepted into an anesthesiology residency program upon completion of medical school. I aspire to become board certified in anesthesiology and complete a fellowship afterward. In my two gap years before matriculating to medical school, I worked in Central Office for Quality & Safety at NYC Health + Hospitals, and as a future anesthesiology resident and physician I hope to again involve myself in this work but as a physician at the front-line of healthcare.

I want to promote best practices for anesthesia and ensure safety for patients in preoperative care, in the operating room, and postoperative care.

Description: -General background-
Despite substantial research in the past fifteen years, the effect of early-life (birth to three years of age) general anesthesia in producing negative long term changes in the human brain is still unclear due to two major reasons. (A) There are three types of anesthetics categorized by the receptors that they predominantly target, the GABAA, the NMDA and the α 2- adrenergic receptors (8). In animal studies, approaches to identifying the long term effects of early-life anesthesia focused on cognition-related behaviors and were not directly associated with the anesthetic's target receptor (3). (B) In human studies, outcome measures used to identifying negative neurological changes were based on those used in animal studies (1,8,11). These results produced strong evidence for cognition-related behavior changes in animals (2, 5, 6, 9), but no convincing evidence for such changes in humans. Therefore, there is a critical need to identify specific long term changes that are directly mediated by the receptor that an anesthetic predominately targets, and then apply that understanding to design an outcome measure for human studies. With such an understanding, one would be able to accurately identify neurological changes/disease vulnerability that may arise as a result of early-life anesthetic exposure.

To address this critical need, our laboratory has previously used mice as a model system to study the long term functional changes in the brain directly mediated by the GABAA receptor that the anesthetic sevoflurane predominately targets. The laboratory identified that early-life exposure to sevoflurane is associated with increased susceptibility to seizure later in life. In this protocol, the laboratory is applying seizure prevalence as an outcome measure to a retrospective human study to establish an association between exposure to GABAA receptor-targeted anesthetic in young children and increased seizure vulnerability later in life. Long term, this work will provide the option for pediatric anesthesiologists to choose components of anesthetic cocktails to minimize adverse side-effects, together with the ability to ameliorate unavoidable side-effects with therapeutic drugs.
-Specific aims and research plan for your proposed project-
This research project aims to gain a comprehensive understanding of neurological change/disease vulnerability associated with each type of anesthetic in order. With this understanding, knowledge will be available to help anesthesiologists develop a safe treatment approach when exposing their patients to early-life general anesthesia. The laboratory's long term goal is to identify an association between exposure to GABA receptor-targeted anesthetics in young children (birth to three years of age) and an increased risk of seizure disorder later on in life (greater than three years and up to 20 years of age). This research project will be one of the steps in a series of research projects toward the attainment of our long-term goal.
This is a feasibility pilot study using Downstate Medical Center to generate preliminary data for a future multi-center study. This study is designed to test the following hypothesis: There is an association between exposure to GABA receptor-targeted anesthetics in young children (birth to three years of age) and the development of a seizure disorder later in life (greater than three years and up to 20 years of age).
-Methods and statistical analysis-
We propose to conduct a retrospective case-control study to identify an association between young children (birth to three years of age) exposed to anesthetic that is predominately GABAA receptor-targeted (e.g., sevoflurane and propofol) and increased risk of seizure disorder later in life (greater than three years and up to 20 years of age).
The study population will come from:
Review charts from patients that came to Downstate Medical Center requiring an MRI in the past 10 years. Date range from which the data will be collected Jan 2009-Dec 2019. The range of age for these patients is greater than three up to 20 years of age.
From the MRI chart information, include subjects that were diagnosed with seizure/epilepsy disorder and had no anesthetic exposure as a young child (between birth up to three years of age).

From the MRI chart information, include patients that were diagnosed with seizure activities/disorder and had anesthetic exposure as a young child (between birth up to three years of age).
From the MRI chart information, include patients that were not diagnosed with seizure and had no anesthetic exposure as a young child (between birth up to three years of age).
From the MRI chart information, include patients that were not diagnosed with seizure and had anesthetic exposure from birth to 3 years (between birth up to three years of age).
Exclude patients with unknown history of medical treatment before the age of three.
Our sample size: is ~1,200 patients.

Method for Screening for Eligibility: Patients who had undergone MRI will be used as a screening tool to capture the group of patients that were diagnosed with seizure. The rationale is that all patients who were diagnosed with seizure disorder would require an MRI scan.

Inclusion of Vulnerable Populations: Data on children and minorities are included; however, since the study involves a retrospective medical records review, there are no interactions with these individuals.
Statistical Considerations: We will analyze our preliminary data according to the inclusion/exclusion criteria with the following two-way frequency table:

	General anesthesia 0 to 3 years (+)	General anesthesia 0 to 3 years (-)
Seizure >3 and <20 (+)		
Seizure >3 and <20 (-)		

We will generate an odds ratio number based on the table. The odds ratio number will indicate the feasibility of the research.
Procedures and Data Collection: N/A, this is a feasibility retrospective study using data from patient's charts
Duration of Study: We anticipate to spend 4 months on this feasibility study. The first two months will be dedicated to gathering patient information from the charts. The remaining two months will be to analyze the data.
References to prior publications:
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Make ups: N/A

Andrew Porrazzo
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Title: Association of Tobacco Use and Psychotic Symptoms in Patients with Bipolar Disorder
Sponsor: Dr. Michele Pato
Psychaitry
Co-Advisor:
Location: SUNY Downstate Institute of Genomic Health

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: I was a research assistant at the University of Pennsylvania Rhinology Lab. I maintained cell cultures of epithelial tissue extracted from patients with chronic rhino-sinusitis. I was also responsible for embedding the epithelial tissue in paraffin wax, sectioned the tissue using a microtome and mounted tissues on slides to be stained with antibody. I used immunofluorescence staining technique on slides. Used a confocal microscope to analyze the TR38 bitter taste receptor and analyzed pictures taken from a confocal microscope to choose optimal antibodies to stain the desired protein.
Other research experience I have is working in the Ptasisnska Lab at the University of Notre Dame where I conducted projects related to atmospheric pressure plasmas for biomedical applications. I also gained experience using different laboratory techniques, such as pipetting, statistical analysis and gel electrophoreses, to understand the effects that plasma radiation has on DNA and more specifically its implication for a cancer treatment. Some of my most relevant research experience come from working in the Marital Therapy & Research Clinic. I used various statistical analysis techniques to compose a meta-analysis of the effects of relationship functioning and psychopathology. I also gained experience in observational coding of videos and statistical analysis in order to develop a new assessment for marital satisfaction.

Career goals: In the future I plan to be a practicing physician. While I am not exactly sure what I would like to specialize in, I am very interested in psychiatry, neurology, and internal medicine. After graduation I want to work with the most vulnerable patient population. I have always been a deeply religious Christian. In the Bible, Jesus states that "whatever you did for one of the least of these brothers and sisters of mine, you did for me." This quote has always inspired me to try and work with the most vulnerable populations and in the areas that need my help the most. In society today, some of the most vulnerable people in our population are people with mental illnesses. Therefore this study will give me better understanding into a patient population I care deeply about and a patient population I may work with in the future. I also believe that this summer research opportunity will give me greater insight into the field of psychiatry and give me great experience seeing psychiatric interviews of patients with Bipolar Disorder and Schizophrenia.

Description: Bipolar Disorder is a severe and chronic psychiatric disorder with a prevalence of 1-3% worldwide. Bipolar Disorder is characterized by periods of depression and abnormally elevated moods states termed mania. The transition between mania and

depression is characterized by measurable shifts in mood, energy, activity, and concentration, often resulting in incapacitation. Individuals with severe mental illnesses, like Bipolar disorder, may die up to 25 years earlier than the general population, and the cause of this early death is often related to medical illness that can be attributed to substance use disorders and not specifically their psychiatric condition (Hartz et al. 2014).

The particular "substance" we will study in this study is tobacco. According to the 2018 National Survey on Drug Use and Health identified adults with serious mental illness (based on 14 items related to psychological distress and disability) and found that 37.2% of adults with severe mental illness are current smokers compared to 16.3% of adults without mental illness. In the general population, according to the Center for Disease Control, increases the risk of the development of coronary heart disease and the likelihood of a stroke both by 2 to 4 times, respectively. The effects of smoking on human health are most evident in the development of lung cancer. Smoking increases the chance of developing lung cancer by 25 times in men and 25.7 times in women. Overall, smoking causes diminished health, increased absenteeism from work, and increased health care utilization and cost. While efforts to curb smoking among the general population have been met with much success, efforts to decrease smoking rates among some of the most vulnerable people in the population, specifically those with mental illness have failed (Hartz et al. 2014). In addition to tobacco use in general, there are gender differences that may be modulating factors in the increased tobacco use among patients with Bipolar Disorder (Filia et al. 2014).

Prior studies have shown conflicting results regarding the impact of smoking on psychotic behaviors, if they are present, in Bipolar disorder (Corvin et al. 2001 and Kreinen et al. 2012). Thus this proposed analysis will add meaningfully to the literature not only because it can compare those with BID who have psychosis to those without psychosis, but because the sample will be larger than many of the previous studies that have been published so will have more power. More specifically this study will utilize a sample size of approximately 1000 subjects to increase the power. Secondarily, this research will focus on covariates in the development of tobacco dependence in Bipolar Disorder, such as gender, which have yet to be examined in a population sample of this size. The results of this study will be important to advise physicians whose patients' chronic tobacco use may be exacerbating their manic symptoms. It will be important to understand comorbidities that may be associated with psychosis during manic states, so that physicians are aware that many of their patients who have Bipolar Disorder may also have other Substance Use Disorders, particularly Tobacco Use Disorder. They will also be aware of how smoking may be affecting genders differently in patients with Bipolar Disorder. This may lead to greater mood stabilization and better overall health outcomes for their patients.

Study Aims:

Aim 1:

To examine the differences in Bipolar Disorder symptoms in subjects with and without tobacco use, across variable severity of use.

Aim 2:

To examine any difference in tobacco, use among subjects with Bipolar Disorder with and without psychosis.

Aim 3:

To examine the differences in smoking severity between the male and female subjects, as it relates to Bipolar Disorder and the presence or absence of psychotic symptoms.

Methods and Statistical analysis:

The analysis will involve getting familiarity with the administration of the DIPAD and screening tools used in the collection of phenotypic data on subjects with and without Bipolar Disorder (BID) and with and without psychosis in the active genomic psychiatry cohort studies (GPC) done in the IGH. We will combine this current ongoing data collection with the use of the existing GPC data on BID with and without psychosis. To date the GPC group has approximately 400 cases with BID with psychosis and 600 BID without psychosis that we can use in our analysis. The data on current medical conditions and tobacco use, using the CAGE criteria for tobacco use, come from the GPC screening tool and the DIPAD (Hartz et al. 2014), which has been used for the past 15+ years with well-established reliability and validity. (Pato M, et al 2013)

In addition, to the analysis of the data for medical and psychiatric symptoms, we can also analyze the database for ethnicity: African Ancestry (AA), Latino Ancestry (LA) and European-Caucasian Ancestry (EA). Analysis of this data will include: t-test, ANOVA's, chi-square, and linear regression, depending on whether the variable are ordinal or continuous. For instance, comparing smoking severity (continuous variable) in men and woman with BID, with and without psychosis will require a t-test. But, a chi-squared analysis will be used to analyze differences in symptom presence or absence of patients with BID with and without tobacco use.

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Make ups:

Ed Throckmorton

From: Stanley Friedman
Sent: Friday, May 8, 2020 3:23 PM
To: Ed Throckmorton
Cc: Mark Stewart
Subject: Fwd: Alumni Summer Research Fellowship

Ed,
Can you add this e-mail to the document containing the student applications?

Regards,

Stan
Outlook for iOS

From: Andrew Porrazzo <Andrew.Porrazzo@downstate.edu>
Sent: Friday, May 8, 2020 2:56:56 PM
To: Stanley Friedman <sFriedman@downstate.edu>
Cc: Michele Pato <Michele.Pato@downstate.edu>
Subject: Alumni Summer Research Fellowship

Hello Dr. Friedman,

My name is Andrew Porrazzo and am a first year medical student applied for the Alumni Summer Research Fellowship program earlier this year in March. Much has changed since I have submitted my application due to the situation surrounding COVID-19, and I have been in contact with Dr. Michele Pato, who is my faculty sponsor, in order to accommodate the strange situation at hand. We have discussed the ability for all of my research to be done remotely. The only thing that I may not be able to do remotely, which we set as one of our aims of this summer, is gain experience interviewing some subjects with the DIPAD; however, Dr. Pato has stated that I may even be able to accomplish this by sitting in on some sessions through FaceTime. I just wanted to update my application and let the review board know that Dr. Pato and I have been considering the unique situation posed to us by the coronavirus. We believe that all of our aims can still be met this summer despite the situation and wanted to supply an update incase this was a consideration taken place during the allocation of the research fellowship awards.

Thank you for your time and consideration,

Andrew Porrazzo

Jacob Robinson
Email: jacob.robinson@downstate.edu
Phone: 3159753460
Title: Excitability of Entorhinal Cortex and the Hippocampus Circuit in a Sphingomyelin Deficiency Mouse Model
Sponsor: Dr. Herman Moreno
Neurology, Physiology, Pharmacology
Co-Advisor:
Location: Laboratory of Dr. Herman Moreno at BSB 6-16. I will have access to a setup for electrophysiology that consists of: Warner amplifier, DP314 4 Channels, axon digidata 1550B plus perfusion system, chambers and temperature control equipment.

Fellowship period: Yes
Involve any? Yes

Review Board Type: IACUC
Study#: 15-10475
Dates: 9/17/2018-9/17/2021
Title: Interdisciplinary Research to Understand the vascular contributions to Alzheimer's Disease
Site: Moreno Lab
Type: IBC

Additional Study: 18-102
Dates: 9/17/2018-9/17/2021
Title: Interdisciplinary Research to Understand the vascular contributions to Alzheimer's Disease
Site: Moreno Lab

When/Where:

Research Experience: My research background is in neuroscience. I completed an undergraduate degree in Neuroscience, which gave me foundational principles and a framework to build upon. It also included laboratory coursework in chemistry (inorganic and organic), molecular and cellular biology, anatomy, physiology, and neuroscience. These exposed me to the methods and procedures of laboratory work. Working as a teaching assistant in the organic chemistry laboratory helped me to become comfortable with issues regarding lab safety and also with explaining lab procedures, results, and reasoning to others.
The most important and relevant part of my research experience was working for about 1.5 years in a basic science research lab. I worked with Dr. Jeffrey Edwards at BYU where I attended. I was part of his electrophysiology group. I performed in vitro field electrophysiology recording in the hippocampus, amygdala, and prefrontal cortex of rat and mouse brain slices. The studies I worked on involved measuring how long-term potentiation (LTP), used as a measure of synaptic plasticity, changed in response to different variables. One study examined the use of prophylactic medical intervention as a protective mechanism against PTSD, and the other examined the effect of ketone bodies on LTP in the hippocampus. Following baseline recording, LTP was induced with high-frequency stimulation via theta burst and 90 minutes of post-stimulation activity was recorded. I analyzed the data I recorded during experiments to assess the degree of LTP in the slice. I presented the preliminary findings of our study on ketones in the brain at the Utah Conference for Undergraduate Research 2019 as a 15-minute oral presentation.

Career goals: I plan to pursue a career in academic neurological surgery. I have always been interested in neuroscience and want to continue to study it throughout my life. There is so much more to be discovered about the brain and the diseases that affect it. I am not sure yet of the exact direction of research I will pursue during my career, so I plan to explore this during medical school, incorporating both basic science and clinical research projects. Neurological surgery is a research-heavy field, and I expect to be able to find opportunities to incorporate research into my career. I would like to work in an academic setting in which I can care for patients, carry out research, and possibly be involved with medical education.

Description: General background:
The burden of late onset Alzheimer’s dementia (LOAD) and its antecedents is increasing without known prevention or cure, and vascular and metabolic factors are important contributors. According to the Alzheimer’s Association, 11% of people aged 65 years

and older, and a third of people 85 years and older have LOAD (1). LOAD cases in persons 65 years and older are expected to increase by 40% by 2025 (1). The predominating causal model in Alzheimer's disease (AD) research is based on the amyloid hypothesis (2), which posits that amyloid β (Aβ) deposition in the brain causes synaptic dysfunction (3) resulting in memory deficits and progression to mild cognitive impairment (MCI) and dementia (4). Tau is also an important AD pathology feature, biomarker, and treatment target (5,6,7). In addition, cerebrovascular disease (CVD) is thought to play a role in the manifestation of dementia in approximately half of cases of AD (1), probably by decreasing the threshold of AD neuropathology needed to manifest dementia (8). The interaction between CVD and AD seems to be complex and may share mechanisms (9,10). In order to elucidate these mechanisms linking AD and CVD the National Institute on Aging (NIA) established the consortium called "Molecular Mechanisms for the Vascular Etiology of Alzheimer's disease (M2OVE-AD)", to which my advisor's main project belongs. The AD Metabolomics Consortium (ADMC), as part of M²OVE-AD, is building a comprehensive metabolomics database and a metabolomics Atlas for AD research. Metabolomic signatures serve as a readout capturing net influences of genetic/epigenetic variation, protein expression, gut microbiome and environmental and lifestyle differences. Metabolic signatures can inform about disease mechanisms, progression, heterogeneity, and treatment response. Major findings of the ADMC (11) highlight common pathways between diabetes, CVD, and AD that include altered phospholipid and sphingomyelin metabolism related to changes in membrane structure and function (12). My research project will use the discovery approaches used by the ADMC to examine a piece of the metabolic contribution to AD in mouse models: specifically, the role of sphingomyelin (SM). Decreases in SM have been associated with AD (13). For my research project, I would like to study the effect of SM deficiency on the entorhinal cortex (EC) and the hippocampal circuit. I will concentrate on the EC and hippocampus because they are early sites of AD pathology and dysfunction. This has been studied in my advisor's lab, not only in AD models, but also in AD risk factor models such as APOE4 mice (14,15).

Specific aims and research plan:

My project will use in vitro electrophysiology to explore the effect of SM deficiency on EC-hippocampus function. This will take place in a mouse model that has SM levels similar to those found in human AD. We expect to find abnormalities mimicking what is seen in APP/PS1 mice, a widely used mouse model for AD. Data from my advisor's laboratory (not yet published) show that in an AD risk factor mouse model (ABCA7 knockout), synaptic deficits were rescued by bath application of SM and not by phosphatidylcholine (PC). We hypothesize that our SM deficient mouse model (SMS2 knockout, see below) will have synaptic and circuit abnormalities which will be modified specifically by SM. My research will therefore focus on the following specific aim: to evaluate EC-hippocampus synaptic transmission and circuit properties in a mouse modeling SM deficiency and the effects of SM supplementation.

Methods and statistical analysis:

My lab training will be given by a postdoctoral fellow expert in electrophysiology and my advisor, Dr. Moreno. I will be using sphingomyelin synthase 2 (SMS2) knockout mice as a model for reduced SM production, approximately 40% of normal. Dr. X Jiang at SUNY Downstate has a colony of sphingomyelin synthase 2 (SMS2, the last enzyme of SM biosynthesis) knockout mice (SMS2-KO)(16,17). The SMS2KO is available in my advisor's lab and this line has already been characterized behaviorally: significant hippocampus and frontal cortex-dependent behavioral deficits were observed. To study EC-hippocampus function, I will measure spontaneous field potentials in superficial and deep layers of EC and 2 hippocampal areas, the dentate gyrus and subiculum. For superficial fields, 4 electrodes will simultaneously record in the medial entorhinal cortex, lateral entorhinal cortex, transentorhinal cortex, and perirhinal cortex as a measure of EC output to the hippocampus (18). For deep fields, the 4 electrodes will record in the MEC, LEC, subiculum, and dentate gyrus as a measure of hippocampal output (18).

Electrophysiology methods: LFPs will be recorded (at 34°C in artificial CSF with 5 mm KCl) using glass electrodes of 2MΩ resistance filled with NaCl, in all layers with/without pharmacological blockade of GABA-A receptors (Picrotoxin, Sigma) and with/without 20 uM of SM or PC micelles. EC-hippocampal slice will be prepared as previously described by my advisor's lab (14).

Statistical analysis: I will measure spontaneous local field potential (LFP) duration in 7-month-old (the age at which SM decreases by 40% and animals have cognitive deficits) wild type and SMS2KO mice and obtain means and SD per group. I propose to use a minimum of n=8 mice per group, and to obtain at least two or three slices per mouse, increasing the number of samples. This power calculation was based on two group Satterthwaite t-test calculations performed by my advisor using LFP durations in APP vs WT mice. In the statistical analysis, we will control for random effect per mouse using mixed models. Data will be analyzed using generalized linear models (once distributions are assessed) where we will covariate for sex. The data will consist of duration, frequency, and amplitude of LFPs using MATLAB routines developed in the lab to detect events.

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Make ups:

Molly Schneider
Email: molly.schneider@downstate.edu
Phone: 3018026017
Title: Overcoming Barriers to Mental Health Treatment Access: A Single-Session Growth Mindset Intervention for Adolescent Depression
Sponsor: Dr. Eugene Dinkevich
Pediatrics
Co-Advisor:
Location: Downstate Pediatrics Associates

Fellowship period: Yes
Involve any? Yes

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where: The intervention that we plan to pilot at Downstate Pediatrics Associates (Project Y.E.S.) was classified as exempt from Institutional Board Review (as a program evaluation) by the Office of Research Compliance at Stony Brook University. The online progra

Research Experience: As a research coordinator at the Depression and Anxiety Center at Mount Sinai for two years before medical school, I ran the daily operations of three research protocols under supervision of the principal investigator (PI). One study investigated the efficacy of a ketamine-like drug to reduce suicidal ideation in patients with major depressive disorder (MDD); the second study collected biological specimens from patients with MDD and PTSD, both pre- and post- investigational treatment. The goal was to identify biomarkers predictive of treatment response, focusing on markers of systemic inflammation. The third study used 7 Tesla MRI to explore neuroanatomical biomarkers of MDD. In addition to recruiting participants, collecting data, and maintaining study databases on REDCap, I administered psychiatric interviews to monitor symptom changes throughout the studies. I also drafted regulatory documents and study instruments, submitted to the Institutional Review Board (IRB), and helped prepare grant submissions to the NIH and private foundations.
While working at Mount Sinai and during my undergraduate education, I completed several independent projects. Using data that I helped collect from the 7 Tesla MRI cohort described above, I presented a poster at the Friedman Brain Institute's Neuroscience Retreat (Mount Sinai; April 2019). The poster explored the relationship between specific childhood trauma subtypes, including physical abuse and neglect, emotional abuse and neglect, and sexual abuse, on anterior cingulate cortex and insula gray matter volume, regions implicated in stress and suicidality.
For my senior psychology project at Barnard College, I evaluated how college students use metacognitive knowledge and cues about task difficulty to make problem-solving choices; specifically, how difficulty-level of an initial math test influenced subsequent performance and willingness to attempt harder problems. For this project, I submitted an IRB proposal, ran subjects through the task, and wrote up the results.
Publications
Brown SSG, Rutland JW, Verma G, Feldman RE, Schneider M, Delman BN, Murrough JW, & Priti Balchandani. Ultra-High-Resolution Imaging of Amygdala Subnuclei Structural Connectivity in Major Depressive Disorder. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. August 2019.

Jacob Y, Morris LS, Huang K-H, Schneider M, Rutter S, Murrough JW, & Priti Balchandani. Neural correlates of rumination in major depressive disorder: A brain network analysis. NeuroImage: Clinical. 2020;25:102142.
Morris LS, Kundu P, Costi S, Collins A, Schneider M, Verma G, Balchandani P, & James W. Murrough. Ultra-high field MRI reveals mood-related circuit disturbances in depression: a comparison between 3-Tesla and 7-Tesla. Transl Psychiatry. 2019;9(1):1-11.
Posters
Schneider M, Morris L, Verma G, et al. Gray Matter Volumes and Childhood Trauma Subtypes. 11th Annual Neuroscience Retreat, Icahn School of Medicine, April 2019

Career goals: As a future pediatrician or adolescent medicine specialist, I envision having my own outpatient clinical practice while also conducting clinical research projects to address childhood health disparities. I am particularly interested in the impact of adverse childhood experiences (ACEs) on physical and mental wellbeing, and how primary care physicians can intervene early and most effectively to mitigate the long-term health consequences of early life stress. To that end, I hope to work in an academic medical setting that supports research and scholarship to improve the health of vulnerable patient populations. At some point during my training, I plan to pursue a master's degree in public health or biostatistics to gain a solid foundation in research methodology and statistics to support my academic career.

Description: One-third of New York City public school students reported feeling sad or hopeless almost every day for 2+ weeks in a row in the past year [1]. 16.3% reported seriously considering suicide [1]. Despite the great need for treatment, most teenagers who experience a major depressive episode do not receive mental health care [2]. Furthermore, members of racial and ethnic minority groups – particularly men – are less likely to access treatment than white Americans [3]. At Downstate Pediatrics Associates, a faculty practice affiliated with SUNY Downstate, almost one in five adolescents screen positive for depression but only about 20% of those referred for treatment make at least one appointment [4].
Structural barriers such as financial cost, as well as stigmatization of mental health diagnosis, likely play a role in low rates of treatment uptake and adherence [5, 6, 7, 8] For that reason, interventions to address mental health concerns in adolescents must be easily accessible and also change stigmatic beliefs about the cause of symptoms and the capacity for improvement. Single-session interventions (SSIs), which can be delivered in the doctor's office immediately upon diagnosis, can engage patients in early treatment and motivate them to seek further care [9]. One promising SSI for adolescents, developed by Schleider and Weisz, teaches theories of growth mindset, the idea that personality traits are malleable [10]. In a 20-30 minute self-administered, computer-based program, participants learn about the concept of neuroplasticity, how people can change given the brain's malleability, and how growth mindset can be used to cope following stressful situations [10].
Despite their brevity, single session growth mindset interventions (GM-SSIs) have the potential to improve adolescent depressive symptoms. In a study by Schleider & Weisz, youth ages 12 – 15 (N=96) with anxiety and/or depression-related symptoms were randomized to receive the 30-minute, computer guided GM-SSI or a supportive-therapy control [10]. Participants in the GM-SSI group experienced significantly greater improvement in depression symptoms across the 9-month follow up period and also more rapid improvement compared to the control group [10]. In another randomized control trial, tenth grade female adolescents from rural, low-income high schools in the southeastern United States (N=222) completed a 45-minute GM-SSI or an active control [11]. Students in the GM-SSI group had significantly greater reductions in depressive symptoms after 4-months compared to the active control group [11]. In addition to its clinical impact, GM-SSIs can improve youth and parent perceptions of mental health treatment [12]. A randomized-control trial of 430 parents of youth ages 7-17 showed that a 15-minute online GM-SSI significantly increased parents' beliefs that psychotherapy could be effective for themselves and their children [12].
Altogether, these findings attest to the potential for GM-SSIs to improve depression symptoms, change perceptions of mental health treatment, and thereby improve treatment uptake and adherence. One outstanding question, however, given that culture, income, race, and ethnicity all play a role in treatment access and outcomes, is whether this intervention will also be effective for the patient population at SUNY Downstate. In the Schleider & Weisz study discussed above, most participants were Caucasian, received prior treatment for depression/anxiety, and had annual household incomes over $60,000 [10]. By comparison, 85% of adolescents seen at Downstate Pediatrics Associates are Afro-Caribbean or African American. In East Flatbush where the clinic is located, the average household income in 2017 was $50,290 [13].
We believe single-session growth mindset interventions can significantly improve treatment uptake among adolescents at SUNY Downstate, but the program must first be piloted to assess whether the positive results described above can be replicated here in Brooklyn.
Specific Aims and Research Plan

The goal of the present study is to validate the acceptability and effectiveness of an online GM-SSI called Project Y.E.S. (Youth Empowerment & Support) for adolescents who screen positive for depression during routine care at Downstate Pediatrics Associates [14]. The aims are as follows:

Aim 1. To assess baseline perceptions of mental health treatment among depressed adolescents and their parents.

Aim 2. To measure rates of GM-SSI uptake and completion among depressed adolescents who are offered the intervention by their PCP.

Aim 3. To collect data on patients' perception of the intervention after completion.

Aim 4. To assess whether the intervention influences rates of treatment uptake and adherence among patients referred to the clinic's Licensed Mental Health Counselor (LMHC).

Design: Depressed adolescents will be introduced to Project YES by their primary care provider (PCP). Data will be collected regarding the number of patients who agree to participate and, if applicable, reasons for refusal. Participants will provide written feedback and complete a feedback scale. For those patients referred to the in-house LMHC, the number of sessions attended, and subsequent PHQ-9 scores will be recorded.

Methods

In the waiting room, all adolescents over age 11 who are seen at Downstate Pediatrics Associates will complete the PHQ-9, a self-administered assessment for DSM-IV depression symptoms, and the Adverse Childhood Experiences (ACEs) questionnaire. The forms will be reviewed by their PCP. Patients who score 10 or above on the PHQ-9, indicating moderate depression (and not requiring immediate referral due to possible self-harm) will be provided with information about Project Y.E.S. and encouraged to complete it on a computer in the clinic after their appointment. Those who prefer to participate at home will be given instructions and encouraged to complete it within one week. Beforehand, participants will be asked to complete the Barriers to Accessing Care Evaluation (BACE), a validated assessment of barriers to accessing mental health treatment, particularly as they relate to stigma. Project Y.E.S. is web-based intervention, delivered via Qualtrics, that is publicly accessible through the Lab for Scalable Mental Health (PI: Jessica Schleider) at Stony Brook University: http://www.schleiderlab.org/yes.html [14]. Dr. Schleider was named to the 2020 Forbes 30 Under 30 list in the Healthcare category for her work on brief, effective interventions to treat depression in youth [15].

The current study will use Project Personality, one of the three activities that comprise Project YES [14]. After exposing participants to the concept of growth mindset, Project YES asks them to complete a worksheet describing strategies for applying these principles to their own lives. Afterwards, participants write notes to younger children, using the concepts they just learned, about the malleability of personality traits to help them cope with challenges [11]. Upon completion, Project Personality prompts participants to complete an Intervention Feedback Scale [11]. We will also administer our own, Downstate-specific intervention feedback scale.

References

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Make ups: N/A

Moshe Schneiderman
Email: moshe.schneiderman@downstate.edu
Phone: 347-931-4380
Title: Patient-Reported Outcome Measures on Sexual Satisfaction after Hand/Upper Extremity Surgery
Sponsor: Dr. Steven Koehler
Department of Orthopedic Surgery
Co-Advisor:
Location: BSB 3-7

Fellowship period: No
Involve any? Yes

Review Board Type: IRB
Study#: 1299140
Dates: 10/9/2018
Title: Developing the HAND-Q: Phase 2 Field Test
Site: SUNY Downstate
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: Prior Research Experience: Previously, I assisted with data collection and entry with Dr. Allan Geliebter at Mt. Sinai-St. Luke's Hospital in an obesity study that examined whether bariatric surgery alters brain activity. I've also assisted in a research study that investigated feeding practices in infancy and resultant BMI at ages 2-5 years. I assisted with the literature review and in scrubbing the data for a study comparing duration of breastfeeding and the resultant trajectory of childhood BMI. Outcome measures included: BMI, BMI percentile, infant weight for length, infant weight for length percentile, and head circumference. Head circumference was included as an indicator of brain development. The study was a retrospective one, using chart data from electronic health records, which are more accurate than maternal recall of infant feeding practices years later-- the way most studies of this nature have been carried out in the past. I gained experience in manuscript writing, in research design, and in statistical analysis. The study will soon be submitted for publication.

Career goals: I am interested in a career in academic medicine in keeping with the physician-scientist model. From my proposed research project, I will gain experience in experimental design, research methodology and statistical analysis. This will be valuable in giving me practice with all of these for conducting research in the future. Moreover, I found learning about the hand this semester to be fascinating. Doing research on hand surgery will give me the opportunity to learn more about the hand and the field of hand surgery in particular, as well as providing me with experience about the process of research in general-- experience with research methods and design.

Description: Introduction/Background:
As modern medicine shifts toward patient-centered care, patients are becoming key stakeholders in their healthcare decisions. While traditional methods like radiographic imaging and post-operative complication rates have been used by surgeons to interpret surgical outcomes for decades, recent literature describes the incorporation of patient satisfaction into this evaluation. Patient-reported outcome measures (PROM) have since emerged as a fundamental method for assessing patient morbidity and suffering, as well as satisfaction with care [1-5].
Multiple survey techniques have implemented this general PROM model to quantify the post-surgical patient experience while simultaneously quantifying surgical outcomes. Examples of these PROMs include the Disability of the Arm, Shoulder and Hand

(DASH) [7] and the Boston Carpal Tunnel Questionnaire (BCTQ) [8]. The DASH questionnaire offers a unique view into self-interpreted post-surgical outcomes including symptoms and disabilities. This is achieved through a 30-item disability/symptom scale that can effectively detect changes in a disability over time in patients undergoing surgery for upper extremity musculoskeletal disorders. Meanwhile, the BCTQ incorporates a 19-item symptom severity/functionality scale that reflects on post-surgical relief of symptoms, strength and dexterity, time to resumption of activities and work and clinical measures of sensation. Although DASH and the BCTQ are revolutionary in the way that patient outcomes are interpreted, they offer only a brief look at the patient experience with a focus solely on functionality outcomes.

As PROMs have gained traction and reputability in the field, new surveys have begun to push the boundaries. The recent creation of the Hand Questionnaire (HAND-Q) offers an extensive survey that expands on basic outcomes questions and delves deeper into the personal lives of patients undergoing a multitude of surgeries. This survey is generalized to many upper-extremity conditions involving the hand while thoroughly assessing hand functionality satisfaction, hand appearance satisfaction, symptom severity, emotional dissatisfaction, sexual dissatisfaction and overall treatment satisfaction. The wide variety of patient-centered questions asked in HAND-Q allows for a cross analysis of various post-surgical patient experiences to better understand patient satisfaction. One unique facet of HAND-Q is the section of the survey that pertains to sexual satisfaction, as this topic is often overlooked in assessing the impact of hand/upper extremity disease on patients' lives. We believe that this section of HAND-Q offers a new instrument to initiate conversation about a topic that many patients may be hesitant to discuss with their healthcare providers. Sparse literature exists on the implications of sexual satisfaction in treatment outcomes, especially in reference to the upper extremity. However, one study on breast augmentation demonstrates the effectiveness in PROMs in facilitating a conversation on sex, while also demonstrating surgical impacts on sexual satisfaction and the patient experience as a whole [6].

Specific Aims and Research Plan:

The goal of this project is to assess the effects of upper extremity surgery on patient's perception of their sex life and overall experience. We will be using patients' composite scores on the Hand Questionnaire (HAND-Q) and conducting statistical analyses of the questionnaire responses. We hypothesize that the hand is a uniquely sexual organ and self-reported measures of disease severity, quality of life, and emotional impact would correlate with sexual dissatisfaction among patients actively receiving treatment for conditions of the hand/upper extremity.

Methods and Statistical Analysis:

Patients presenting to a single, board-certified and hand/microsurgery fellowship-trained orthopaedic surgeon at an outpatient hand clinic will be given the option to complete the Hand Questionnaire (HAND-Q) while waiting to be seen. Consenting patients will be consecutively enrolled in a Phase II Hand Questionnaire (HAND-Q) Pilot Multicenter International Validation Study [9]. All patients with valid responses to the following question types will be included in this study: Functionality, Symptom Severity, Hand Appearance Satisfaction, Emotional Dissatisfaction, and Treatment Satisfaction.

Composite scores (CS) will be created for each individual section by collating scores from individual questions. CS for each section will be calculated by summing all recorded patient answers, ranging from (1-4), for each question in the section, and dividing by the maximum score attainable for each section, then multiplying by 100, which established a generalizable CS scale (0-100). In order to be included in the CS analysis, patients will be required to have answered, at a minimum, all but one question. Interpretation of CS will vary for each individual section: sexual dissatisfaction (range, 0 [not at all bothered] to 100 [extremely bothered]), diminished quality of life (range, 0 [not at all] to 100 [very much]), emotional dissatisfaction (range, 0 [never] to 100 [always]), hand appearance satisfaction (range, 0 [very dissatisfied] to 100 [very satisfied]), symptom severity (range, 0 [none] to 100 [severe]) and hand functionality (range, 0 [not at all difficult] to 100 [extremely difficult]). T-test analysis will be used to compare sexual dissatisfaction CS for males versus females. Next, individual sexual dissatisfaction CS for each patient will be compared to their CS for diminished quality of life through Spearman correlation coefficient analysis. This same method will be applied to compare sexual dissatisfaction CS to each of the following: emotional dissatisfaction, hand appearance satisfaction, symptom severity, and hand functionality. All analyses will be performed using SPSS version 24 (IBM Corp., Armonk, NY, USA), and a p-value <0.05 will be set as threshold for statistical significance.

My role in the study will include administering the questionnaire, collecting and analyzing the data, as well as drafting the manuscript.

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Make ups: No make-up work

Jaewoo Shin
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Title: Does lateral quadratus lumborum nerve block versus intrathecal morphine affect postoperative opioid consumption and pain control after Cesarean delivery? A prospective randomized controlled trial.
Sponsor: Dr. Ming Zhang
Department of Anesthesiology and Cell Biology
Co-Advisor: Cheng, TzuHsuan, Department of Anesthesiology
Location: SUNY Downstate Medical Center

Fellowship period: Yes
Involve any? Yes

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where: 4/1/2020

Research Experience: From 2015-2016, I had volunteered as part of a team of research assistants in the Mount Sinai Hospital emergency room where I performed data collection and obtaining informed consent from patients across 7 different clinical studies occurring at the time. The topics had ranged from pain management to looking for bacterial indicators of asthma.
I also spent 2015-2016 as a volunteer research assistant in a biochemistry lab under Dr. James Borowiec at NYU Langone where I studied the function and mechanism of Replication Protein A (RPA) binding with single-stranded DNA in the presence of various cellular co-factors. This was largely a basic-science wet-lab where I performed DNA/protein purification, bead-binding assays, and other standard biochemistry experiments.
Finally, from 2016-2018, I had moved to a neighboring biophysical lab run by Dr. Eli Rothenberg at NYU Langone to pursue my own independent research project. My project was part of a larger collaboration with Nobel laureate Dr. Aaron Ciechanover in Israel. I had led the super-resolution microscopy imaging of the proteasome. I had shown that there was nuclear to cytoplasmic shuttling of the proteasome as an adaptive mechanism in response to stress (amino acid starvation) for promoting cancer cell survival. This project served as my honors thesis for my undergraduate degree in biochemistry.

Career goals: My primary goal has long been to practice medicine at an academic institution so that I could care for patients while performing clinical research and advance the field I'm practicing in. The particular field I am currently interested in is Anesthesiology. By doing clinical research in this department, I thought it would be a great way for me to gain greater exposure to the type of patient care that anesthesiologists do and the type of research I would be doing in the future.

Description: General background
Effective acute post-operational pain management is critical for women undergoing cesarean delivery. Cesarean deliveries often result in large amounts of pain for 48 hours post-operation (1). This acute pain has been linked to increased rates of postpartum depression, persistent pain and decreased recovery for 8 weeks after the delivery, and is seen as an increased risk for insecure infant attachment (2). The morbidity associated with post-operative acute pain highlights the need for effective pain management.

Current guidelines on post-operational acute pain management after cesarean section by the Enhanced Recovery After Surgery Society (ERAS) recommend a multimodal approach with many different forms of analgesics and techniques. These first involve a nerve block in which local anesthetic is given around a nerve, with the subsequent use of acetaminophen and NSAIDS around the clock; if the combination fails to control the pain, then more potent analgesics such as opioids are used as needed (3). The ultimate goal of this multimodal pain management is to improve care by reducing patients' reliance and usage of perioperative morphine. The use of opioids leads to common side effects like vomiting, constipation, and physical dependence, as well as the more fatal complications of respiratory depression and death (4). Thus, determining the most efficacious perioperative pain management method to minimize opioid use is critical.

In exploring the optimal nerve blocking technique for post-cesarean analgesic management, there are four nerve blocking techniques to choose from. The primary recommendation is thoracic epidural analgesia (TEA), with the alternatives being intrathecal morphine (ITM), transverse abdominis plane (TAP) nerve block, and the most recently introduced Quadratus Lumborum block (QLB) in 2015 (3, 5). In terms of efficacies, patients who had ITM instead of TEA for colorectal surgery had earlier mobilization and discharge from the hospital post-operation (6). Patients who had QLB had reduced morphine consumption compared to TAP block for cesarean deliveries (7). Following these results, there was interest in comparing the efficacy between the ITM and QLB analgesic technique in reducing post-operative morphine use.

In 2019, the efficacies of ITM and QLB have been compared in two different randomized controlled trials that produced contradictory results. Tamura et al. reported that spinal morphine produced lower visual analog scores (VAS) for pain than did QLB, suggesting the inferiority of QLB to ITM in managing post-operative pain (8). However, Salama reported that the QLB reduced post-operative morphine use than the ITM method and decreased the incidence of morphine related side effects (9).

The goal of our study is to compare the degree of post-operative opioid use with ITM and QLB in order to investigate the apparent conflicting results between Tamura et al. and Salama. Tamura et al. used the VAS—where patients rate their pain on a scale—to compare the efficacies of ITM and QLB. However, these scores are subjective. Thus, they are not a preferable primary outcome measure to quantify a patient's level of pain. To address this, our study will measure post-operative opioid consumption as a primary measure, with VAS as a secondary measure. Moreover, Tamura et al. used the posterior approach to the QLB while our study investigates the lateral approach to the QLB. It is unknown what effect, if any, these two different methods will have on our primary outcomes measured. Finally, Salama and Tamura et al. used opioids as the standard starting analgesic given to patients after the anesthetics (QLB/ITM) were applied. However, we wish to study the effects of ITM versus QLB on opioid consumption in the context of a more multimodal approach to pain treatment. Thus, our standard of care for post-operative cesarean pain will start with non-opioid medications (acetaminophen and ibuprofen) for all patients after QLB/ITM is applied, and opioids will subsequently be given and tracked as needed on an individual basis.

Specific Aims and Research Plan of Your Proposed Project

The specific aim of this project is to explore the effectiveness in QLB and ITM in managing the first 48 hours of post-operative pain and reducing opioid use in patients who choose to undergo elective cesarean births at SUNY Downstate. Patients will receive either a QLB or ITM as part of the multimodal approach to post-caesarian pain management in the first 48 hours after surgery. The primary outcome measure will be opioid consumption in morphine milligram equivalents (MME). Secondary outcomes measured will be the length of time before a patient first requests for rescue pain medication, the VAS using a numerical rating system, and the incidence of opioid side effects.

Our hypothesis is the non-inferiority of the QLB in comparison to ITM as part of the post-cesarean multimodal analgesic management.

I, as part of the research team, will be involved in obtaining the consent of patients, data collection, and data analysis of the project.

Methods and Statistical Analysis

The study will be performed as a prospective, randomized, controlled, single-blinded study at SUNY Downstate Medical Center. 70 patients undergoing elective cesarean delivery will be randomized into either QLB receiving (group 1) or ITM receiving groups (group 2), for a total of 35 patients per group.

After the cesarean delivery and application of the QLB or ITM, all patients will be prescribed a standardized analgesic regimen of oral acetaminophen (650mg) and ibuprofen (600mg) every 6 hours. For rescue analgesia, patients will have a call button. If pain medication is requested, oral oxycodone (5mg) will be given. The minimum time between oxycodone doses per request is every 30 minutes. If the pain score does not change or increases after 1 hour of the initial oxycodone, the oxycodone will be replaced with IV morphine. The VAS will be assessed for both at rest and during movement every 2 hours and during any change in medication.

The amount of opioid use in morphine milligram equivalents in timed intervals will be recorded as the primary outcome. The secondary outcomes such as whether a patient mentioned pain as their complaint, the number of patients who switched from oral oxycodone to IV morphine, the time of rescue analgesic administration, incidence of side effects from the opioids, and VAS pain scores will be recorded. VAS is recorded as a 11-point numerical scale ranging from 0 to 10 with 0 representing no pain and 10 representing the most extreme level of pain for the patient.

For statistical analysis, SPSS program will be used for analysis. The primary and secondary outcomes will be compared between the QLB-receiving and ITM-receiving cohorts. All descriptive statistics will be reported as a mean +/- standard error of mean. To compare baseline characteristics of the two cohorts for quantitative variables including BMI and age, we will use the Mann-Whitney U test. To compare the baseline characteristics of the two cohorts for categorical variables including categories of BMI and comorbidities, the Fisher exact test will be used. Kaplan–Meier Survival analysis will be used for analyzing time to request first rescue medication (Plotted as percent requesting rescue medication vs. time intervals post operation). Between the two cohorts, the MME over time will be analyzed with a mixed linear model. The same analysis will be performed for the VAS numerical scores. For all analysis, statistical significance will be defined to be a p-value of less than 0.05.

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Make ups:

Omar Siddique
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Title: Time-course of changes in tPA expression after steroid treatment
Sponsor: Dr. John Danias
Ophthalmology
Co-Advisor:
Location: SUNY Downstate

Fellowship period: Yes
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: I spent two years at my undergraduate college involved in basic science research on the effects of methamphetamine on serotonin and dopamine receptors throughout the brain. During these years, I have learned various skills necessary for basic science research of all disciplines. These skills range from the utmost basic such as proper pipette technique and animal care to more specialized tasks such as brain slicing, film development, and euthanasia of animals according to protocol. Although I have stayed in the same neuroscience lab throughout all two years, I have taken on many roles and responsibilities in the lab including assisting in research activities, compiling and analyzing data, and training new assistants. I have learned how to manage through the processes of gaining approval from IRB and IACUC and have used this knowledge to ensure the smooth operation and conduction of the research. Additionally, I have experience presenting my research at school-wide poster conventions. Apart from basic science research, I also have experience in clinical research in a hospital setting. My role involved recruiting patients in the emergency room for research studies they may be eligible for.

Career goals: Ultimately, my goal for my career is to become a practicing ophthalmologist and to use the various skills and knowledge I have gained throughout my career to treat my patients to the best of my ability. Staying up to date with novel treatments developed and understood through research will be crucial to my work. I am also interested in becoming involved in academic medicine that may include a professorship or as a researcher and ideally I would strike a proper balance between academic medicine and clinical practice.

Description: Tissue plasminogen activator (tPA) has a storied and well-studied history in the context of thrombolytic therapy. It has been shown to effectively decrease aqueous outflow obstruction due to fibrin clots post-glaucoma surgery [1, 2] and in the treatment of open-angle glaucoma secondary to blood clots [3]. While the therapeutic efficacy of tPA has been reported and studied in various eye-related conditions, further research is required in order to fully understand its importance in the pathogenesis and treatment of said conditions. The current application proposes to study and clarify the role of tPA in open-angle glaucoma, the most common form, and, in particular, steroid-induced ocular hypertension. Our lab has previously investigated the effects of tPA in open-angle glaucoma and steroid-induced ocular hypertension. We found that recombinant human tPA is an effective treatment in the reversal and prevention of steroid-induced ocular hypertension in a sheep model and that this treatment may be beneficial in steroid-induced glaucoma as well [4]. Additionally, we have also shown that a deficiency in tPA in

trabecular meshwork cells reduced outflow facility in a mouse model [5], suggesting that the tPA pathway may be critical in the maintenance of a patent trabecular meshwork. Also, our work with human trabecular meshwork cells has shown that steroid usage downregulates the expression of the PLAT gene and, therefore, decreases tPA, further establishing a clear connection between tPA levels, steroid administration, and potentially steroid-induced ocular hypertension and open-angle glaucoma [6].
The effects of steroid usage on intraocular pressure have been studied in various animal models with results reporting consistent intraocular pressure elevation post-steroid administration [7, 8]. However, these results are not limited to just animal models. One particular study has shown that children treated with topical steroids for vernal keratoconjunctivitis presented with blindness in one or both eyes or were characterized as having low vision due to glaucomatous optic neuropathy, indicating a possible link between topical steroid usage and the development of glaucoma in children [9]. While steroid-induced ocular hypertension has been shown to be reversible on cessation of steroid usage [10], topical steroids remain commonly used and prescribed due to their ease of access, relatively low cost, and transient sense of improvement in symptoms of the pathology [11]. It is due to this consistent usage of steroids and the established link between it and elevated intraocular pressure that a proper therapy is needed to treat and prevent the downstream ocular effects of glaucoma and blindness.
tPA is one such potential therapy that has been shown to reduce steroid-induced intraocular pressure. It has been theorized that plasminogen activators in general increase the activity of matrix metalloproteinases [12], extracellular proteins responsible for tissue growth, turnover, and remodeling. Increased metalloproteinase activity has, in turn, been shown to increase aqueous humor outflow facility in a human model [13]. Additionally, tPA levels have been noted to be substantially elevated in trabecular cells compared to normal vascular cells, resulting in higher levels of trabecular outflow [14], indicating a possible natural increased usage of tPA in maintaining a patent trabecular meshwork. However, it has been shown that corticosteroid treatment results in decreased tPA activity and decreased aqueous outflow, further establishing a connection between tPA and trabecular meshwork outflow [15]. The studies mentioned above have clearly indicated a promising potential therapeutic role of tPA in steroid-induced ocular hypertension and it is crucial to expand upon these findings.
Despite an evident connection between the treatment of tPA and a reduction in intraocular pressure in steroid induced glaucoma, it is still unclear how exactly tPA functions in maintaining proper trabecular meshwork outflow. Our project aims to deepen the fundamental understanding of tPA, its upstream regulation by steroids.
Methods:
Experiment 1.1 Determination of time course and dose response curve of PLAT expression changes and tPA, amount and activity in HTM cells exposed to steroid.
Hypothesis: PLAT expression decreases early after application of steroid to HTM cells in culture and results in changes in tPA amount and activity
Experimental Design: HTM cells from multiple donors (>3) will be seeded in 12-well plates and exposed to prednisolone (2µM-2mM) or vehicle. Cells and media will be harvested at 30mins, 1h, 3h, 6h, 12h, 24h, 48h and 96h for mRNA extraction, protein extraction or tPA activity determination using standard methodology. mRNA will be used for quantitative PCR (qPCR) with human PLAT specific primers. mRNA will be normalized to 18S mRNA, protein amounts to actin and activity values to total protein. Comparisons between cultures exposed to steroid and those exposed to vehicle at all individual time points and steroid concentrations will be performed using ANOVA with post-hoc comparisons.
Rationale: It is important to confirm that steroids downregulate PLAT in humans, determine whether they affect tPA activity and resolve the time course of these changes. In preliminary experiments we have detected PLAT expression downregulation 1h after prednisolone administration in HTM cells from one donor. We will test multiple time-points to determine the exact time-course of PLAT mRNA and tPA protein amount and activity changes as these may vary in cells from different donors.
Expected results and interpretation: We expect that prednisolone will downregulate PLAT mRNA expression in a dose dependent manner in HTM cells. We also expect that this occurs early (30min-3h) after exposure to steroid and leads to decreased tPA production which in turn results in reduced tPA activity (although reductions in amount and activity may be delayed compared to mRNA changes). Expression changes delayed for more than 3-6 hours would suggest that steroid modulates PLAT transcription indirectly (through effects on the synthesis of another protein). Although we expect a dose-dependent effect of steroid on PLAT expression, alternatives could include the presence of a threshold or a rather flat dose effect.
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Make ups: N/A

Nicholas Tan
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Title: Association between Corneal Hysteresis and Vision Loss in a Glaucomatous Hispanic Population following Ahmed Glaucoma Valve Surgery
Sponsor: Dr. Nathan Radcliffe
The New York Eye and Ear Infirmary of Mount Sinai, NYC, NY
Co-Advisor:
Location: The New York Eye Surgery Center
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Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: Prior to and since enrolling at Downstate, I have been active in behavioral, basic, and clinical research. On the behavioral end, I worked as a research volunteer from 2016-2018 at NYU Langone's Center for Healthful Behavior Change. I performed academic literature review, data entry, and data analysis with actigraphy for multiple projects involving sleep, cognitive functioning, nutrition, and metabolic disease among underrepresented groups. From that experience, I co-authored three abstracts presented at national conferences.
On the basic sciences side, I completed research at two labs at Downstate in 2019. First, I volunteered in the Department of Allergy and Immunology under Dr. Maja Nowakowski. I evaluated the viability of cells after freezing, cultured cells, and measured nitric oxide production. I performed peripheral blood monocyte isolation, cell counts, and freezing using samples from patients suffering from angioedema, asthma, and allergic rhinitis. I am co-author of an abstract accepted for presentation at The American Academy of Allergy, Asthma, and Immunology in 2020. Second, I worked within the Department of Surgery, in Dr. Chongmin Huan's lab, where I learned and performed various lab procedures such as processing DNA and performing PCR with gel electrophoresis to genotype samples from mice. I co-wrote a review paper on the role of the regeneration protein family (Reg) in the pathophysiology of inflammatory bowel disease, describing Reg' s bactericidal, anti-inflammatory, and tissue repair effects. I am second author in the manuscript that is currently under review by the World Journal of Gastroenterology.
My most notable clinical research experience is that of a sub-investigator for the New York Eye Surgery Center, where I currently coordinate a research project. Under the mentorship of Dr. Nathan Radcliffe, I developed and wrote the protocol, proposal, clinic data forms, and an informed consent form for a Phase IV clinical trial funded by Ocular Therapeutix, Inc. The clincialtrials.gov ID is: NCT04200651. The study is designed to compare the safety and efficacy of dexamethasone ophthalmic insert (Dextenza) to the current standard of care, prednisolone acetate eye drops, after concomitant cataract and minimally invasive glaucoma surgeries. I wrote the IRB application and prepared the materials for FDA investigational new drug approval. I also correspond regularly with the drug company liaison on costs, documents, approvals, enrollment, and beyond. Dr. Radcliffe and I enrolled the first patient for the clinical trial on January 13th, 2020. Separately, I also performed a chart review on the outcomes of patients who received dexamethasone intraocular suspension (Dexycu) at Dr. Radcliffe's practice since April 2019. I subsequently authored an abstract that was accepted for presentation at the Association for Research in Vision and Ophthalmology's 2020 conference.

Career goals: Currently, my strongest specialty interest is in ophthalmology. I shadowed Dr. Nathan Radcliffe after he performed glaucoma and cataract surgeries on my father this past summer. I was enthralled by the diversity of pathology, balance between clinic and OR, patient satisfaction, and technological marvels of the field. Watching a monocular patient embrace Dr. Radcliffe after he operated on the patient's remaining eye for the fifth time, saving his vision, left a lasting impression. I seek to impact lives to such a capacity. Requisite competencies include deep medical knowledge, surgical expertise, creativity, and dedication to service. I have been honing most of those capabilities since starting medical school. With Dr. Radcliffe's oversight, I wrote the protocol for, secured IRB approval of, and am enrolling patients into a clinical trial comparing a novel sustained-release drug to the standard of care. The potential for innovative approaches to solve health care problems excites me. I hope to have both academic and private practice options available in my career. I am active in the Brooklyn Free Clinic as both a volunteer on clinic nights and as the Chief Financial Officer for the 2020-2021 clinic council. BFC work not only allows me to help patients, but also prepares me for situations where efficiency, bureaucratic navigation, and financial literacy are paramount. I am also a member of the clinical educator pathway, which I will use to gain more exposure to academics.

Description: Aims and Research Plan

The Ahmed Glaucoma Valve (AGV) is a surgically inserted tube shunt that redirects aqueous humor from the anterior chamber to the posterior subconjunctival space. It is designed to slow glaucoma progression by reducing the eye's intraocular pressure (IOP) (1). However, even a well-placed AGV can fail to prevent further vision loss. The aim of this study is to evaluate corneal hysteresis, a biomechanical measure of the cornea, as a potential variable independently associated with post-AGV surgery vision loss. Specifically, this study will examine glaucomatous eyes from Hispanics/Latinos, a group that faces ocular health disparities (2, 3). This study will focus on eight baseline variables for a retrospective case-control analysis. They include corneal hysteresis (CH), IOP, age, central corneal thickness (CCT), best-corrected visual acuity (BCVA), visual field mean deviation, central vision defects, and number of glaucoma medications. CH is the primary variable of interest. It is a relatively new glaucoma risk factor that may indirectly measure the ability of the optic disc to withstand pressure changes (4,5,6). Next, preoperative IOP will be included due to prior research suggesting that it is a risk factor for AGV failure (7). Age is a risk factor for glaucoma progression (8). Visual field mean deviation and glaucoma medications will provide general measures of glaucoma severity prior to surgery (8). Central vision defects will reveal late-stage glaucomas, and prior research suggests central vision defects may increase risk for post-glaucoma surgery blindness (9). Preoperative BCVA will be included because some instances of postoperative blindness may occur in patients who simply have little vision left to lose. Finally, central corneal thickness will help distinguish the influence of overall corneal health from corneal hysteresis alone.

Background information

Glaucoma affected as many as 2.9 million Americans in 2016 (10). Glaucoma involves damage to optic nerve head architecture and the retinal ganglion cells composing the retinal nerve fiber layer. Multiple risk factors contribute, with some including elevated intraocular pressure, increased age, myopia, family history, and ethnic background (8). In terms of ethnicity, Hispanics/Latinos face disparities in glaucoma. Data from the Los Angeles Latino Eye study showed that prevalence of open-angle glaucoma was significantly greater for Hispanics in age groups 50 and older compared to the values reported for whites in equivalent cohorts (3).

Since IOP is the only modifiable risk factor for glaucoma, various drugs and surgeries target IOP to limit vision loss. One such intervention, the Ahmed Glaucoma Valve, is a drainage valve used for refractive glaucoma. It can reduce IOP by over 12 mmHg in 12 months (11). However, various complications exist, such as corneal damage from tube abrasion and postoperative infection (1). Rarely, tube shunt glaucoma surgery in advanced glaucoma patients can result in "snuff-out phenomenon," where mysterious, severe central vision loss occurs soon after an uncomplicated surgery (9). Preoperative central vision defect was significantly associated with snuff-out after tube shunt implant (9). Directly opposing the AGV's goal of IOP reduction, another complication called the hypertensive phase occurs in as many as 30-80% of AGV patients 1-3 months after surgery (12). This phase involves a paradoxical increase in IOP that seldom resolves spontaneously. Higher preoperative IOP is associated with greater chance of hypertensive phase occurrence (12). More broadly, overall success rate for AGV surgery was reported as 49% after 5 years in one study, and 44% at 10 years in another (7, 11).

Other factors may contribute to AGV failure, however. The AGV directly reduces IOP, but IOP differs from how the optic disc biomechanically responds to pressure changes. This is where corneal hysteresis may fill a risk factor gap (13). Corneal hysteresis, measured by the Reichert ocular response analyzer, indicates the viscoelastic ability of the cornea to dissipate energy after being bent by a force. Low CH has been significantly associated with glaucoma progression in prospective longitudinal studies (4, 6).

Mechanistically, it has been proposed that CH may approximate the biomechanical state of the lamia cribrosa, a connective tissue structure within the optic nerve head that serves as the site of retinal ganglion cell axon exit (14). Low CH may indicate poorer ability of the lamina cribrosa to tolerate intraocular pressure changes, leaving retinal ganglion cell axons more vulnerable to damage from elevated IOP (5). Supporting this are studies showing that decreased CH is significantly associated with both an increased rate of retinal nerve fiber layer loss and the posterior displacement of the lamina cribrosa (5, 15). Given the evidence on CH's mechanism and glaucoma effects, it is possible that a low CH may be linked to worse AGV implantation visual outcomes, since a patient with a weak lamina cribrosa may remain vulnerable to retinal ganglion cell damage even if IOP is reduced by the surgery.

Methods and Statistical Analysis

Data will be collected through a retrospective chart review using the Medflow electronic medical record system and recorded on a Microsoft Excel spreadsheet. Participant confidentiality will be protected through alphanumerical coding. A sample will be assembled of 200 Hispanic, glaucomatous eyes that have undergone AGV surgery at the New York Eye Surgery Center in The Bronx, NY since 2014. The sample will be divided based on the main outcome of interest: postoperative vision loss. Significant postoperative vision loss will be defined as no light perception or losing at least two Snellen eye chart lines within one year post-operation.

Using that criteria, two groups will be formed: 100 eyes that experienced significant vision loss 1 year after AGV surgery, and 100 eyes that did not. Values for the eight baseline preoperative variables (CH, IOP, age, CCT, BCVA, visual field mean deviation, central vision defects, and number of glaucoma medications) will be recorded for each eye and analyzed for inter-group differences. Snellen fraction (e.g. 20/20) will be converted to logMAR score for ease of analysis. Both visual field mean deviation and central vision defects will be based on the 24-2 algorithm of the Humphrey visual field analyzer. Per eye, the values for all independent variables that will be used in the analysis will be the preoperative values that were input closest to the time of AGV surgery.

For this study, multivariable logistic regression analysis will be performed to determine which of the baseline variables contributed to significant vision loss by 1 year after AGV surgery.

Multivariable logistic regression will allow for possible colinear associations between variables to be accounted for and independent associations to be elucidated. Odds ratios, p-values, and 95% confidence intervals will be calculated using SPSS as the primary data analysis software.

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Make ups:

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Title: Understanding Anti-epileptic Drug Adherence using NYS Prescription Monitoring Program
Sponsor: Dr. Arthur Grant
Neurology
Co-Advisor: Nakhutina, Luba, Neuropsychology
Location: Epilepsy clinics are SUNY Downstate Medical Center

Fellowship period: Yes
Involve any? Yes

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where: Application will be sent for IRB expedited review for expected approval prior to June 15, 2020

Research Experience: In college, I assisted in a meta-analysis project on self-regulation and anxiety/depression. My tasks included conducting literature reviews, selecting relevant articles and identifying which measures were used. For my first clinical research experience, I worked with an emergency physician at Bellevue Hospital. I collected basic patient information including sex, age, and chief complaint. I asked a series of questions regarding alcohol, tobacco, and recreational drug use, including opioid use. Additional information was collected If patients screened positive for alcohol and/or drugs using a condensed AUDIT and/or DAST-10. I engaged in motivational interviewing for all patients screening positive for substance use. If patients attested to opioid use, we offered them a naloxone kit and trained them on proper use. This past year, I worked in ophthalmology research in a series of industry-sponsored projects for retinal diseases. As part of those studies, I performed refraction and visual field exams, and assessed patients' visual acuity, contrast sensitivity and intraocular pressures. The information collected was analyzed to assess drug efficacy.

Career goals: In my future career, I would like to be a practicing physician in medicine or neurology. I am interested in engaging in clinical research as part of my practice. This could include projects that are industry-sponsored and independent research projects. I think research is one of the best ways to continue being part of the learning process.

Description: Background:
Epilepsy is a very common neurologic disease with a prevalence of about 1.5% [2]. Compared to the general population, people with epilepsy (PWE) have lower quality of life (QOL) and higher rates of musculoskeletal injuries, burns, accidental death, anxiety, depression and sudden unexplained death, all of which correlate with seizure frequency. Patients with frequent seizures also experience higher levels of stigma and are less likely to be employed than those with infrequent seizures [1]. For these reasons, seizure freedom is the main goal of treatment.
Imperfect adherence is by far the most common cause of preventable seizures in PWE. It is believed to have a greater impact on seizure control than any specific medication adjustment. Imperfect adherence includes missed or delayed medication doses and prescription delays [3]. A study showed that patients who adhere to their antiepileptic drug (AED) regimen have continuous remissions lasting 6 - 24 months compared to those non-adherent patients. The literature distinguishes two types of imperfect adherence. Primary non-adherence is when the patient does not have a prescription for their medication. Secondary non-

adherence is when the patient does not take their medications as per their treatment regimen, despite having the medication [2]. This research group has shown a correlation between self-report of adherence and adherence measured by medication event monitoring system (MEMS) devices. MEMS devices are a pill bottle with an electronic cap that records the time the bottle is opened. Measuring adherence with a MEMS device relies on the assumption that the patient takes the correct amount of pills every time the bottle is opened. A weakness of the MEMS device is that it is too large to carry in a pocket or small purse, and requires that the pills be placed in the associated MEMS bottle rather than a pillbox or other container that may facilitate adherence. The MEMS also requires the patient to come to the physician office to have the data downloaded [2,5].
At Downstate Medical Center, the patient population is primarily of low socioeconomic status (SES), Caribbean-American and African-American. This population group is understudied in adherence research in general, and in adherence research in PWE specifically. Factors contributing to non-adherence, and therefore interventions to improve adherence, are likely to differ between patients of different SES, culture, and ethnicity [3,6]. This research group has shown that negative beliefs about AEDs were significantly associated with self-rated nonadherence in our patient population [6,7].
Rationale:
Improving adherence in PWE will reduce seizures and consequently result in fewer injuries, ED visits, sudden unexplained deaths and overall higher quality of life. However, in order to improve adherence, it must first be accurately measured and patient awareness of their adherence pattern must be determined. In order to improve adherence, potential barriers to non-adherence must be determined, which may differ in the DMC population compared to PWE of different SES and racial and ethnic backgrounds [6]. A literature review revealed that no study has used the New York State Prescription Monitoring Program (NYS PMP) Registry to analyze adherence in PWE. Several commonly used AEDs are DEA controlled drugs, and therefore detailed data on when and where prescriptions are filled are readily available on-line to medical practitioners. This will be the first study to use the NYS PMP database as an objective measure of adherence.

Hypotheses:
1. Self-reported adherence will correlate with objective adherence determined by NYS PMP registry data.
2. Non-adherent patients will fall into two groups: a) those who are aware of their non-adherence and therefore self-report poor adherence, and b) those who are unaware of their non-adherence and therefore self-report good adherence which is contradicted by the NYS PMP data.
Specific Aims:
1. Measure self-reported adherence to DEA controlled AEDs and objective adherence using the NYS PMP Registry in PWE seen in DMC epilepsy clinics.
2. Determine the association between self-reported and objective adherence.
3. Examine barriers to AED adherence based on patients' self-report.
Methods:
Participants:
Participants in this study will be epilepsy patients receiving care at a Downstate Medical Center epilepsy clinic between June 15 and August 15, who are ≥ 18 years old, treated with ≥ 1 DEA controlled AED, and able to complete the questionnaires.
Measures:
Prior to the outpatient visit, the attending physician will access the patient's prescription record from the NYS PMP Registry. This registry displays all the controlled substance prescriptions that the patient has filled in the last twelve months. The compiled information includes the date the prescription was written, the date it was dispensed and the number of pills dispensed. Perfect adherence will be assumed if the patient picked up their latest prescription on or before the day the pills should have run out based on the most recent prior date of picking up the prescription. Non-adherence will be quantified by the number of days between when the pills should have run out and when the patient picked up their prescription.
Self-reported adherence:
At their outpatient visit, study participants will be asked to rate their adherence in the past one week, two weeks and one month (from 1-very poor to 6-excellent) using a validated self-report measure. This measure is drawn from validation research that demonstrated close concordance with electronically monitored adherence in HIV/AIDS [4]. Self-ratings using this measure were significantly associated with seizure frequency in PWE in previous studies [6].
Background information questionnaire:

This questionnaire will include basic demographics including age, gender, education level, country of origin. Epilepsy-related information will include age of seizure onset, seizure type, and seizure frequency, as documented in the patient's medical record. It will also contain the current AED regimen.

Barriers to adherence questionnaire:
A questionnaire will be used to assess the potential barriers of adherence. The questionnaire will comprise 3 main items about 1) routine when taking AED (e.g., at set times of the day, related to specific activities like tooth brushing) and the use of adherence aids (pill boxes), 2) how they deal with a missed dose, for example taking an extra pill with their next dose 3) reason for their nonadherence including forgetfulness, fear of side effects, discomfort after taking AEDs, seizure- free period, no access to refill medications, and used-up AEDs meaning the patient has run out of medication before obtaining a refill.
Statistical Analyses:
Descriptive statistics: Calculate percent adherence, as measured by the NYS PMP Registry. Pearson's correlation to examine the association between the objective and self-reported adherence. Determine the most common barriers to adherence as reported by patients (i.e., percent of patients endorsing the barrier).
Student Role:
I will have a dedicated desk and computer workstation in Dr. Grant's research laboratory. Each week I will access the patient schedules for epilepsy clinics (both private practice and hospital based), and through medical record review will determine which patients are taking a DEA controlled AED. I will provide the attending physician with a list of these patients and he/she will download the relevant prescription information from the NYS PMP record for the two most recent refills. I will record the name of the AEDs, the dates the prescriptions were dispensed, and the number of pills dispensed. I will prefill the demographic information questionnaire as much as possible using the patient's medical record. On the day of their visit, I will give each patient the questionnaire to collect any remaining demographic or clinical data, their self-reported adherence and potential barriers to adherence questionnaires. I will input the data to an SPSS database throughout the summer. We expect to collect data on at least 100 patients by the end of the project. Half-way through the project and at the end of the summer I will run the statistical analyses described above, with the assistance of Drs. Grant and Nakhutina.

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Make ups:

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Title: Multipolar Pacing and Ventricular Arrythmias
Sponsor: Dr. Adam Budzikowsky
Division of Cardiovascular Medicine-EP Section
Co-Advisor:
Location: SUNY Downstate

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: I previously conducted oncology research in Albert Einstein College of Medicine. I was working in a wet lab setting. I interned in the cancer research department at AECOM where Dr. Maitra has been studying the effects of the KRAS mutation on colorectal cancer in human cell lines and murine models. I participated by conducting the Western Blots that would detect the effects on the protein level. We selected antibodies to detect the deviations in protein expression, and I was charged with running the gels and preparing the blots. Afterwards, I would proceed to the dark room to develop the chemiluminescent films. In between, I spent some computer time investigating statistics related to KRAS mutants' protein expressions and tracking the numerous blots and their applied antibodies.

Career goals: As a first year medical student in SUNY Downstate, I most certainly am looking forward eagerly to life as a practicing physician. I see the opportunity to assist patients in the medical setting as an opportunity that is incredibly rewarding and fulfilling. I am especially interested in the field of cardiology; I find the heart and its associated physiology fascinating. As I proceed in my studies, I continuously see the importance and relevance of research and how it has revolutionized medicine. It is something I want to incorporate into my career, and I anticipate that this alumni summer research fellowship will allow me to continue developing the skills necessary to make research a mainstay of my career.

Description: Heart failure has been singled out as an epidemic that is a staggering clinical and public health problem that affects 5.8 million people in the US and 27 million worldwide. It is associated with significant mortality, morbidity, and healthcare expenditures, Hospitalizations for HF remain very frequent and readmission rates continue to rise.(1) Cardiac resynchronization therapy (CRT)is a well-established method of treatment for people with heart failure. (2). With the advent of multipolar pacing of the left ventricle (LV), research has demonstrated that it can outdo multipolar pacing. It is associated with lower mortality rates, hospitalizations, better hemodynamic response, and overall clinical outcomes (3-6). Although all these effects may be a result of reverse remodeling, reduction in burden of ventricular arrhythmias (VA) may contributing to this effect. At the very fundamental level, the presence of myocardial scar and viable tissue creates milieu for ventricular arrhythmia by allowing non-homogenous spread of depolarization hence creating a reentry (7-10). At the same time, one could construe that under correct circumstances colliding wavefronts of depolarization resulting from CRT may also extinguish the reentry. Furthermore, creating more complex waveform associated with multipolar pacing may further contribute to a reduction of ventricular arrhythmias. Additionally,

further reduction in intraventricular conduction delay may contribute to lowering ventricular arrhythmia burden. In our previous study with bipolar only pacing we demonstrated a 24.3% reduction in ventricular burden most significantly pronounced in women (11).

Therefore, we seek to determine whether the multipolar LV pacing is associated with further reduction of VA.

Methods:
We will be seeking access to Abbott remote device monitoring database Merlin. Merlin database contains from several hundred thousand of patients with implantable Abbott devices that are undergoing remoted device monitoring. Detailed data is available for each patient including model of the LV lead pacing factors and whether multipolar pacing is turned on as well as burden of VA. We will select patients with implanted defibrillator connected with a quadripolar left ventricular lead. Comparison will be made between the patient with only bipolar pacing turned on as compared to patients with multi polar pacing turned on. Only patients with true bipolar and multipolar pacing will be enrolled since earlier reports have suggested that extended bipolar pacing (particularly LV electrode to device) may not result in effective cardiac resynchronization.
Classification of ventricular events:
All episodes will be reviewed by 2 independent electrophysiologists. If disagreement is present, the event will be classified by a consensus. Ventricular tachycardia was identified by a rate greater than 170 bpm, regularity of rate and the following:evidence of V-A dissociation and a local electrogram morphology different from baseline. If 1:1 A:V relationship was present, V-V changes had to drive A-A changes. Ventricular fibrillation was identified by rate greater than 240 bpm and disorganized ventricular electrograms. All ventricular events will be collected, which included those that were non-sustained or that required either ATP or shock therapy.
Statistical analysis
Arrhythmic burden will be measured as the sum of ventricular episodes. All data will be checked for normalcy. Wilcoxon signed rank test will be used to compare the differences in cumulative ventricular events. SPSS software will be used for statistical analysis. A p-value of <0.05 will be considered considered significant. The study protocol will be reviewed and we will seek approval by the SUNY Downstate Institutional Review Board. This proposal will be also submitted for approval and access to Merlin database to Abbott.

Sample size calculation:
The purpose of this study is to determine the reduction in ventricular burden in patients received quadripolar CRT, where ventricular burden is measured by the number of ventricular events. We have used the standard sample size calculation formula (Power = 0.8; Confidence = 0.95) to determine the number of patients we will need to study to determine these effects. In this study, we are hoping to demonstrate a 30% decrease in ventricular event in patients received quadripolar CRT.

That is,
Post-CRT VA = Pre-CRT VA * 0.7

From our previous study, the average pre-CRT ventricular event per patient was 7.4 (11). Hence, a 30% decrease in post-CRT ventricular event will be 5.6. Applying these to the standard sample size calculation formula, the sample size is calculated to be 215 patients.

With sample size of 215 patient, data collection should take about 4 weeks. Remainder of the time will be used for data analysis and draft of the manuscript.

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Make ups:

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Title: Pulmonary Edema Development Secondary to Obstructive Apnea
Sponsor: Dr. Mark Stewart
Department of Physiology and Parmacology
Co-Advisor:
Location: SUNY Downstate Basic Science Building

Fellowship period: Yes
Involve any? Yes

Review Board Type: IACUC
Study#: 14-10429
Dates: 6/25/2018 - 6/24/2021
Title: Laryngospasm during seizures
Site: SUNY Downstate
Type: IACUC

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: My research experience began at NYU Langone's Voice Center during the summer after my first year of college. Mentored by Dr. Ryan Branski, PhD, I was able to involve myself in all aspects of the research process. I worked with a large team of doctors and students to plan, execute, and analyze various projects. The main project I worked on was focused on studying the progression and treatments of Recurrent Respiratory Papillomatosis, which resulted in a paper publication in The Laryngoscope.

In addition to the NYU Voice Center, I was also a member of NYU's Presidential Honors Scholars Program, which is a resource consisting of seminars and faculty mentoring to develop the skills necessary for honors-level research. As a Psychology honors student, I connected with Dr. Emily Balcetis, head of the Social Perception, Action, and Motivation Lab. With the help of Dr. Balcetis and a doctoral candidate, I crafted a research proposal based on my interest in health-related issues. I received my first NYU Dean's Undergraduate Research Fund Grant for a study to examine the effects of social support on health-related behavior, such as eating and exercise.

I was also a member of NYU's Psychology Honors Research Seminar Program. During my senior year I attended a full-year honors research seminar to further cultivate my investigative skills and conducted an independent research project. I received my second NYU Dean's Undergraduate Research Fund Grant to examine visual attention strategies on running efficacy. My work culminated in an Honors Thesis in Psychology and a panel presentation at NYU's Undergraduate Research Conference in the Spring of 2019. My experiences to date have taught me a balance between analytical and creative thinking, and I have learned many skills necessary to engage in efficient collaboration throughout the research process.

Career goals: As a medical student, my main (and maybe obvious) goal is to become a physician in order to care for patients. More specifically, I am interested in a career in academic medicine where I can pursue research opportunities in addition to caring for patients. I would also like to help educate the next generation of physicians, which is exemplified in my involvement on the Downstate American Medical Association E-Board. In terms of a specific medical field, I am keeping my options open, as I am still very early into my medical education. However, I have always had an interest in Otolaryngology. My interest began while working in NYU's Voice Lab during college and has only grown since then. As a Downstate medical student, I have gained a deeper understanding and appreciation of head and neck anatomy and feel that I am in a much stronger position now to contribute to

the field in a meaningful way. The Alumni Summer Research Fellowship will afford me the opportunity to pursue my interest in Otolaryngology research, which will ultimately support my career development in the field.

Description: Pulmonary Edema Development Secondary to Obstructive Apnea

Background

In the United States there are approximately 3.4 million Americans living with epilepsy [8]. Among this population, sudden unexpected death in epilepsy (SUDEP) is responsible for 2% to 17% of deaths, depending on the cohort [2]. This proportion may be even higher among children, reaching up to 36% [7]. Additionally, the incidence of SUDEP increases with the severity of epilepsy and may be as high as 1% in individuals with refractory epilepsy [1]. SUDEP is defined as the sudden, unexpected death in a patient with epilepsy, excluding status epilepticus, drowning, trauma, or other structural or toxicologic cause of death [4]. The exact pathophysiology of SUDEP, however, is somewhat unknown. Proposed mechanisms range between cardiac, pulmonary, autonomic, and neurologic etiologies.

One model for SUDEP that has been put forth by our lab, and demonstrated in a rat model, is that seizure induced laryngospasm results in obstructive apnea and respiratory dysfunction, leading to death [6]. In a rat model, laryngospasm induced by seizure activity affecting the laryngomotor areas of the brainstem are sufficient to cause complete airway obstruction [3]. During periods of obstructive apnea, inspiration attempts are associated with large negative airway pressures [6]. These repeated negative airway pressures against a closed larynx cause pulmonary edema, which is the most common post-mortem finding in humans with SUDEP [6]. EEG and trans-tracheal pressure measurements from the 2013 Mortality in Epilepsy Monitoring Unit Study support that this phenomenon in rat models translates to humans [5]. The biomechanics resulting from ictal laryngospasm generate acute pulmonary edema. This may be an effective measure of the severity of the seizure induced laryngospasm, which could have implications for evaluating near-miss SUDEP cases.

Specific Aim

We will test the hypothesis that the severity of pulmonary edema in rats increases with the magnitude and number of inspiratory attempts made during obstructive apnea.

The aim of the study is to evaluate the time-course and level of pulmonary edema development in rats during controlled airway occlusion to simulate laryngospasm-based obstructive apnea. With controlled airway occlusion, we can manipulate the duration of obstructive apnea to test the hypothesis that the magnitude and number of inspiratory attempts determines the degree of pulmonary edema development. We will continuously monitor changes in lung density with either sonography or transthoracic electrical impedance to measure the level of pulmonary edema, but also its time course. We will also measure postmortem lung water as a definitive indicator of pulmonary edema.

Method and Expected Results

We will use a previously established rat model with urethane or ketamine/xylazine anesthesia to monitor the development of pulmonary edema during simulated acute laryngospasm-mediated airway obstruction. A t-shaped tracheal tube will be implanted such that one arm is sealed into the distal trachea and two arms initially remain open to the atmosphere. One of the two exterior arms will be connected to a pressure transducer to measure intratracheal pressure. The other arm will be used for breathing or close to cause obstructive apnea for specific periods. The airway will be completely blocked for periods of 60 seconds. ECG, transtracheal pressure, and oxygen saturation will be measured continuously for all animals. In a set of animals, an ultrasound probe will be placed on the thorax throughout experimental procedures and evaluated for the development of B-lines, a clinical hallmark of pulmonary edema. In other animals, transthoracic impedance will be continuously monitored during experiments. Thoracic air in the lungs and pleural cavity contributes to a relatively high impedance value. The accumulation of pulmonary edema (water with electrolytes) results in a lower transthoracic impedance. Both measures will be evaluated for the temporal profile of changes in relation to the periods of obstructive apnea. At the end of each experiment, the lungs will be harvested and any pleural effusion collected. Lungs will be weighed wet and then dried to yield total lung water.

There will be two main groups of rats. One group for sonography analysis and the other for transthoracic impedance analysis. Each analysis group will be split in half. Half of the animals in each analysis group will experience airway occlusion; the other half will experience equivalent surgical manipulations performed, but with their airways left open.

Ultrasound density of the thoracic cavity will serve as one measure of pulmonary edema. Continuous recordings of the left or right lung will be obtained. An optimal imaging position will be obtained for each animal and used throughout the experiment. Recordings will occur continuously for 5 minutes, starting at 60 seconds prior for baseline, 60 seconds during controlled occlusion, and 180 seconds post occlusion. It is expected that ultrasound density will increase as pulmonary edema develops due to airway occlusion.

Transthoracic electrical impedance will function as another measure of pulmonary edema. We will record a low current sine wave between surface electrodes on the chest wall, allowing for the calculation of electrical impedance. Transthoracic impedance is expected to decrease as pulmonary edema develops in the airway occluded rats.

Following controlled occlusion applications, all animals will be euthanized, and their lungs harvested to assess edematous contribution to total lung water (TLW). There will be an immediate postmortem weighing of both lungs, followed by a drying period of 3 days at 70 °C and then another weighing. The extent of pulmonary edema development in test animals is expected to have a positive correlation with TLW and be greater than that of control animals. The lung weight from both groups can be pooled for comparison because the only differences between the animals studied with transthoracic impedance or ultrasound will be the method used to evaluate pulmonary edema development during the occlusion.

The statistical approach to evaluating these experiments will be analyses of variance (ANOVAs) with obstruction (experimental) vs. no obstruction (control) as the independent categorical variable and the results of the three experimental approaches described above—ultrasound density of the thoracic cavity, transthoracic electrical impedance, and total lung water—as the dependent continuous variables.

Implications

The main goal of this experiment is to shed light on the physiologic process that occurs during acute laryngospasm-mediated airway obstruction. More specifically, we are looking to pulmonary edema as a marker of obstructive apnea. The results of our study may elucidate the importance of evaluating postmortem findings in SUDEP cases to analyze whether preventative action (i.e. minimizing pulmonary edema in cases of acute laryngospasm-mediated airway obstruction) is a useful therapeutic approach. In addition, for near-miss SUDEP cases, there may be a residual impact of the seizure that influences health outcomes. Assessing pulmonary edema after incidents may be a useful way of identifying patients at the highest risk levels for sudden death and for gauging compromise in pulmonary function that contribute to or are indicative of increased mortality.

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Make ups:

Esther Yoo
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Phone: 5163060510
Title: Simulating a BG network model comprised of biophysically realistic dSPNs and iSPNs
Sponsor: Dr. William Lytton
Department of Physiology and Pharmacology
Co-Advisor:
Location: SUNY Downstate Health Science University

Fellowship period: No
Involve any? No

Review Board Type:
Study#:
Dates:
Title:
Site:
Type:

Additional Study:
Dates:
Title:
Site:

When/Where:

Research Experience: Experience:
Case Western Reserve University, Pentzer Lab
September 2017-January 2019
Pickering-type emulsions to template new hybrid materials with 2-D nano sheets
UH Digestive Health Institute, Dr. Keyur Parikh
September 2016-June 2017
L-Menthol infusion as a novel technique during colonoscopy
Cold Spring Harbor Laboratories, Egeblad Lab
September 2013-July 2014
Role of neutrophils in breast cancer metastasis

State University of New York, Stony Brook
September 2011-December 2013
Role of gap junctions in carbon dioxide chemosensitivity
Publications:
1. Ionic Liquid-Containing Pickering Emulsions Stabilized by Graphene Oxide-Based Surfactants Qinmo Luo, Yifei Wang, Esther Yoo, Peiran Wei, and Emily Pentzer Langmuir 2018 34 (34), 10114-10122 DOI: 10.1021/acs.langmuir.8b2011
2. Pickering Emulsion-Templated Encapsulation of Ionic Liquids for Contaminant Removal Qinmo Luo, Yifei Wang, Zehao Chen, Peiran Wei, Esther Yoo, and Emily Pentzer ACS Applied Materials & Interfaces 2019 11 (9), 9612-9620 DOI: 10.1021/acsami.8b21881

Career goals: In addition to becoming a clinician, I'd like to be involved in research on a large capacity throughout my career. Specifically, I'm interested in a systematic approach to learning about the human brain and behavior, and believe pursuing computational neuroscience will facilitate my understanding so that I can eventually contribute to the field. With the development of so much new technology, especially in healthcare, I believe this skillset will allow me to help my peers understand the ever-growing overlap between humanity and technology as applied in medicine.

While there are certain medical specialties that I'm interested in more than others, at this point it would be premature to comment definitively. Regardless of the field I choose, I would like to be involved in academia and the next generation's medical education. Society has changed rapidly in the past few years, with industry becoming a major producer of innovation - nonetheless, academic institutions provide the foundation for which these novelties are founded upon. They are safe havens for new ideas to be fed and grown.

Description: BACKGROUND
Spiny projection neurons (SPNs) are the primary cells of the striatum, which is the input area of the basal ganglia (BG). SPNs can be subdivided into two populations: dSPNs, which project into the direct pathway, and iSPNs, which project into the indirect pathway. These cells and pathways are pharmacologically and functionally distinct: [1] dSPNs express D1-type dopamine (DA) receptors (D1Rs) and functionally allow movement release -- the "GO" pathway. [2] iSPNs express D2Rs and have "NOGO" functionality. This is illustrated by Huntington's disease (HD), in which patients have too much GO, and Parkinson's disease (PD;) patients have too much NOGO. Improving clinical treatments of these major neurological disorders and other conditions involving dysfunctional BG require an improved understanding of the functional organization of SPNs.
Signal processing in CNS neurons is fundamentally an electrical phenomenon[1-3]. One of the limitations of the pertinent studies so far is that they have not been able to directly interrogate membrane potential changes in dendrites[4-7], thus leaving the computational neuroscience without critical model parameters[8-11], which in turn precludes the mechanistic understanding of the BG function in health and disease. As a result, the basic science research on BG inadequately influences the clinic[12-15]. SPN dendrites are too small to record from with electrodes. To overcome this obstacle we will use voltage-sensitive dye imaging of membrane potential transients[16].
dSPNs and iSPNs may differ mostly in their dendritic properties. We hypothesize that these differences will lead to vastly different signal handling properties, which we will assess with a combination of experiments and computer simulations. Current understanding of synaptic integration and initiation of regenerative potentials in SPN dendrites is based on somatic recordings[5]. We will be able to directly measure voltage waveforms at multiple sites along dendrite while simultaneously recording from cell body, and use this to tightly constrain computer simulation parameters. The majority of the proposed experimental measurements can stand alone and provide unique descriptions of signal processing events in dSPNs & iSPNs. When combined with computer simulations, this approach will not only yield the interpretations of multi-site multi-dendrite recordings, but also allow investigation of the computational networks made of dSPNs and iSPNs with realistic dendritic properties.
AIM
Simulate a simple BG network model comprised of biophysically realistic dSPNs and iSPNs
Given the mutual inhibition of these two cell classes (dSPNs and iSPNs) and their different dendritic excitabilities, we predict dominance of the BG direct pathway under the basal conditions, the same net cortical and thalamic glutamatergic input on both pathways with no neuromodulation. Reduced network models (few cell types) and absence of confounding factors, such as DA and cholinergic neuromodulations, permit better understanding of the phenomenon under study: how does differential dendritic excitability of dSPNs and iSPNs impact patterns of network activity. The development of this simple network will then provide the basis for the development of a full striatal model (addition of interneurons and neuromodulatory ambient-s).
METHODS AND STATISTICAL ANALYSIS
The SPNs used in a partner experiment will be filled with biocytin, then reconstructed via Neurolucida and MBF Bioscience, then converted into NEURON code (protocol for aforementioned experiment can be provided upon request). Passive and active membrane properties will be optimized by fitting the experimental data through BluePyOpt in Python. The mullti-site dendritic voltage imaging data will comprise: [a] steady-state attenuation, [b] membrane time constant, [c] bAP amplitude, latency and half-width, [d] spike-order dependent changes in amplitude and duration, [e] TTX-induced changes in AP waveform amplitude, latency and duration, and [f] of α-dendrotoxin/4-AP/ML133-induced changes in AP amplitude, latency and duration.

Biophysically realistic models of dSPNs and iSPNs will be integrated into a computational neuronal network. We will develop a multiscale BG model, starting from the molecular level, with the goal of developing a model at the network level to assess the contributions of dendrites in providing additional and complementary support of continuing activation in the network. The network will contain 400 compartmental neurons arranged in matrix regions connected using synapses containing AMPA/NMDA/GABAA/GABAB receptors, without striosomes: striosomes only occupy about 10%–15% of the total striatal volume. Striosomes are acetylcholinesterase-poor regions, and some, but not all, striosomes have a predominance of dSPNs (up to 70%). The Matrix, on the other hand, contains approximately equal numbers of dSPNs and iSPNs. The simpler and more homogenous

cellular composition of the BG Matrix will permit us to determine the effect of differential dendritic excitabilities on the shape of network activity pattern, since this will have a fixed corticostriatal input and no modulators.

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Make ups: N/A