



GMS Presents:

**SUMMER TRAINING AS
★ RESEARCH SCHOLARS
(STaRS) PROGRAM ★**
Research Symposium

Thursday, August 5, 2021



Boston University Graduate Medical Sciences
Summer Training as Research Scholars

STaRS Research Symposium

Boston University School of Medicine

Thursday, August 5, 2021
12:00 PM – 1:30 PM

Welcome to the Annual Summer Training as Research Scholars (STaRS) Research Symposium, hosted by the Graduate Medical Sciences.

The STaRS program would like to acknowledge the achievements of our students and the faculty and researchers across BU Medical Campus whose mentorship has enhanced both the quality of our students' work and their overall summer experience.

The students have spent this summer conducting research in labs across the BU Medical Campus and we hope you enjoy learning about their projects.

Dr. Isabel Dominguez, STaRS Director

2021 Scholars

The summer 2021 cohort of STaRS scholars included 22 scholars selected from almost 400 applicants.

The STaRS program has also hosted scholars from the AHA-SURE program since its inception, that are also participating in the symposium.

STaRS Scholars

Shantalle Martinez
Hieu Nguyen
Hailey O'Brien
Nicole Briand
Ronald Yang
Sofia Uranga
Julie Aguiar
Ainsley McDonald-Boyer
Claire Gray
Mariana Castaneda
Abraham Sontay
Kamari Weaver
Noah Fields
Jack Friend
Estefania Rivera
Victoria Ontiveros
Liliveth Nwanguma
Nelia Lara-Torres
Zach Yung
Jean Devera -MD
Frances Lara Rodriguez - MD
Arturo Toro - MD

AHA-SURE Scholars

Chelsea Akubo
Corban Jackson
Destiny Jackson
Sheila Pagtakhan



Ronald Yang

Rowan University, Class of 2023

Heart- Brain Axis

Ronald Yang; Ann Fefferman; Daniel Park¹, PhD; Jonathan Wisco, PhD²

¹Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital

²Department of Anatomy and Neurobiology, Boston University School of Medicine

Background: The so-called heart-brain Axis is the neurological and physiological connection between the heart and the brain. The stellate ganglia and superior cervical ganglia are the location of the sympathetic neuronal cells that innervate the vasculature of the heart and brain, respectively. The paravertebral chain connects the ganglia on either side of the neck. In a recent study, the stellate ganglia were shown to remodel with regard to cell body number, size, density, and clustering in the presence of cardiac diseases. As cardiac diseases are a leading cause of death, it is important to develop a tool that is able to quantify disease progression based on nearest neighbor density and size of ganglion neurons. Knowing this, it is possible to create a tool that quantifies cardiac diseases based on these variables in the stellate ganglia.

Hypothesis/Objective: Developing a tool that can quantify cardiac diseases based on current understandings of the heart-brain axis and variables in the stellate ganglia.

Study Design and Research Methods: Biopsies of the stellate ganglia were collected bilaterally from an opportunity sample of 17 willing body donors with and without histories of self-reported myocardial infarction (MI) and/or cerebrovascular accident (CVA). The ganglia were stained with luxol fast blue and cresyl violet which allowed for histological analysis of local neurons. Images of the ganglia after staining were processed using multiple libraries in python, primarily PIL and OpenCV. The images first underwent multiple filters: a high contrast filter and a smoothing filter. After this filter, the image passed through a color threshold that obtained the location of each neuron; the locations of each neuron were used to make a binary image. The binary image was passed through various parameters such as neuron area, radius of the minimum enclosing circle, and a ratio of the area of the neuron and area of the minimum enclosing circle. A heatmap was generated from this last image by calculating the size and nearest neighbor density of the neurons on the binary image. The heat maps were then qualitatively categorized by disease.

Results: A pipeline was created that generates heatmaps of the nearest neighbor density and size of the neurons on the stellate ganglia. The resulting heatmaps require analysis based on the donor's cardiac disease status in order to determine any relationship.

Conclusions: Heatmaps of the nearest neighbor density and size of the neurons potentially show signs of cardiac diseases. Developments within computation pathology is an easily accessible and pioneering way for new technological innovation.



Hieu Nguyen

Washington and Lee University, Class of 2021

Investigating Melanocyte Dynamics in order to Treat Melanoma Metastasis

Hieu Nguyen; Laura Lowery, PhD

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Background: Skin cancer is the most common form of cancer in the United States. Of those, melanoma only accounts for a small fraction of these cases, but it is the most deadly. Once the malignant melanocytes metastasize, current treatments for melanoma such as radiation therapy and immunotherapy are often ineffective and can cause severe side effects. To remedy this problem, our collaborator, Dr. Alani Rhoda, has developed the novel drug corin, a synthetic epigenetic modifier that targets the CoREST complex. Previous preliminary studies have shown that corin effectively reduces CoREST complex activity via the modification of H3K4 and H3K9 and has promisingly dampened the proliferation of multiple melanoma cell lines.

Objective: The objective for this summer is to understand the baseline melanocyte dynamics *in vivo* and to apply this knowledge to determine the effectiveness of corin in treating melanoma metastasis.

Methods: To study melanoma, *Xenopus laevis* is used as our animal model because the melanocytes are easily visible. In addition, a chemical called ivermectin has been demonstrated to induce a melanoma metastasis-like condition in the tadpoles. The experiment is set up to have three groups: the control group which receives neither ivermectin nor corin; the melanoma-metastasis group which receives ivermectin; and the treatment group which receives both ivermectin and corin. Afterward, timelapse videos of these tadpoles in their respective solution are recorded. Next, my specific role in this experiment is to break down the immense information in the time lapse videos into smaller, analyzable data. Specifically, I follow all the individual cells and record their dispersion by using different cell dynamic parameters such as pigment granule expansion and retraction.

Results: After analyzing the control time lapse video, the total cell population is 346 melanocytes. From the time lapse video of the control group, the average time of initial dispersion is **148.3 minutes**. In terms of the percentage of melanocytes expanding, **5.2%** of the melanocytes expand zero-time within the video, **52%** expand one time, **20.2%** two times, **6.6%** three times, and **15.9%** four or more times. Looking at the baseline melanocytes dynamics in detail, melanocytes expand an average of **2.15 times** and each time for **67.78 minutes**. In addition, melanocytes retract an average of **1.219 times** and each time for **10.21 minutes**.

Conclusions: After determining the baseline melanocytes dynamics, we have successfully operationalized and quantified melanocytes dynamics. The next step is to determine the effectiveness of corin. The goal of this research is to comprehensively understand the mechanism behind melanocytes dynamics and utilize this knowledge to test potential therapeutic inhibitors of metastasis.



Mariana Castañeda

University of Texas at El Paso, Class of 2021

Risk Factors for CES-D-10 Depressive Scores from the Bogalusa Heart Study

Mariana Castañeda, Ileana de Anda Duran MD, MPH, Phillip Hwang PhD, MPH

BACKGROUND: Depression is the emotional and mental disorder through which people express a feeling of deep pain, guilt and sadness. It is a common illness that requires treatment that can last for many years and its sequelae may be irreversible. There are multiple reasons why depression is identifiable in some, but almost undetectable in others. There is not a unique cause or causes for depression, it may result from a combination of multiple factors, such as genetic, biochemical, and physiological factors. Experiences such as a traumatic episode, grievance, as well as external stressors, may also contribute to the development of depression. Yet, studies have shown that there are multiple factors that can increase the risk of depression.

OBJECTIVE: This study examined differences in demographic and clinical factors between participants with depressive CES-D-10 scores and those without depressive CES-D-10 scores. This knowledge will help to decrease the percentage of undiagnosed patients with depression by facilitating a more complete screening process to those who are at risk.

STUDY DESIGN AND RESEARCH METHODS: A total of 1291 participants from the Bogalusa Heart Study (BHS), which is a long-term epidemiologic investigation of cardiovascular disease, were included in this study. The Center for Epidemiologic Studies Depression Scale (CES-D-10) scores were recorded to examine the degree of depression. A score of 10 or more indicated a strong marker of depression. Statistical analysis to assess differences between CESD-10 score groups included conducting two-sample t-tests for continuous measures and Chi-square tests for binary categorical measures using SPSS. Level of significance was set at 0.05.

RESULTS: From a total of 1291 participants, 395 had a CES-D-10 score higher than or equal to 10. Among the 395 participants with a CES-D-10 score ≥ 10 , 62% had an education level of high school or less, whereas among the 896 participants with a CES-D-10 score < 10 , 67.40% had an education level of high school or less. This difference of 5.40% in education level between CES-D-10 groups was significant ($p = 0.04$). It is also important to note that there was a trend in BMI between CES-D-10 scores in patients with CES-D-10 scores higher than 10 and high BMI levels.

CONCLUSIONS: The results indicate a significant difference in education levels between participants who obtained a CES-D-10 score higher than or equal to 10 and those with less than 10. However, further research is needed to evaluate whether differences in educational level are independently associated with depression.

Jack Friend

Boston University, Class of 2021



Review of Wnt Signaling component expression in the *Xenopus* Nervous System

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Background: The Wnt/b-catenin signaling transduction pathway is an autocrine and paracrine pathway essential for cell proliferation, body-axis planning, and cell fate. This pathway is conserved across vertebrates, with each intermediate protein having several paralogs (e.g. there are 19 Wnt ligands that bind to 7 Frizzled receptors and 2 LRP-5/6 co-receptors, which acts on 3 Dishevelled proteins). Wnt signaling plays a key role in the development of *Xenopus*, a key model of developmental research. To the new *Xenopus* developmental researcher, the many Wnt component paralogs can be intimidating. One way for the new researcher to learn the role of Wnt component paralogs is to learn their expression pattern during embryo development.

Methods: We collected published information on the expression of Wnt components across *Xenopus laevis* and *Xenopus tropicalis* embryonic development, which are staged according to the normal table of development by Nieuwkoop and Faber. We used the gene expression functionality on Xenbase, the *Xenopus* model organism database, to source selected literature and figures for each Wnt component. Two experimental techniques were commonly used: whole mount *in situ* hybridization, which depicts the localization of the gene's mRNA transcripts, and whole mount immunohistochemistry or immunofluorescence which depicts the location of the transcribed protein.

Results: We summarize the expression patterns of Wnts, Frizzleds, Lrp-5/6, and Dishevelleds in *Xenopus laevis*. Wnt1 is expressed throughout the Mid-hindbrain Boundary, and Wnt3a is expressed along the dorsal brain, a finding that is conserved between chicken and *Xenopus*. In early tailbuds, LRP-5 is preferentially expressed in the hindbrain, notochord, optic vesicle, and somites, but disappears from the notochord and shows in the pharyngeal arches and otic vesicle in late tailbuds. LRP-6 is preferentially expressed in the pharyngeal arches of early and late tailbuds.

Conclusion: The results indicate that different paralogs of Wnt signaling components show different expression patterns. Next, we will look at the binding affinities of each *Xenopus* Wnt-Fzd-LRP receptor complex to learn how these combinations of paralogs may have an agonist or antagonist effect on Wnt target gene expression. Lastly, we will investigate the differences and homology among amphibian and mammalian Wnt signaling, which will help us to translate findings from *Xenopus* to mammalian models.



Ainsley McDonald-Boyer

Rice University, Class of 2022

Comparing Proteoglycan Structures in the Brain Using Proteomics and Glycoproteomic

Ainsley McDonald-Boyer, Margaret Downs, Dr. Joseph Zaia

Department of Biochemistry

Background: Adult cognitive function is contingent on the perineuronal nets which surround neurons and glia cells. A component of the extra-cellular matrix, perineuronal nets are organized networks of proteoglycans and glycoproteins. The proper function of these proteins in the brain is critical; however, its functions can be greatly altered depending on the attachment of glycans through a process called glycosylation. Glycosylation affects the binding properties of the protein which in turn affects its function. Typically, the proteins in the perineuronal nets are highly glycosylated and it is suspected that glycosylation changes with respect to neurological phenomena. With millions of people negatively impacted by conditions such as neurodegenerative diseases, understanding the role of changes in glycosylation states is imperative for improving diagnostic and treatment procedures.

Objective: This research investigated the proteoglycan structures typically found in perineuronal nets through proteomics and glycoproteomics.

Methods: Commercially acquired samples were prepared through enzymatic digestion using Trypsin. Following digestion, the samples underwent liquid chromatography – mass spectrometry. The output from the mass spectrometer was compared to information from the protein sequence database UniProt to identify the protein present in the samples. Using Glycosoft, the glycan structures attached to the proteins identified were then examined. Additionally, the final data was represented in graphical form using R.

Results and Conclusions: This research has produced critical information about glycoform abundance for both Aggrecan and Syndecan, which are important proteins found in the perineuronal nets. From this study, experiments can be built to test glycosylation states of proteins in neural tissue from varying demographics. Such work could lead to a better understanding of neurological conditions and how best to treat them



Nicole Briand

Marist College, Class of 2022

Molecular mechanisms of aortic aneurysms in vascular smooth muscle *Bcl11b* knockout mice

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Background: BCL11B is a transcription factor known to regulate neuronal and T lymphocyte development. Surprisingly, a genome-wide association study showed that a highly conserved enhancer region downstream of BCL11B is highly conserved and harbors single nucleotide polymorphisms associated with increased arterial stiffness. When BCL11B was knocked out of vascular smooth muscle (VSM) of mice treated with the hypertensive drug angiotensin II (angII), development of aortic aneurysms (AAs) was observed. AAs are a ballooning of a weakened vessel wall, and their potential to rupture or dissect is increased with hypertension. Due to a lack of limited knowledge on the molecular causes of AAs and the lack of therapeutics, it is important our goal was to identify molecular regulators of aortic gene expression in BCL11B knockout mice treated with angII.

Methods: RNA sequencing was performed on the aortas of wild type (WT) and VSM *BCL11B Bcl11b* knockout (BSMKO) mice treated with angII, as well as on untreated WT and BSMKO and BSMKO-angII mice (n=5 mice in each group). I focused my analysis on these group comparisons: For both data sets (1) WT/angII vs BSMKO/angII; (2) BSMKO vs BSMKO/angII to identify genes differentially in *Bcl11b*-deleted aortas. For both data sets, genes with known cardiovascular functions were analyzed using Ingenuity Pathway Analysis (IPA). The canonical pathways feature was utilized to examine pathways that were significantly activated or inhibited. Through the upstream regulators and network features, the predicted regulators and central nodes in the comparisons were identified.

Results: Three canonical pathways with an activity z-score < -2 or > 2 had significant overlap with genes in the WT/-angII and vs BSMKO/-angII comparison dataset. Five predicted upstream regulators were present in the data set identified: ABCA1, BRCA1, FST, IL1B, and PPARG. Three networks had scores > 40, indicating high connectivity within the network and close match with IPA literature databases. In the BSMKO and vs BSMKO-angII dataset, there were 42 canonical pathways with an activity z-score < -2 or > 21 and had significant overlap with genes in the database. There were 29 predicted upstream regulators. The networks had weak connectivity and literature match, with 22 out of 25 networks scoring 18.

Conclusions: The results from the upstream analysis and networks features suggest that probable regulatory molecules that are differentially expressed in aortas lacking BCL11B compared to WT after -angII versus BSMKO-angII gene expression include IL1B, CD36, THBS1, PPARG, and SRC. Moreover, probable regulatory molecules of BSMKO versus BSMKO-angII include IL1B, ANGPT2, HGF, and LDB1 were differentially expressed in BSMKO mice treated with angII compared to BSMKO mice not treated with angII. The interaction of these probable regulatory molecules could underlie the development of AAs in BCL11B knockout mice under hypertensive stress. Validation of the molecules' RNA levels of the identified regulatory molecules by qRT-PCR and investigation of their downstream targets are warranted in future studies.



Arturo Toro

Boston University School of Medicine, Class of 2024

Manual segmentation of the caudate tail in high resolution MRI

Arturo Toro³ and Jarrett Rushmore^{1,2,3}

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2. Center for Morphometric Analysis, Massachusetts General Hospital, Boston, MA, USA;
3. Department of Anatomy and Neurobiology, Boston University School of Medicine, Boston, MA, USA

Background: The caudate nucleus is part of the basal ganglia, a collection of subcortical brain structures that facilitate goal-oriented behavior. The caudate is a comma shaped structure with three main parts: the head anteriorly, the body posteriorly, and the tail posteriorly. While the volumes of the head and the body have traditionally been measured on MRI scans, the small size of the caudate tail has not yet been measured on MRI scans. Recent advances in MRI resolution have made it possible to measure the caudate tail, however a protocol to reliably delineate its borders does not yet exist. This gap in knowledge limits our ability to assess how the caudate tail may change in pathological states, or to identify the connections of the caudate tail using non-invasive diffusion-based MRI tractography.

Methods: Neuroanatomical characteristics of the caudate tail were evaluated in 12 neuroanatomical atlases, in 4 hemispheres in human brain sections, and in high resolution ex vivo structural MRI (Edlow et al. 2019). This information was used to design a segmentation protocol, which was employed to label the caudate tail in four high resolution MRI scans from the HCP Young Adults dataset. Segmentation was performed using the 3D Slicer v4.10 software package. Eight caudate tails were independently segmented by two raters and by the same rater on two different occasions, and we then used the Dice-Sørensen similarity metric to determine inter/intra rater reliability. Finally we used our tail segmentation together with filtered diffusion data from the same subjects to illustrate the connectivity of the caudate tail.

Results: Across the eight segmented tails, we achieved a relatively high intra- (mean=0.65, S.D 0.11) and inter- (mean=0.64, SD=0.08) rater reliability, indicating consistent protocol application. The reliabilities of brain 1 and 2 were lower than those of brains 3 and 4 ($p = 0.0046$). We found no relation between the relative sizes of the caudate tails and reliability. Tractographic analysis recapitulated established connections between the caudate tail and multiple brain regions including the prefrontal cortex, premotor cortex, and amygdala.

Conclusions: We produced the first reliable segmentation of the caudate tail on high resolution T1w MRI scans. Reliability scores showed consistency between raters' definition of the caudate tail of the caudate, and also revealed two of the brains had a lower reliability. This result was not due to differences in volume, but is likely to be due to poor signal contrast between the tail of the caudate and the surrounding white matter. These data indicate that more reliable caudate tail can be achieved with better MRI scans, and ensuring these types of scans would lead to more consistent morphometric and tractographic measures.



Shantalle Martinez

University of Miami, Class of 2022

Effects of Exercise on the Hippocampus and Navigation-related Brain Regions

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Background: The hippocampus is a region of the brain that is known to be an integral part of memory, with one subset of memory being navigation and spatial memory. Aging is associated with the deterioration in the structural and functional integrity of the hippocampal memory system. Around 16.5% of the United States population is over the age of 65 and this number is growing rapidly. With the population becoming more vulnerable to memory-loss, it is imperative to find preventative measures that will safeguard the hippocampus and other parts of the brain that are related to navigation. One preventative measure that has been studied is aerobic exercise, with previous literature finding that it is associated with better navigation skills and spatial memory. However, the underlying mechanisms of memory at the hippocampal subfield level - and how exercise impacts this - are not well understood.

Objective: The overall goal is to examine whether hippocampal volume increases following an aerobic exercise intervention compared to baseline.

Study Design: Thirty-two older adults across two randomized controlled trials participated in our study. The participants underwent a series of neuropsychological tests, physiological tests, and an MRI scan. They were instructed to do a 12-week exercise intervention and were randomly assigned to perform either Resistance Training or Endurance Training. Afterwards, the participants underwent the same testing as before. As part of the data analysis, T1- and T2-weighted MRI scans that were collected were processed to calculate hippocampal subfield volume through the Freesurfer 7.1.0 program using scripts on BU's Linux-based shared computing cluster. After the statistical output generation in Freesurfer, the data points were exported to SPSS to run repeated-measures analysis of variance (ANOVA).

Results: We found that aerobic exercise intervention significantly increases the right DG in the Endurance Training group compared to the Resistance Training group, $F(1, 26) = 4.494$, $p = .044$. An exploratory analysis for the effect of exercise intervention on the body of the hippocampus indicated a significant increase in the body of the left CA1 only in the RT group following the exercise intervention, $F(1, 26) = 4.667$, $p = .040$. There were no other significant differences between the two groups and no significant difference in VO_{2Max} .

Conclusion: Aerobic exercise intervention significantly improved the volume of the right DG head subregion, after controlling for sex and intracranial volume. An exploratory analysis for the effect of exercise intervention on the body of the hippocampus indicated a significant increase in the body of the left CA1 only in the RT group following the exercise intervention. Our results indicate that aerobic exercise intervention can attenuate age-related decline in the head of DG, a hippocampal subregion that shows adult hippocampal neurogenesis.



Zach Yung

Trinity College, Class of 2022

Systemic AL Amyloidosis And N-glycosylation

Zach Yung, Gareth Morgan, PhD

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Oncology

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Background: Amyloidosis is a rare disease in which there is a buildup of an abnormal protein caused by protein misfolding. These misfolded proteins then aggregate into ordered structures called amyloid fibrils in tissues which causes organ damage. We are specifically interested in monoclonal immunoglobulin light chain amyloidosis (AL amyloidosis) in which B cells produce faulty antibodies that form fibrils. Past research has suggested that N- glycosylated antibodies may be linked with AL amyloidosis. N-linked glycosylation is a post-translational modification in which carbohydrate attaches to a nitrogen atom, usually from an asparagine residue. It usually occurs in the endoplasmic reticulum and the golgi body at the sequence motifs N-X-S or N-X-T where X is any amino acid but proline.

Hypothesis/Objective: We aim to see whether this possible link is a distinctive feature of AL amyloidosis or just a normal distribution of glycosylated light chains. Additionally, we aim to determine whether the position of the glycosylated residues are compatible with observed AL fibrils.

Study Design and Research Methods: We took 4,232 light chain sequences from our database (AL Base) which have been categorized as AL-PCD and Non-PCD. AL-PCD sequences were ones which were known to be amyloid associated. Non-PCD sequences were supplemented with observed antibody space (OAS) sequences and were healthy sequences which served as our control. We also categorized them according to their type of light chain as either kappa or lambda. We then isolated the sequons within the sequences and determined their distribution and positions in three observed AL fibrils. The three fibril structures we used were PDB entries 6i3c, 6hud, and 6z1o. For each sequence, we made a pairwise alignment against the IMGT germline sequence and then converted the position of the residue of interest to IMGT numbering. Afterwards, we mapped the positions of glycosylated residues to the three fibril structures.

Results & Conclusions: When comparing glycosylated residues between OAS and AL-PCD on each fibril, there were many similar residues that are highlighted in both. The absence of a subset of distinct glycosylated antibodies suggests that glycosylated residues, particularly in the observed positions, are not a distinctive feature of AL amyloidosis. In all 3 fibrils, it was found that a lot of residues that are commonly glycosylated are buried within the structure. Since glycosylated residues cannot be buried within the fibril, these structures are not compatible with glycosylated light chains. This suggests that there is more structural diversity among light chain amyloid fibrils than has so far been observed.



Kamari Weaver

University of Massachusetts, Amherst, Class of 2022

A Review of Site-Directed Mutagenesis Studies in Protein Kinase CK2 α

Kamari Weaver, Isabel Dominguez, Ph.D.

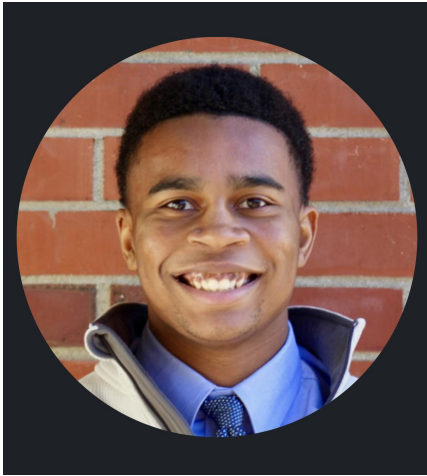
Boston University School of Medicine, Department of Hematology & Medical Oncology, Boston, MA, USA

Background: Protein phosphorylation is a reversible post-translational modification catalyzed by protein kinases - one of the largest families of mammalian genes. Protein kinases regulate many cellular functions including signal transduction, metabolic pathways, and cell proliferation. In our study we focused on protein kinase CK2 α , a well-studied serine/threonine kinase with unique features that distinguish it from other protein kinases. Unlike many other protein kinases, CK2 is second-messenger independent, able to use both ATP and GTP as phosphoryl donors, and is constitutively active. CK2 α can phosphorylate in vitro over 300 substrates involved in diverse biological functions. Mutations in CK2 α have been observed in numerous human pathologies including cancer, neurodevelopmental disorders and neurodegenerative disorders. Questions remain unanswered about the full scope of mutations in CK2 α and how those mutations impact the unique biochemical features of the protein and lead to these pathologies. This project presents a review of the many publications that have generated novel mutants in CK2 α through site-directed mutagenesis. The analysis of these studies gives key insights into biochemical features of the CK2 protein. Hypothesis/Objective: This is a hypothesis-generating literature review project to review and analyze all CK2 α mutations that have been studied in the laboratory to date.

Study Design and Research Methodology: The search terms “Protein Kinase CK2”, “Site-Directed Mutagenesis”, “Inactive mutants”, “Active mutants” were used in PubMed, Google Scholar, and Science Direct search engines to find the studies. There were no limitations in the publication date. Relevance to CK2 α was determined first by the title, then by the methods section including site-directed mutagenesis and evaluation of the mutant with well-established kinetic and biochemical assays. After a publication was selected, the full-text article was reviewed and information about each mutant including the potential role of the mutation was extracted and transferred into a chart for further analysis. Articles were excluded from the study if they were missing mutagenesis studies, performed mutagenesis in other proteins, or were not peer-reviewed.

Results: This study identified, analyzed and categorized over 100 mutations from over 30 publications from 1991 to 2016. Mutants were found in many diverse regions of CK2 α including mutations in basic regions, catalytic subdomains, the glycine-rich loop, and the C-terminal region. Of special attention, Val66 and Trp176 residues were proposed to give CK2 α its ability to utilize GTP as a phosphoryl donor. Mutagenesis studies where these two residues were mutated to the amino acids conserved in 95% of protein kinases presented with a modest decrease in the affinity for GTP, indicating that at least one other residue is involved in the co-substrate ability of CK2 α .

Conclusions: Mutagenesis studies are crucial methods for exploring the biochemical mechanisms that give protein kinase CK2 α its unique and vital role in cellular function. This work presented an up to date review of past mutagenesis studies in diverse regions of CK2 α . It can be a reference point for additional mutagenesis studies to be performed. This information will be used to further investigate the role that CK2 α plays in neurodevelopmental disorders and cancers.



Noah Fields

Stanford University, Class of 2022

Identifying Possible VNTRs using Read Mapping Coverage

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Background and Significance: Tandem repeats (TR) are sequences of two or more DNA base pairs repeating in such a way that the copies lie adjacent to each other on the chromosome. In humans, tandem repeats are associated with a number of diseases and illnesses including Huntington's disease, diabetes, and cancer. The Benson Lab is interested in detecting genetic variation at TR loci, because this variation affects gene expression. TRs that vary in the number of repeated copies are called Variable Number of Tandem Repeats (VNTRs), and the Benson Lab has devised VNTRseek to find these VNTRs. VNTRseek performs well in finding VNTRs for TR Loci shorter than sequencing reads (150bp in our study), however, VNTRseek is unable to find VNTRs with ranges longer than sequencing reads. Improving VNTRseek will allow us to find previously unknown VNTRs which could change the way we understand gene expression. The goal of this project was to perform a series of analysis to look at how mapped read coverage (frequency at which reads map to a region of DNA) at TR loci may provide insight into whether a TR locus is a VNTR or not.

Methods: Sequencing reads from patient HG00096 at the New York Genome Center were aligned to the GRCh38 reference genome using the Burrows-Wheeler Aligner software program (BWA). VNTRseek was given the sequencing reads and a Tandem Repeat reference set to identify variant TR loci and non-variant TR loci. Alignments of sequencing reads to the reference genome were examined to see how and where sequencing reads were mapping to TR loci regions. We focused on TR loci that were designated as nonvariants from VNTRseek. A randomly generated distribution of regions was created for comparison. From the outputs of BWA and VNTRseek, we graphed average read coverage for TR loci and read mapping at locations within the TR loci.

Results: There was no statistically significant difference in average read mapping coverage amongst the TR Loci that varied in size and or variant status. There was also no statistically significant difference in the location in which reads mapped to within the TR Loci and background regions that we looked at.

Conclusion: Because there were no statistically significant findings from our analysis of read coverage TR Loci, we suggest that future studies also incorporate pattern length of TR loci as a feature when analyzing data. Additionally looking at several human subject's sequencing read data may provide more statistically significant results.



Julie Aguiar

Assumption University, Class of 2022

Neural Markers of Effort-Based Decision-Making in Individuals With Schizophrenia

Julie Aguiar; Daniel Fulford; PhD

Department of Occupational Therapy and Psychological and Brain Sciences

Background and Significance: Schizophrenia, a psychiatric disorder affecting approximately 1% of the population worldwide, is characterized by positive and negative symptoms. Positive symptoms are characterized by delusions and hallucinations. Negative symptoms reflect an absence of normal mental functioning, including anhedonia (i.e. an inability to experience pleasure) and avolition (i.e. a lack of motivation). Effort-based decision-making (EBDM), is the process in which individuals weigh the effort costs of a certain task, against the anticipated reward, in order to determine whether certain tasks are worth engaging in. Impaired EBDM is a mechanism underlying motivational deficits. Compared to positive symptoms, patients with schizophrenia typically report the negative symptoms as having a more negative impact on their lives. Additionally, antipsychotic medications, which specifically treat positive symptoms, tend to exacerbate the negative symptoms of schizophrenia. Since most research in Schizophrenia focuses on the positive symptoms, the negative symptoms remain mostly untreated. Given the debilitating nature of negative symptoms, it is imperative to understand which the neural markers of effort-based decision-making are implicated in this process, and how it relates to real-world functioning in order to develop proper treatments.

Methods: A literature review was first conducted on motivational deficits and negative symptoms of schizophrenia as they relate to effort-based decision-making in order to understand which neural regions are implicated and how these were associated with real-world functioning. Once several articles were selected by adhering to the given criteria, they were screened by two raters. 7 articles were then synthesized, and data was extracted from them and organized onto an excel sheet. The results from these articles were then used to design a model of brain structures implicated in EBDM in schizophrenic individuals.

Results: After reviewing, synthesizing, and collecting the necessary information, the implicated brain regions were determined to be: caudate, anterior cingulate cortex, insula, posterior cingulate cortex, and the ventral striatum. It was found that the caudate and anterior cingulate cortex were inhibited during effort-based decision-making in schizophrenic individuals. The ventral striatum showed similar activation to that of healthy controls and the posterior cingulate cortex and insula were found to be inconclusive, suggesting further research should be done on those regions. It was also determined that ventral striatum activation was associated with symptom severity and that, overall, schizophrenic individuals were less willing to exert higher levels of effort in order to gain a reward when compared to healthy controls. Furthermore, decreased connectivity in the associated brain regions was also observed in schizophrenic individuals during the task when compared to healthy individuals.

Conclusions: The collected results suggest that the ventral striatum and associated pathways are impaired in SZ during EBDM. This is related to impaired cognition, reward processing deficiencies, and reduced anticipatory pleasure. Individuals with high levels of negative symptoms likely experience a hard time when attempting to go about everyday activities. This may prevent them from getting or maintaining a job which, in turn, can lead to poverty and consequently homelessness. It may also exacerbate negative health behaviors, such as smoking, poor diet, and lack of physical activity. By understanding which regions are implicated and how they are affected, this allows for further research to be conducted in order to generate the necessary treatments that target the affected regions.



Victoria Ontiveros

Emory University, Class of 2023

Association Between Change in Alcohol Use and Change in sCD14 in People With HIV (PWH)

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Background: Harm reduction of alcohol use is an important public health endeavor. sCD14, a biomarker of monocyte activation in the innate immune system, is associated with alcohol use as well as with disease progression and mortality in PWH. However, it is unclear whether there is an association between reduction in alcohol use and reduction in levels of sCD14; information about this may be clinically relevant to developing interventions to reduce morbidity and mortality for PWH.

Hypothesis: Decreasing alcohol consumption will be associated with a decrease in sCD14 over the same time interval in PWH.

Methods: PWH selected from the Russia ARCH study population in St. Petersburg, Russia had no antiretroviral therapy exposure. The study was 2 years long with 3 checkpoints (baseline, year 1, year 2). Alcohol use was measured with a 30-Day Timeline Follow Back survey and a phosphatidyl ethanol (PEth) blood test; sCD14 levels were measured by ELISA. Primary analysis assessed the association between change in PEth and change in sCD14 over the same 1 year time intervals. Secondary analyses compared change in self-reported alcohol with change in sCD14 over the same 1 year time intervals, and also compared change in alcohol use (PEth and self-reported) in the first year compared to change in sCD14 in the second year in a staggered analysis. We used piecewise linear regression models, adjusting for demographics and comorbidities.

Results: The 349 participants had a mean age of 34 and 71% were male. No association was detected between change in PEth and change in sCD14 levels in the same year ($\beta=47$, CI 95%: [-19, 112]). The relationship between change in self-reported alcohol use and the change in sCD14 over the same time interval was nonlinear. Increasing alcohol use was associated with a shallow decrease in sCD14 ($\beta=0.2$, CI 95%: [-4, 4]) until a threshold of a 10 drink increase was met; thereby, an increase in reported number of consumed drinks was associated with a 9 ng/mL decrease in sCD14 ($\beta=9$, CI 95%: [-15, -3]). No association was detected in the other secondary analyses involving change in PEth and self-reported alcohol use and change in sCD14 over staggered time intervals ($\beta=-12.20$, p -value=0.72; $\beta=3.16$, p -value= 0.14)

Conclusion: We did not detect a significant relationship between change in PEth and change in sCD14 over the same year. The lack of detection of significant results in the primary analysis is contrary to other studies that find higher alcohol use is associated with higher levels of sCD14. Future studies should consider using more frequent checkpoints in order to more precisely determine whether decreasing alcohol use stimulates or suppresses monocyte activity in the innate immune system.



Claire Gray

Brown University, Class of 2023

Identifying strain-specific mutations in the genes encoding the polymerase of Nipah virus

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BACKGROUND and SIGNIFICANCE: Nipah Virus (NiV) is a zoonotic non-segmented negative-strand RNA (nsNSVs) virus belonging to the family Paramyxoviridae. NiV was first recognized in Malaysia where it spread from pigs to humans. The second outbreak, occurring in Bangladesh, showed more human-to-human transmission. NiV is deadly with a case fatality rate estimated at 40% to 75%. Currently, there is no vaccine or treatment for NiV. The viral polymerase which carries out transcription and replication is thought to be a good drug target for nsNSVs. Therefore, it is important to understand how the viral polymerase complex mutates between the two strains of NiV.

METHODS: The Bangladesh (AY988601) and Malaysia (NC_002728.1) NiV sequences were obtained from the NCBI nucleotide database. Benchling was used to translate the sequence for the large polymerase subunit (L), phosphoprotein (P), and nucleocapsid (N) proteins of both strains. An alignment between the two strains was created to identify the amino acid differences in N, L, and P. Next, it was determined which ones had chemically different amino acids indicating a possible impact on function. These mutations for L and P were then modeled on the three-dimensional protein structure using UCSF Chimera software. There is yet to be a structure determined for NiV polymerase, so a polymerase structure of a related virus, parainfluenza virus 5 (PIV5), was used. The structure was obtained from the Protein Data Bank with ID code 6V85. An alignment of PIV5 and NiV was used to find the corresponding residue site on PIV5 L and P.

RESULTS: There were 37 mutations of L found between the two strains. Of these 37 mutations, 20 were chemically distinct amino acids indicating a possible impact on function. The L mutations that were modeled using the PIV5 structure showed that most of the mutations were on the outer region of the polymerase complex, indicating they could impact protein binding. There were mutations found in all the functional domains of L except the capping domain. Interestingly, there was a mutation of L p.K183E found in a highly conserved region between related viruses. The PIV5 polymerase structure is not complete, so not all the mutations could be three-dimensionally modeled. There were 49 mutations of P and 30 of these had chemically distinct amino acids.

CONCLUSIONS: These results indicate that NiV does have mutations of the viral polymerase and other proteins that comprise the viral transcription/replication machinery. Future experiments can be designed to test if and how these mutations impact these processes. Further research could also investigate if these mutations had any impact on the different transmission of the NiV strains. These findings could give insight into how N, L, and P play a role in viruses' ability to adapt to different species. Overall, a better understanding of these mutations could lead to ensuring potential therapeutics target conserved aspects of the polymerase.

Liliveth Nwanguma

Johns Hopkins University, Class of 2023



A Comparison of Digital Biomarkers and Blood-Based Biomarkers for Alzheimer's Disease Dementia Prediction

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Background and Significance - 50 million people are living with dementia worldwide, and this number is predicted to triple by 2050. There is no clear understanding of the risk factors for dementia. Despite the rising dementia population – cognitive assessment tools that apply to age, education, and language/culture are still lacking. Biomarkers that can predict onset/risks of dementia are necessary tools in helping understand dementia risks and can give more accurate results when modeling high-dimensional, heterogeneous, clinical data.

Hypothesis/ Objective - A literature review was conducted to understand the digital and blood-based biomarker approaches to detect Alzheimer's disease (AD).

Study Design and Research Methods - The EBSCOhost database was used through Johns Hopkins University for the literature search. Inclusion criteria were: Publication year 2015-2021, biomarker of interest was addressed, and article focused on AD. The search terms include “deep learning”, “Alzheimer's disease”, “blood-based biomarkers”, “digital biomarkers”. There were 31 results for “Digital biomarkers and Alzheimer's disease” search. The first 31 articles were assessed for inclusion, and 4 met the criteria for inclusion. There were 452 results for “Blood-based biomarkers and Alzheimer's disease” search. The first 50 articles were assessed for inclusion, and 4 met the criteria for inclusion. There were 2301 results for “machine learning and Alzheimer's disease” search. The first 100 were assessed for inclusion, and 4 articles met the criteria for inclusion. Three articles for “digital biomarkers and Alzheimer's disease” were selected from the BU PBHI archive. In total, 15 articles were reviewed in this study.

Results - Blood-based biomarkers demonstrate greater feasibility to be applied at the population level than digital biomarkers. Also, CNS-derived proteins are present in very low concentrations in the periphery, and the form of amyloid-beta (the hallmark of AD) changes constantly, and various proteins in the blood bind with it. However, longitudinal and continuous data collection can be achieved using digital biomarkers. One of the limitations seen in digital biomarkers is data storage and privacy concerns.

Conclusion - AD is a whole-body disease including the peripheral system, thus biomarkers that can induce AD pathology in the CNS provides new perspectives and should be considered in the future for AD research. Non-invasive and easily reliable biomarkers are essential to detect preclinical AD and control disease progression.



Hailey O'Brien

University of Central Florida, Class of 2022

**Putting the 'A' in Pneumonia:
Impact of Supplemental Vitamin A on Pneumonia
Prevention and Treatment**

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Background: Pneumonia is a leading cause of morbidity and mortality worldwide. It affects nearly 450 million people annually, resulting in approximately 4 million deaths. It is well established that proper nutrition contributes to the maintenance of optimal immune function, thus reducing the impact of infections. The micronutrient vitamin A, via its bioactive metabolite retinoic acid (RA), is critical for supporting the cells of the immune system and enhancing resistance to infections. Numerous studies have been conducted to investigate the efficacy of vitamin A administration on the prevention, severity, and mortality of pneumonia. However, vitamin A supplementation remains controversial with regards to preventing or treating pneumonia.

Objective: This project aims to conduct an analysis of the existing literature on the impact of vitamin A supplementation on pneumonia prevention and treatment.

Methods: An online literature review using PubMed was performed for this study. Only randomized controlled trials that evaluated the effect of vitamin A on pneumonia prevention or treatment were included in our analysis.

Results: While vitamin A supplementation does not reduce the incidence or mortality of pneumonia in all kids, it greatly reduces the risk of acquiring pneumonia in those with poor nutritional status. This benefit is lost in well-nourished children. Adjuvant vitamin A therapy does not affect pneumonia-associated mortality, but it reduces the duration of illness, length of hospital stays, and overall severity of the disease in malnourished children. Evidence on the use of vitamin A for preventing or treating pneumonia in adults is lacking.

Conclusion: Based on our analysis, we do not recommend that everyone receive vitamin A to prevent or treat pneumonia. Vitamin A supplementation is most effective in children with poor nutritional status. It remains unclear whether vitamin A administration effectively prevents or treats pneumonia in the adult population as the data are insufficient. Our analysis is limited by the poor methodological quality in some of the included trials. Further research in this field, particularly in adult and elderly populations, is needed to understand the importance of Vitamin A in respiratory health.



Abraham Sontay

University of California, Santa Barbara

Potential Biomarkers to Predict Immunotherapy Responses in HNSCC

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Background: Head and Neck cancer accounts for approximately 650,000 cases and 330,000 deaths worldwide. HPV associated head and neck cancer cases have shown overall better survival rates, however, little is known about the difference HPV infections causes to the tumor microenvironment. Current immunotherapy treatments that target checkpoint inhibitors such as PD-L1 and PD-1 work for a small subset of patients and potential prognostic biomarkers could bring insight into patient responses to certain immunotherapy. Interleukin expressions have been associated with the regulation of M1 and M2 macrophages and their potential as biomarkers is a new area of research in HNSCC. With this, we explored the role of interleukins and their potential as independent prognostic biomarkers.

Hypothesis/Objective: The objective of the study was to analyze gene expression levels in interleukins and explore differences between HPV associated head and neck cancer. This was done by establishing a set of parameters such as HPV status, sample type, and demographics. Kaplan Meier graphs were created for individual interleukins and overall, progressive-free, and disease-free survival rates were analyzed and continued to be studied.

Methods: UCSC Xena browser was used to analyze databases by the Cancer Genome Atlas Program and the genomic data portal. Expression levels and correlation patterns between potential genes are noted and Kaplan Meier plots were determined to see whether regulation of genes lead to better overall survival, disease free survival, and progression free survival. Based on this data, we can hypothesize if a particular interleukin can be potentially used an independent prognosis biomarker.

Results: The Kaplan Meier graphs showed no significant overall survival differences based on single gene expression of interleukins in overall, progressive-free, and disease-free survival rates. However, statistically significant expression levels between interleukins in HPV + and – were observed and may suggest significant differences within the tumor microenvironments.

Conclusion: We concluded that the interleukins show no significant data when it comes to survival rates in patients with HNSCC, suggesting that they cannot be used as independent prognostic factors. However, further analysis on survival rates of a group of interleukins based on function could bring insight into a potential gene signature that may be significant as a biomarker. In addition, exploring expression levels of interleukins in serum samples such as saliva could bring significant statistical differences in HPV + and – related HNSCC.



Frances Lara Rodriguez

Boston University School of Medicine

Aging and prevalence of Enlarged Perivascular Spaces in the population-based Framingham Heart Study

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Background and purpose: Enlarged Perivascular Spaces (ePVS) are considered markers of small vessel disease, associated with stroke and cognitive decline. We characterized the age and sex-specific prevalence of ePVS, and assessed risk factors of ePVS overall and by brain region, in a large community-based sample.

Methods: We included 4,101 Framingham Heart Study participants aged 61.4 ± 14.6 years, 1873 women, with available brain MRI. We used a validated method to rate ePVS in the centrum semiovale (CS) and basal ganglia (BG) regions. Vascular risk factors included systolic and diastolic blood pressure (SBP, DBP respectively), hypertension, smoking, total cholesterol, HDL, LDL, triglycerides, plasma glucose, and diabetes mellitus. Individual risk factors were related to ePVS burden using logistic regression analyses adjusted for age, sex and Framingham Heart Study cohort.

Results: The prevalence of severe ePVS increased substantially with age and was similar in men and women. Older age was associated with greater burden of ePVS in CS, BG and mixed regions ($p < 0.0001$). Hypertension, smoker status, increased DBP and SBP were related to higher burden of CS- and BG-ePVS ($p < 0.05$). Antihypertensive medication use was related to CS and BG-ePVS ($p < 0.05$) and borderline for mixed regions ($p = 0.05$) while HDL was significant only for CS-ePVS ($p < 0.05$). No other significant associations were observed.

Conclusions: We found a strong relation of age with higher ePVS burden across all brain regions. Our observations suggest that ePVS may be a marker of aging, and its relation with vascular risk factors support its role as a cerebral small vessel disease marker.



Estefanía Rivera

Cornell University, Class of 2022

Gender/Sex Science Myth Busters in the Field of Athletics

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BACKGROUND: Despite the efforts through Title IX legislation to equalize the playing field, females continue to face systemic challenges and disparities in athletics. Title IX declared that no person should be excluded from participation of any activity on the basis of sex, which only differentiates males from females on a biological basis. Thus, the amendment failed to address the concept of gender. Gender is a social construct and how a person chooses to identify: women, men, transgender, etc. Many athletes born as males, who identify as women, could undergo hormone therapy to transition into their preferred gender. Hence, this research will highlight the scientific evidence regarding the effect of hormone therapy on the performance of transgender athletes. Secondly, this study will expose the underlying reasons behind the gender disparities that affect both transgender and cisgender athletes.

OBJECTIVE: To determine the challenges that an athlete faces due to their gender, in regards to society's myths/stereotypes about gender and athletics.

STUDY DESIGN AND RESEARCH METHODS: A conceptual framework was designed, which highlighted two main categories of science and culture. For the science category, the subcategories of physical characteristics, athletic performance, genetics, hormones and nutrition were selected. A grounded-theory thematic meta-analysis of existing literature was conducted. Theoretical sampling was performed through literature search utilizing the PubMed database. For this project, only the scientific variables have been coded and analyzed. The principle of constant comparison was applied to redefine and reorganize thematic categories. New major themes were identified and axial coding was employed to define the connection between categories. Memo-writing will be employed to produce an explanation/theory for the research question.

RESULTS: A total of 245 studies were found to be related to the science of athletics. A final determination of themes included: sports/training (41), physiology (38), nutrition (37), endocrine (30), menstrual cycle (29), fatigability (25), medicine (20), youth (13), and transgender (12). All themes were also stratified into subcategories. In particular, transgender subthemes included: hormones (7), team and staff (3) and case studies (2).

CONCLUSIONS: Our results suggest that there are gaps in the scientific literature regarding gender science in the field of athletics: women's varying nutritional needs during the menstrual cycle; transgender athletes' fatigability after hormone therapy; and, the potential benefits of oral contraceptives in thermoregulation. Addressing these gaps will allow for a better understanding of the obstacles an athlete faces due to their preferred gender and how to tackle these in order to ensure equal athletic opportunity for all.



Nelia Lara-Torres

University of Texas Rio Grande Valley, Class of 2022

Breastfeeding and Opiate Use: Annotated Bibliography to Support the ABM Guideline Update

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Background: There has been a greater than fourfold increase in the number of mother-infant dyads impacted by maternal opioid use disorder (OUD), estimated to now affect 6.5 per 1000 live births in the United States (US). There is strong evidence that breastfeeding has specific benefits to opioid exposed mother-infant dyads. Despite this, current US breastfeeding guidelines reduce opportunities for breastfeeding among women who may be interested due to prenatal substance use, that, based on recent evidence, shows little correlation with postpartum use and hence breastfeeding safety. Additionally, new evidence on opioid use and OUD treatment in the perinatal period has emerged since the last guideline publication in 2015. Objective: Therefore, to support an update to the Academy of Breastfeeding Medicine (ABM) guidelines on breastfeeding in the substance exposed mother-infant dyad we aimed to complete an updated literature review and annotated bibliography focused on opioids. The review will support up-to-date, evidenced based, recommendations for breastfeeding to guide physicians and patients in breastfeeding choices and safety.

Research Methods: A search strategy was created using key and mesh terms from PubMed for breastfeeding and opioid use, OUD, and OUD treatments. Meetings were set up with a Boston University librarian for guidance on creating the most inclusive yet focused searches, that ultimately included the following terms: breastfeeding, opioid-related disorders, opioids, illicit drugs, OUD drug therapy, narcotic antagonist, and opiate substitution treatments. After establishing the PubMed search terms the searches were translated, with the help of the librarian, to the Web of Science and Embase to widen the literature search. As the latest ABM guidelines were from 2015, the search was limited to studies published after 2015 to focus the review on the most up to date literature. All citations were exported to Zotero and Rayyan, a systematic review software, to store and include studies that were relevant to the guideline update.

Results: After creating and translating the searches, 813 studies were identified, of which 583 were excluded based on publication prior to 2015. An additional 45 studies were excluded due to duplications. Following deduplication, 165 citations with 73 citations from PubMed, 72 citations from Embase, and 40 citations from Web of Science were reviewed for inclusion. Eight additional studies were excluded because they were animal studies, and 44 were excluded for not being related to breastfeeding and opioid use. 98 studies were ultimately included and summarized in the annotated bibliography.

Conclusions: We identified 98 relevant studies on breastfeeding and opioid use to support updated breastfeeding recommendations. The update to the ABM guidelines will aim to balance mother-infant dyad safety and patient-centered breastfeeding promotion using up-to-date evidence gathered in this annotated bibliography

Sheila Pagtakhan



Longitudinal Changes in Stage B Heart Failure in Individuals with Obesity

As many as half of all patients diagnosed with heart failure in the United States suffer from diastolic heart failure. Results from tests indicate that the problem with the heart is not its ability to pump blood, but its ability to relax. Additionally, this condition can coincide with other medical problems such as diabetes, obesity, hypertension and abnormal lipids.

Preclinical changes in cardiac structure and function prior to incident heart failure in obese individuals can be labeled as metabolic heart disease (MHD). Diastolic dysfunction (DD), left ventricular hypertrophy (LVH), and pulmonary hypertension (PH) are all elements of MHD. Both MHD and obesity escalate the risk of heart failure with preserved ejection fraction (HFpEF).

Although a correlation between MHD and obesity exists, the relationship is not completely understood. Our research was conducted with the purpose to better understand the impact of obesity and weight changes on heart failure. Specifically the effects it has on Stage B heart failure parameters.

We've concluded that these parameters progress over time in individuals with obesity. A new finding not previously reported is that compared to those who have weight loss, those who gain weight have significantly accentuated elevated pulmonary artery systolic pressures over time. Early prevention efforts to minimize weight gain may also be helpful in decreasing the incidence of HFpEF.



Destiny Jackson

An Evaluation of Gender Bias in AI using the Alzheimer's Disease Neuroimaging Initiative

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Gender bias in Artificial Intelligence (AI) is a growing concern in the scientific community as its applications gradually expand into healthcare. We evaluated gender bias in AI via a case study analysis of data from the Alzheimer's Disease Neuroimaging Initiative (ADNI). The goal of this project is two-fold: (1) evaluate the performance of models that are trained on neuroimaging measures with varying levels of gender representation on testing data of equal representation; (2) identify high and low performance areas of these models to improve our understanding of how selection bias impacts the accuracy, precision, and recall of the machine learning models. This project employed three model types, support vector machine (SVM), k-nearest neighbors algorithm (KNN), and random forest classifier (RF) to train and predict Alzheimer's disease (AD) status. These three models were trained using participant-level data from the ADNI GO and ADNI 1 cohorts (n=312) and tested on data from ADNI 2 cohort (n=190). These participant-level data contained the neuroimaging measures (i.e., intracranial volume, the thickness, surface area, and volume measures of 34 selected cortical brain regions, and the volume of subcortical brain regions) and sociodemographic information (i.e., apolipoprotein E4 protein status, age, educational attainment, ethnicity, gender, marital status, and race) of each participant. The models were trained on datasets with graded interval gender representation ranging from 10% female and 90% male to 90% female and 10% male. Subsequently, the models were tested on datasets that were 100% male, 100% female, and 50:50 male to female representation to observe their performance across gender. The desired output of the models was the AD status of each participant (i.e., cognitively normal or AD). Model performance was assessed using accuracy, precision, and recall measures. The preliminary results indicated that the RF classifier outperformed the KNN and SVM classifiers in predicting AD status in the 50:50 male to female, 100% female, and 100% male datasets. Furthermore, the accuracy and precision of the RF model were consistently ~80% across gender representation levels (i.e., the RF model predicts AD status at ~80% in each dataset from 10% to 90% female representation). As part of our future work, we will look to validate our model findings in other AD cohorts that use similar neuroimaging features. This project is among the first to evaluate gender bias in the context of neuroimaging and AD, and its contribution in the context of medical diagnosis is integral to current efforts to mitigate AI bias.



Chelsea Akubo

Effects of Pod-Based Electronic Cigarette Use on Indices of Heart Rate Variability

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Background: Prior studies indicate altered autonomic function with both combustible and earlier generation electronic cigarette use. We sought to evaluate the effects of pod-based electronic cigarettes (ecig) on autonomic regulation in young adult habitual users.

Methods: We recruited healthy young participants aged 18-45 without cardiovascular risk or disease who were tobacco nonusers, pod-based ecig users, or combustible cigarette users. Using a sphygmomanometer, we measured parameters of HRV including standard deviation of the NN intervals (SDNN) and the root mean square differences of successive NN intervals (RMSSD) after a 6 hour product fast and following 10 minutes of structured use of the subject's own product.

Results: In 153 subjects (age 26 ± 7 , 51% women), baseline HRV measures were similar across the tobacco non-user ($N=45$), pod-based ecig ($N=74$), and combustible cigarette users ($N=34$). In analyses adjusted for age, sex, and race, acute pod-based ecig use reduced SDNN (-4.2 ± 2.5 ms) similar to combustible cigarette use (-13.3 ± 3.7 ms) and greater than non-use (6.8 ± 3.1 ms) consistent with a reduction in overall HRV (overall $P=0.003$). Further, parasympathetic function measured by RMSSD was reduced by acute pod-based ecig use (-4.1 ± 3.2 ms) similar to combustible cigarette use (-14.4 ± 4.6 ms) and greater than non-use (7.0 ± 3.9 ms) consistent with a reduction in the short term component of HRV (overall $P=0.02$).

Conclusion: Our data show that acute use of pod-based ecigs is associated with alterations in heart rate variability and cardiac autonomic function.



Corban Jackson

Evaluation of Prediction Models Accounting for Race in the Risk of Atrial Fibrillation

Jackson: Prediction Models Accounting for Race

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Background: Early prediction of atrial fibrillation (AF) could enable the prevention of heart disease and reduce morbidity. However, most existing AF risk prediction models consider a narrow range of biological variables. Race, along with socioeconomic factors and social determinants of health (SDOH) could have a major impact in determining who is most at risk for AF. Identifying opportunities to include these additional factors could increase the accuracy of prediction models across populations.

Methods and Results: A literature search was conducted from electronic databases, PubMed and ScienceDirect, between 2009 and 2019. Eligible studies included atrial fibrillation as the outcome and race as a risk factor. Race was dichotomized as white and black in all of the prediction models. Non-white individuals comprised 0-30.3% across the study samples. White race was associated with an increased risk of AF in all of the models evaluated. Socioeconomic risk factors and SDOH were not included or considered in 3 of the 6 of prediction models.

Conclusion: Race was tested on a superficial level in all included studies without examination of additional factors that may vary across race and ethnicity, making it difficult to ascertain whether the predictive utility of race for AF risk reflects biological, social, demographic, or other factor. Examined models displayed both a lack of population-representative inclusion among non-White populations and insufficient analysis of socioeconomic factors and SDOH in the risk of AF. Studies that did include SDOH lacked adequate exposure data to model interactions between these variables and race. While common AF risk factors have some association with race and AF with varying consistency, consideration of socioeconomic and SDOH information may offer an opportunity to further improve AF risk modeling and advance understanding of the roles of ancestry and sociocultural components of risk mediation in AF.

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THANK YOU ALL!