Scientific Posters

Poster Theme Group A2. Genetics

Poster # 1: REVEALING THE HIDDEN SPATIAL HETEROGENEITY IN HUMAN BRAIN TRANSCRIPTOMES

Presenting author: Hu Chen (Baylor College of Medicine)

Background: Tremendous molecular heterogeneities in AD have been revealed, significantly expanding our understanding of this disease. Nevertheless, many studies have not adequately considered potential latent factors, which are unobserved variables that can significantly impact the observed data and could, therefore, significantly impact biological discoveries. To address this, we aimed to conduct a rigorous statistical inference of potential latent factors inherent in the transcriptome sequencing data of AD. Method: We applied DASC, a latent factory discovery algorithm, on RNA-seq datasets derived from various regions of AD patients and controls. We then conducted an integrative multi-omics analysis to characterize the nature of the identified latent factor. Result: We discovered a latent factor that manifests in RNA-seq data of the human brain from about ~ 2,500 samples, which gives rise to three major transcriptional groups exhibiting distinct molecular activities. We demonstrated and validated that this hidden factor arises from spatial sampling variations. Adjusting for the hidden factor led to the discovering of a new set of RNA signature genes for Alzheimer's disease. In addition, the latent factor was also observed in other data types, including metabolome and proteome profiling. Conclusion: Overall, signatures of spatial heterogeneity are pervasive across various cellular and molecular brain profiles and should be considered in future studies of Alzheimer's disease and related conditions.

Funding: Huffington and Chao endowment; COI: None

Poster # 2: ASSOCIATION BETWEEN EPIGENETIC MARKERS FOR METABOLIC DISEASE AND COGNITIVE IMPAIRMENT IN MEXICAN AMERICANS

Presenting author: Adrian Ballesteros, BS (UNT Health Science Center)

The Mexican American (MA) population is heavily burdened by metabolic conditions such as obesity, metabolic syndrome (MetS), T2D, and an earlier onset of cognitive impairment (CI). These metabolic conditions are significantly associated with risk of CI. Epigenetic markers for MetS (cg06500161 & cg17058475) and T2D (cg07960624, cg06500161, & cg19693031) have been identified in MAs in previous studies. This project aims to determine if epigenetic markers for MetS and T2D found in Mexican Americans are significantly associated with CI in MAs compared to non-Hispanic whites (NHW). DNA obtained from peripheral blood of 551 participants (n=299 MAs, n=252 NHWs) from the Texas Alzheimer's Research and Care Consortium was analyzed for methylation via Infinium® MethylationEPIC BeadChip array (Illumina). Participants were stratified by ethnicity and cognitive status, and methylation data for the epigenetic markers were adjusted and analyzed via t-test and linear regression. Two epigenetic markers for T2D (cg07960624 and cg19693031) were found to be significantly associated ($p=0.0012$ and $p=0.0016$) with CI in MA's compared to CI in NHWs. These epigenetic markers were significantly hypomethylated in MAs with CI compared to NHW with CI. cg07960624 is found within the SAMD12 gene, which regulates RTK signaling, and cg19693031 is found within the TXNIP gene, which is associated with elevated triglycerides in diabetics. Future studies may further investigate how these genes are integrated with other pathways that contribute to cognitive impairment, such as inflammation, oxidative stress, and mitochondrial dysfunction.

Funding: Research reported in this presentation was supported by the National Institute on Aging of the National Institutes of Health under Award Numbers R01AG054073 and R01AG058533, P41EB015922 and U19AG078109. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors would like to thank the Health and Aging Brain Study: Health Disparities

(HABS-HD) research team and participants. This study was made possible by the Texas Alzheimer's Research and Care Consortium (TARCC) funded by the state of Texas through the Texas Council on Alzheimer's Disease and Related Disorders; COI: This study was made possible by the Texas Alzheimer's Research and Care Consortium (TARCC) funded by the state of Texas through the Texas Council on Alzheimer's Disease and Related Disorders.

Poster # 3: COMPARING METHYLATION OF CRP AND IL-6 ASSOCIATED GENES IN COGNITIVELY IMPAIRED MEXICAN AMERICANS TO NON-HISPANIC WHITES

Presenting author: Joseph Sotelo, MS (UNT Health Science Center)

Background: A large pool of literature shows that Alzheimer's Disease (AD) results from inflammatory processes and neuronal loss via tau protein accumulation and amyloid-β plaques. Mexican Americans (MA) are among those with the highest risk of AD, and research into the epigenetics of this association is lacking. C-reactive protein and interleukin-6 are well known for their roles in measuring systemic inflammation. Method: 551 Participants were selected from the Texas Alzheimer's Research and Care Consortium (TARCC). Array probes measured methylation at CpG sites as beta values. CpG sites were identified via literature review. Any differences between cognitively impaired (CI) participants and normal controls (NC) were assessed using a standard two-sample t-test assuming unequal variances in Rstudio. Linear regression analysis was performed in Rstudio. Result: In MAs, there were six significant methylation sites in the CI group compared to the NC group. Cg25325512, cg19821297, and cg10636246 were all significantly hypomethylated in the CI group and are associated with CRP. Cg19638572, cg17412005, and cg20789595 all show significant methylation in the CI group and are associated with IL-6. In NHWs, there was one significant hypermethylated site, cg06690548, which is associated with CRP. Conclusion: The results suggest there is an association between hypomethylated CRP and IL6 genes and cognitive impairment in the Mexican-American population. Further studies should adjust for inflammatory comorbidities, such as metabolic syndrome.

Funding: Research reported in this presentation was supported by the National Institute on Aging of the National Institutes of Health under Award Numbers R01AG054073 and R01AG058533, P41EB015922 and U19AG078109; COI: None

Poster # 4: METHYLATION ANALYSIS OF GENES INVOLVED IN LIPID METABOLISM, TRANSPORT, AND SYNTHESIS IN MEXICAN AMERICANS WITH COGNITIVE IMPAIRMENT

Presenting author: Ryan Liou (UNT Health Science Center)

Introduction: There is a paucity of research investigating epigenetic modifications associated with Alzheimer's Disease (AD) in a metabolically burdened Mexican American (MA) population. Our study aims to elucidate differentially methylated CpG sites associated with AD between MA and Non-Hispanic Whites (NHW) in genes associated with lipid metabolism. Methods: Genes of interest were derived through the utilization of Gene Ontology, wherein genes were categorized based on their association with lipid synthesis, transport, and metabolism. Peripheral blood samples from 551 participants were run on the Illumina Infinium MethylationEPIC chip array. Within each ethnic group (N = 299 MA, N = 252 NHW), participants were stratified by cognitive status (control vs. cognitively impaired (CI)). Beta values, representing the relative degree of methylation, were normalized using the Beta MIxture Quantile dilation method and assessed for differential methylation using the Chip Analysis Methylation Pipeline (ChAMP), limma, and cate packages in R. Results: Upon adjusting to a Bonferroni Correction alpha value of 1.02e-06, examination of 48,748 CpG sites revealed 20 significantly differentially methylated CpG sites across a MA cohort compared to zero differentially methylated CpG sites in the NHW cohort. Notably, the CpG site in the BIN1 gene (cg20973922) is shown to have a decrease in methylation between CI and normal control (NC) in the MA cohort. Additionally, within the GRAMD1A gene, three CpG sites (cg22045942, cg16475416, and cg14640584) displayed decreased methylation between CI and NC in the MA cohort. Conclusions: These findings underscore the presence of differential methylation in specific genes associated with lipid metabolism between CI and NC within the MA cohort compared to NHW. This suggests a unique metabolic-related risk for AD in Mexican Americans, emphasizing the need for more targeted research to identify ethnicity-specific methylation sites, which could prove valuable in discerning CI risk in MA.

Funding: This research project was supported in part by funding provided to the Texas Alzheimer's Research and Care Consortium by the Darrell K Royal Texas Alzheimer's Initiative, directed by the Texas Council on Alzheimer's Disease and Related Disorders; COI: None

Poster # 5: GENOME-WIDE ASSOCIATION STUDY OF VISUAL MEMORY AND SPATIAL ORGANIZATION IN A COMMUNITY SETTING: THE CHARGE CONSORTIUM

Presenting author: Alison Luckey, PhD (UT Health San Antonio)

Background: Poor visual memory task performance is predictive of cognitive decline and dementia. Additionally, deficits in perceptual organization tasks are sensitive to dementia severity. However, no Genome-Wide Association Study (GWAS) has assessed the genomic basis of cognitive visual-spatial phenotypes in a large sample to date. To inform future epidemiological studies where visuospatial memory may be compromised in normal aging, this study aimed to identify common genetic variants associated with visual memory and spatial organization in the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium. Methods: We included dementia- and stroke-free participants aged 45 years or older from up to eight cohorts that performed cognitive tasks assessing delayed visual memory (e.g., Benton Visual Retention Test (BVRT, n=10,932) and Visual Reproductions, n=5,565) or spatial organization (i.e., Hooper Visual Organization Test (HVOT, n=5,055)). Each cohort used linear regression models to relate common genetic variants imputed to the 1000 Genomes panel to each cognitive phenotype. Models adjusted for age, sex, population stratification, education, and study-specific covariates (if applicable). Summary statistic results for the BVRT were meta-analyzed using METAL. Combined-GWAS was used for a joint analysis of all traits. Results: We identified a genome-wide significant variant related to BVRT performance located near the TSHZ3 gene (rs10425277, p=6.76x10-9). TSHZ3 is important for the development and functioning of cortical projecting neurons and may be implicated in the progression of Alzheimer's disease through the repression of CASP4 transcription. Multi-trait analyses including BVRT, visual reproductions, and HVOT identified two additional variants of interest near CNTNAP5 (rs72842999, p=3.1x10-7) and ZFPM2 (rs2957459, p=6.5x10-7), both of which are overexpressed in the brain and have important implications for neurodevelopment. Conclusion: Our findings suggest variants related to visual memory and spatial orientation are implicated in neurodevelopmental and degenerative pathways. Additional analyses are underway to replicate these findings and extend functional annotations.

Funding: (1) South Texas ADRC (P30AG066546); (2) Cross Cohorts Consortium (CCC) (AG059421), CHARGE infrastructure grant from NHLBI (HL105756), Neurology working group of CHARGE (AG033193)

Poster # 6: SNX19 IN HUMAN AUTOPSY BRAINS AND CEREBRAL ORGANOIDS

Presenting author: Liang Ma (UT Health San Antonio)

Background: SNX19 is a key player in endolysosomal and autophagy pathways, which have been extensively reported in neuronal dysfunction and neurodegenerative diseases. Although genetic and cellular evidence suggests SNX19 contributes to neuropathology, the underlying mechanisms remain unknown. Here, we propose to study the mechanism in aging postmortem brain tissue at single cell level and model SNX19 in human induced pluripotent stem cell (hiPSCs) derived brain organoids. Method: We collected human postmortem brain dorsolateral prefrontal cortex (DLPFC) single-cell RNA-seq data from Religious Orders Study/Memory and Aging Project (ROSMAP N = 48). We obtained two human induced pluripotent stem cells (hiPSCs). Result: Single-molecule in situ hybridization experiments found that SNX19 is highly expressed in neurons, particularly excitatory neurons, compared to glia in human postmortem brains. Our single-cell RNA-seq data further demonstrated that SNX19 gene expression is significantly associated with neuritic plaques in excitatory neurons in postmortem brains. Cerebral organoid technology has made it possible to model human neurophysiology and disease with increasing accuracy in human-derived tissue cultures. We performed advanced CRISPR gene editing in hiPSCs to knockout SNX19. We then differentiated them into 2D neurons and 3D cerebral organoids to evaluate the SNX19 impact. Our preliminary data has shown that SNX19 knockout can increase synaptic markers' expression in hiPSC-derived neurons. We observed morphological changes in SNX19 knockout organoids and replicated the synaptic markers' change in the SNX19

knockout brain organoids. Conclusion: Our study identified novel AD factors at SNX19 in human postmortem brains and will define its role in AD using human-derived tissue cultures.

Funding: none; COI: none

Poster # 7: LONGITUDINAL ASSESSMENT OF ALZHEIMER'S DISEASE GENETIC RISK IN MEXICAN AMERICANS AND NON-HISPANIC WHITES

Presenting author: Xueqiu Jian, PhD (UT Health San Antonio)

Background: The risk of Alzheimer's disease (AD) is influenced by complex genetic factors. Genome-wide association studies (GWAS) have identified several AD-associated loci, primarily in case-control samples. Longitudinal assessment of AD occurrence is limited, especially in Hispanics with a higher disease risk. Method: We imputed the Illumina MEGAEX data available on over 1,000 Mexican Americans (MA) and 1,500 non-Hispanic whites (NHW) from the Texas Alzheimer's Research and Care Consortium to the TOPMed reference panel (r2). We analyzed time-to-event data, comprising up to 684 NHW and 726 MA. To assess the ancestry-specific association, we applied Cox mixed effects model with two different timescales, time-on-study and age, respectively, adjusting for age (except for age as timescale), sex, principal components, genetic relationship matrix (random effect), and/or baseline cognitive status and APOE. Our GWAS restricted to variants with imputation quality score >0.3 and MAF>1%. Genome-wide significance level was set to 5x10-8. Result: In NHW, multiple APOE region variants were significant in both timescale models. Using time-on-study as timescale, except for a locus on chr11 (intergenic), no locus was found significant independent of APOE, yet two loci on chr10 and 9 (both intergenic) reached genome-wide significance after adjusting for APOE. Using age as timescale, the chr11 locus became more significant. In addition, a locus on chr8 (SNX31) survived after adjusting for APOE. In MA, analysis using time-on-study as timescale showed no significant loci with/without adjustment for APOE. When further adjusting for baseline cognitive status, multiple loci on chr2 (intergenic), 3 (CADM2), 4 (ARHGAP24), and 6 (AL606923.2) reached genome-wide significance, respectively. Using age as timescale, in addition to the chr4 locus, a different locus on chr6 (TARID) was identified. Conclusion: Limited overlap was observed between our Cox mixed effects GWAS preliminary results and those from case-control GWAS, suggesting unique mechanisms underlying progression to AD. Ancestry-specific analyzes revealed distinct association patterns between MA and NHW, providing evidence of a unique genetic basis for the higher risk of AD in Hispanics. Replication analysis using independent MA and NHW samples are underway to confirm our preliminary findings.

Funding: NIH grant R21AG075791; COI: None

Poster Theme Group A3. Human Neuropathology

Poster # 8: VASCULAR AND METABOLIC PROFILES RELATED TO WHITE MATTER HYPERINTENSITIES IN A MULTIETHNIC COHORT FROM THE HABS-HD STUDY

Presenting author: Douglas Taylor (UNT Health Science Center)

Background: Alzheimer's disease (AD) commonly presents with vascular dementia. Research has shown the relationship between the two to be complex, with many individuals presenting with mixed dementia. Vascular dementia is related to small vessel disease (SVD), which causes microinfarcts that show up as white matter hyperintensities (WMH) in MRI. It is our goal to use WMH to find further differences in vascular and metabolic factors related to AD among a cohort of non-Hispanic whites (NHW), Mexican-Americans (MA) and African-Americans (AA). Method: A cross-sectional analysis of 2363 subjects from the HABS-HD cohort was conducted (967 NHW, 410 AA, and 986 MA). Participants underwent a clinical evaluation and a 3T brain MRI (Siemens Skyra). WMH volume was measured from FLAIR using the Statistical Parametric Mapping (SPM) Lesion Segmentation Tool. WMH were Log transform to achieve normality, and were adjusted for intracranial volume derived from Free3Surfer V6.0 analysis of T1MPRAGE. Fasting blood samples were collected, and clinical measures were

conducted using standard procedures. Clinical, vascular, and metabolic risk factors (table 1) were used in linear regression models as predictors of WMH volume adjusted by intracranial volume (ICV). Age, sex, and education were entered as covariates. Result: The total sample was 62.3 percent female with a mean age of 65.4 years and 13.07 years of education. NHW were older, had more years of education, had lower BMI, lower systolic and diastolic blood pressure, and levels of triglycerides, HA1c, and EGFR when compared to AA and MA ($p \leq 0.005$). In NHW, age, sex, education, SBP, DBP, and hypertension significantly predicted WMH volumes ($p \leq 0.005$). Age, years of education and BMI were the only significant predictors of WMH volume in AA ($p \leq 0.005$), while age, total cholesterol and T4 levels were significant predictors of WMH volume in MA ($p \leq 0.005$). Having a diagnosis of diabetes or dyslipidemia, also predicted WMH volume in MA. Conclusion: Results showed that different factors contribute to WMH volume among different ethnicities. Results suggest that in NHW, a vascular profile is most relevant, while in MA and AA, a metabolic profile seems to be driven the association with WMH.

Funding: Research reported in this presentation was supported by the National Institute on Aging of the National Institutes of Health under Award Numbers R01AG054073 and R01AG058533, P41EB015922 and U19AG078109; COI: N/A

Poster # 9: DISTINCT PATTERNS OF PLAQUE AND MICROGLIA GLYCOSYLATION IN ALZHEIMER'S DISEASE

Presenting author: Caitlyn Fastenau, BS (UT Health San Antonio)

Background: Glycosylation is the most common post-translational modification in the brain. Aberrant glycosylation patterns have been observed in cerebrospinal fluid and homogenized brain tissue of Alzheimer's disease cases. Specifically, dysregulation of a particular form of glycosylation, known as sialylation, has been identified in Alzheimer's disease; although the location of sialylation bonds on cells or protein aggregates is largely unknown. Previous Alzheimer's disease sialylation studies have been limited by spatial resolution methods to localize sialic acid residues at the cellular or aggregate level. Sialylation modifications help facilitate important cellular functions including cell-to-cell interaction, cell migration, cell adhesion, immune regulation, and others. Others have not investigated the two form of sialylation, N- and O-linked sialic acids, in neurodegeneration. Methods: The present study aims to overcome these limitations with novel combinations of histologic techniques. To do so, α-2,6 N-linked sialic acid modification was labeled with SNA plant-derived lectin and O-linked sialic modifications (neutral or sulfonated) were labeled with combinations of Alcian Blue, Periodic Acid-Schiff, and High Iron Diamine chemical stains. To compare sialic acid modifications to pathology, Aβ plaque and phosphorylated tau pathology were histologically probed. 10 clinical Alzheimer's Disease cases were sampled to quantitatively compare regional distribution of sialic acid intensity relative to pathological aggregates across the frontal cortex, hippocampus, and cerebellum. Results: We confirm significantly increased N-sialylation intensity of microglia within the Aβ plaque microenvironment and identify Aβ plaques with O-sialylation chemical stains. Within the frontal and hippocampal regions, there was significantly greater intensity of N-sialylated microglia near Aβ plaques compared to no plaque control regions. This was not conserved with O-sialylation. Analyses of plaque morphologies led to significantly increased N-sialylation of microglia proximal to cored plaques compared to diffuse. Interestingly, phosphorylated tau pathology led to a slight increase in N-sialylation of microglia and no influence of O-sialylation. Conclusions: These findings support microglia sialylation appears to have a dynamic impact on immune cell's engagement with Alzheimer's disease protein aggregates and shed light on the potential of O-sialylated proteins within Aβ plaques that may influence cellular interactions and clearance.

Funding: This work was supported by The National Institutes of Health [T32AG021890 to CF, NS082145 to KFB, R21AG072423 and pilot funding under P30AG013319 to SCH, and P30AG066546 to KFB]; the Texas Alzheimer's Research and Care Consortium to KFB, and the Bartell and Mollie Zachry Endowment for Alzheimer's Research and Patient Care to KFB; COI: none

Poster # 10: COGNITIVE INTEGRITY IN NON-DEMENTED INDIVIDUALS WITH ALZHEIMER'S DISEASE NEUROPATHOLOGY IS ASSOCIATED WITH PRESERVATION AND REMODELING OF DENDRITIC SPINES

Presenting author: Anna Fracassi, PhD (UT Medical Branch at Galveston)

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the most common form of dementia. We previously described that a particular cohort of individuals that present with full AD signature pathology but remain cognitively intact (Non-Demented with AD Neuropathology" - NDAN) are characterized by phagocytic microglia able to remove damaged synapses around plaques. This ability provides protection from greater damage along the axons and dendrites. To assess the efficiency of microglia in preserving dendrites and dendritic spines in NDAN, we conducted a comparative analysis of dendrites and dendritic spines morphology in the frontal cortex of NDAN versus AD and age-matched healthy controls. Methods: We conducted a detailed study of synaptic structure in the plaque area using Thioflavin S to detect Aβ plaques and DiI dye staining, a fluorescent lipophilic cationic indocarbocyanine dye, to detect axons and dendrites. Two regions of interest (ROI) were identified: i) proximal area (around plaques) and ii) distal area (far from plaques). Using Imaris software, specifically the Filament tracer and Classify Spines XTension, we quantified dendrite length, dendrite diameter, spine density, and types. Results: No significant differences were observed in the proximal ROI among controls, AD, and NDAN for all studied parameters, suggesting an overall damaging effect of Aβ plaques on dendrites and spines, irrespective of the pathological condition. In contrast, analysis of the distal ROI revealed that AD dendrites had a significantly larger diameter than NDAN dendrites, possibly indicating abnormal vesicle accumulation. NDAN exhibited a significantly higher spine density than AD in the distal ROI, implying that microglial phagocytic activity restricted damage to the plaque environment. Notably, we measured the relative abundance of four spine types (mushroom, stubby, filopodia, and long thin), with stubby spines being the most common across all groups. Mushroom spines, the least dynamic, were significantly increased in AD versus NDAN and control subjects. Conversely, NDAN individuals showed a higher density of stubby, filopodia, and long thin spines than AD. Conclusions: These findings suggest that the rearrangement of dynamic dendritic spines in NDAN may underlie the ability of these individuals to replace damaged synapses and preserve cognitive integrity.

Funding: NIH/NIA AG072883, R01AG069433 to GT; R21 AG082230 and AARF 22973974 to AF; COI: None

Poster # 11: SELECTIVE SYNAPTIC VULNERABILITY UNDERPINS PATHOLOGICAL TAU SPREADING IN ALZHEIMER'S DISEASE

Presenting author: Shrinath Kadamangudi, MPhil (UT Medical Branch at Galveston)

Background: In Alzheimer's Disease (AD), the spatiotemporal progression of CNS tau pathology remains the strongest neuropathological correlate of cognitive impairment, thus constituting a likely effective treatment target. This is particularly evident in Primary Age Related Tauopathy (PART), where individuals exhibit little-to-no amnestic changes despite regionally confined pathological tau burden (hippocampal/sub-entorhinal areas). Compelling evidence supports a trans-synaptic framework for pathological tau spreading, driven by the propagation of toxic, soluble tau oligomers (tauO) between neuronal networks. However, the selective vulnerability of human neuronal subtypes (i.e. excitatory vs. inhibitory) at the synaptic interface (i.e. pre- vs. post-synapse) to soluble tauO remains largely unknown. Methods: We developed a three-part system to interrogate synaptic tauO vulnerability directly in autopsy human brain specimen. Brain-derived-tau-oligomers (BDTO) were co-immunoprecipitated from pooled PBS-soluble hippocampal fractions in AD (n=4) and PART (n=4) and assayed via liquid-chromatography-with-tandem-mass-spectrometry (LC-MS-MS) to identify putative synaptic interactors (Part-1). Synaptosomes isolated from normal autopsy temporal cortex specimens (n=8) were treated with recombinant tauO (RtauO) and subject to a) multiplexed flow-cytometric immunophenotyping-allowing simultaneous delineation of pre-, post-, glutamatergic, and GABAergic synapses (Part-2), and b) FACS sorting coupled with LC-MS-MS to discriminate tauO vulnerable vs. resilient synaptic proteome (Part-3). Results: Proteomic analyses for AD-BDTO demonstrate nearly equal enrichment of both pre-and post-synaptic compartments, while PART-BDTO preferentially engage pre-synaptic proteins. In our FC-immunophenotyping assay, we further observe increased pre-synaptic (1.5x higher) vs. post-synaptic engagement of RtauO. At the pre-synaptic interface, we observed preferential engagement of RtauO with GABAergic (1.4x higher) vs. glutamatergic synapses. At the post-synaptic interface, however, we observed preferential RtauO engagement with glutamatergic (3.7x higher) vs. GABAergic synapses. Synaptosome FACS/LC-MS-MS experiments are currently ongoing. Conclusions: This study is the first to investigate selective vulnerability of

human synapses, and their subtypes, to soluble tauO. We report converging evidence for pre-synaptic tauO vulnerability, thus suggesting mechanisms underlying post-synaptic resilience, particularly within the context of stand-alone tau pathology. Selective neuronal vulnerability to tauO, however, diverges between pre-and post-synaptic compartments, exhibiting preference for inhibitory and excitatory synapses respectively. These findings underscore the need to better understand and develop tau-directed therapies within the context of selective neuronal vulnerability.

Funding: This research was supported by the UTMB Jeane B. Kempner Fellowship awarded to SK and NIH/NIH R01AG060718 awarded to GT.

Poster # 12: DEEP LEARNING REVEALS DISEASE-SPECIFIC SIGNATURES OF WHITE MATTER PATHOLOGY IN TAUOPATHIES

Presenting author: Charles L. White, III, MD (UT Southwestern Medical Center)

Background: Although disease pathology of tauopathies is characterized by abnormal tau protein aggregation in both gray and white matter regions of the brain, neuropathological investigations to date have generally focused on abnormalities in the cerebral cortex because the canonical aggregates that form the diagnostic criteria for these disorders predominate there. This corticocentric focus tends to deemphasize the disease relevance of the more complex white matter pathologies, which remain less well characterized and understood. Method: We took a data-driven machine-learning approach to identify novel disease-specific morphologic signatures of white matter aggregates in three tauopathies: Alzheimer disease (AD), progressive supranuclear palsy (PSP), and corticobasal degeneration (CBD). We developed automated approaches using whole slide images of tau immunostained sections from 49 human autopsy brains (16 AD,13 CBD, 20 PSP) to identify cortex/white matter regions and individual tau aggregates, and compared the difference in tau-aggregate morphology across these diseases. Results: Tau burden in the gray and white matter for individual subjects strongly correlated in a highly disease-specific fashion. We discovered previously unrecognized tau morphologies for AD, CBD and PSP that may be of importance in disease classification. Intriguingly, our models classified diseases equally well based on either white or gray matter tau staining. Conclusion: Our results suggest that tau pathology in white matter is informative, disease-specific, and linked to gray matter pathology. Machine learning has the potential to reveal latent information in histologic images that may represent previously unrecognized patterns of neuropathology, and additional studies of tau pathology in white matter could improve diagnostic accuracy. We are currently exploring the cell-biological basis of these disease-specific differences in white matter aggregate morphology using immunofluorescence staining to test whether, for example, they are primarily driven by differences in cell types in which the aggregates reside in the different diseases.

Funding: TARCC grant 2020-28-25-II; NIH grants R21 AG066012 and R01 AG059689; Chan Zuckerberg Initiative grant 2018-191983; Broughton Foundation; Erma Lowe Center for Alzheimer's; McCune Foundation; Winspear Family Center for Research on the Neuropatholog of Alzheimer Disease; COI: No relevant conflicts

Poster Theme Group A4. Molecular and Cell Biology

Poster # 13: CROSSTALK BETWEEN HISTONE DEACETYLASES AND VITAMIN A IN ALZHEIMER'S DISEASE: THE ROLE OF HDAC INHIBITION

Presenting author: Chhanda Bose, PhD (Texas Tech University Health Sciences Center)

Background: In Alzheimer's disease (AD), histone acetylation/deacetylation homeostasis is greatly disrupted. Also, retinoic acid (RA), the bioactive metabolite of vitamin A (VA) is reduced with age in human and animal models. Here, we investigated the roles of VA on histone deacetylases (HDACs) with and without HDAC inhibition and oxidative stress (OS) in vitro. Moreover, we established a dose of vorinostat that crosses the blood brain barrier and inhibits HDAC deacetylation without any toxicity in AD mice. Method: For in vitro studies, mouse HT22 cells were treated with vorinostat with and without RA (up to 100 μM) and H2O2 (1mM). MTT and lipid peroxidation assays were performed. Expression of acetylated histone H3 was examined via western blot (WB) and

immunocytochemistry. For in vivo testing, hA□-KI AD mice were treated with vorinostat via oral gavage (50 mg/kg), intraperitoneal (IP; 50 mg/kg), or food pellets (25 and 50 mg/kg). After two weeks, acetylation level and HDAC activity in brain tissue were examined via acetylated histone H3 expression and colorimetric ELISA. Result: Vorinostat and RA treatment (up to and 20) had no significant cytotoxic effects on HT22 cells. H_2O_2 alone at 25-50 μM caused ~30-40% of cell death ($p<0.0001$). RA (5μm), in combination with vorinostat (0.5 μM), exhibited protective effects against H_2O_2 up to 150 μM. In WB, vorinostat (0.5 μM) significantly induced acetylation of histone H3 ($p<0.001$) and gradually increased with vorinostat treatment at 0.5-3.0 μM for 24h, with no change in total histone H3 levels. In brain tissue lysates, significantly increased levels of histone H3 acetylation were observed after oral administration ($p<0.01$) and diet (25 mg/kg, $p<0.05$), with not with IP or diet (50 mg/kg; $p>0.05$). To explore the relationship between acetylated histone H3 expression and RA signaling, we found that acetylated histone H3 co-localized with markers of RA signaling (via RARE-lacZ mice) in hippocampal dentate gyrus. Conclusion: Doses of vorinostat used in vitro induced acetylation without causing any toxic effects. In vivo, we established that 25 mg/kg is an optimal dose in AD mice. VA, in combination with vorinostat, may exhibit synergistic effects in protecting neuronal cells from oxidative stress.

Funding: NIH_RO1_AG073826-01A1; COI: None

Poster # 14: TRANSCRIPTOMIC PROFILING REVEALS THERAPEUTIC INSIGHTS OF MITOCHONDRIA-TARGETED MOLECULES IN ALZHEIMER'S DISEASE USING HUMANIZED Aβ-KNOCKIN (HAB-KI) MICE

Presenting author: Murali Vijayan, PhD (Texas Tech University Health Sciences Center)

Alzheimer's disease (AD) is a complex neurodegenerative disorder, leading to cognitive decline and memory impairments. To gain insights into the molecular mechanisms underlying AD pathogenesis, particularly in the late onset of AD, we conducted RNA sequencing (RNA-Seq) analysis on cortical tissues from 6-month-old Humanized Aβ-knockin (hAb-KI) mice. In this study, our aim was to elucidate the transcriptional changes occurring in the cerebral cortex of hAb-KI mice following treatment with mitochondria-targeted molecules SS31, Mdivi1, and a combination of SS31 and Mdivi1, in comparison to untreated hAb-KI mice. Our results reveal distinct transcriptomic signatures in each treatment group, highlighting the unique molecular responses elicited by SS31, Mdivi1, and their combination. Notably, we observe significant alterations in genes related to oxidative phosphorylation, apoptosis, cellular senescence, autophagy, synaptic function, inflammation, neurotrophic signaling, and neuroinflammation pathways, all of which play central roles in AD pathogenesis. Furthermore, our differential gene expression analysis identifies candidate genes that may be involved in mediating the beneficial effects of these treatments on cognitive function and neuroprotection. This comprehensive RNA-seq analysis provides valuable insights into the molecular mechanisms underlying the effects of SS31, Mdivi1, and their combination in mitigating AD-related pathology. Our findings contribute to a better understanding of potential therapeutic targets and pathways for the treatment of AD, ultimately advancing the development of novel interventions aimed at improving the quality of life for affected individuals.

Funding: The research and relevant findings presented in this poster was supported by the National Institutes of Health (NIH) grants AG069333, AG082961, and AG079264 (PHR).

Poster # 15: ANTI-AGING AND ANTI-HYPERPHOSPHORYLATED TAU PROPERTIES OF DDQ IN MUTANT TAU EXPRESSED HT22 NEURONAL CELLS

Presenting author: Pradeep Jangampalli (Texas Tech University Health Sciences Center)

The purpose of our study is to develop age-related phosphorylated tau (p-tau) inhibitors, for Alzheimer's disease (AD). Until now there are no such small molecules claimed to show promising results to delay the disease process of AD. However, a recently developed molecule, DDQ, has been shown to reduce abnormal protein-protein interactions and protect neurons from mutant protein-induced toxicities in the disease process. In addition, DDQ reduced age- and

Aβ-induced oxidative stress, mitochondrial dysfunction, and synaptic toxicity. To date, there are no published reports on the p-tau interaction of DDQ and Sirt3 upregulation with CREB-mediated mitophagy activation in AD neurons. In the current study, HT22 cells were transfected with mutant Tau (mTau) cDNA and treated with the novel molecule DDQ. Cell survival, immunoblotting, and immunofluorescence analysis were conducted to assess cell viability and synaptic and mitophagy proteins in treated and untreated cell groups. As expected, we found cell survival was decreased in mTau-HT22 cells when compared with control HT22 cells and DDQ-treated mTau-HT22 cells when compared with mTau HT22 cells. P-tau and total tau proteins were significantly reduced in DDQ-treated mTau-HT22 cells and MAP2 levels were increased. Anti-aging proteins like Sirt3, and CREB levels were increased in DDQ-treated HT22 cells and in mTau-HT22 cells treated DDQ. Mitophagy proteins were decreased in mTau-HT22 cells and these were increased in DDQ-treated mTau-HT22 cells. These observations strongly suggest that DDQ has anti-p-tau and anti-aging properties, via Sirt3 overexpression and increased mitophagy proteins.

Funding: AG079264, AG063162, AG071560; COI: None

Poster # 16: CBLN1 ALLEVIATES COGNITIVE DEFICITS IN J20 MICE

Presenting author: Xiangling Yin, MS (Texas Tech University Health Sciences Center)

The objective of this study is to investigate the potential impact of neuronal network dysfunction at the early stages of Alzheimer's disease (AD) pathology, with a specific focus on cerebellin1 (Cbln1), a synaptic organizer within the central nervous system. Our recent observations of decreased Cbln1 expression in post-mortem brains of AD patients prompted our hypothesis that restoring Cbln1 levels might ameliorate cognitive decline. To explore this hypothesis, 8-month-old male J20 AD mice were used for this study because J20 mice show deposition of amyloid-beta and beginning plaque formation and cognitive behavioral deficits by this age. Recombinant human Cbln1 or vehicle (0.9% NaCl) was administered stereotaxically into the lateral ventricles of J20 mice and in age- and sex-matched wild type (WT) mice. Subsequent behavioral assessments, including the Morris Water Maze and Novel Object Recognition Task, revealed significant learning and memory deficits in vehicle-treated J20 mice, compared with vehicle-treated WT mice and Cbln1-treated J20 mice, suggesting that Cbln1 administration alleviated cognitive deficits of J20 mice. Further electrophysiological recordings of long-term potentiation (LTP) in hippocampal slices from Cbln1-treated J20 mice and vehicle-treated WT and J20 mice showed that Cbln1 ICV could restore LTP in J20 mice. Together, these results suggest that Cbln1 could alleviate cognitive deficits and restore neuroplasticity in 8-month-old J20 AD mice.

Funding: Garrison Family Foundation; COI: None

Poster # 17: TRANSCRIPTOMIC RESPONSE BY BRAIN CELLS TO OXYGEN DECLINE

Presenting author: Camille Ravel-Godreuil, PhD (UT Health Houston)

Background: Oxygen plays a crucial role in the survival of mammals. The brain is one of the organs most dependent on oxygen and thus is prone to hypoxia, a condition defined by a drop in available oxygen. Hypoxia has been linked to cognitive impairment in humans and mice. In conjunction with other pathologies such as sleep apnea and heart failure, hypoxia poses a significant risk factor for Alzheimer's disease (AD). Although hypoxia-related molecular pathways have been implicated in AD pathogenesis, little is known about the intrinsic cell type-specific response of the central nervous system to differing oxygen levels or whether a hypoxia response may pre-dispose brain cells to AD pathogenesis. Method: To comprehend the genome-wide molecular response to hypoxia, we performed an RNAseq in mice on the major cell types of the brain, i.e. neurons, astrocytes, and microglia, cultured at different oxygen levels. Differential gene expression and pathway analysis were performed. Results: As expected, brain cells responded to the reduced oxygen by altering the expression of genes involved in metabolism and glycolysis pathways. Interestingly, neurons, astrocytes, and microglia display varied gene changes relevant to chromatin organization, cholesterol metabolism, cell cycle, and neurodegeneration in a cell-type-specific manner. Conclusion: This comprehensive transcript analysis revealed molecular imprints of hypoxia on brain physiology and pathology, and shed light on a novel element involved in the etiology of AD.

Funding: NIH grants AG057587, AG074283, DK122708-03S1, BrightFocus ADR A20183775, and Brown Foundation 2020 Healthy Aging Initiative

Poster # 18: TRACKING TYPE I INTERFERON SIGNALING IN THE AGING BRAIN

Presenting author: Ethan Roy, PhD (UT Health Houston)

Age-related changes underlie the onset of many neurodegenerative diseases. Brain aging is associated with increased inflammatory tone which may contribute to cognitive decline. Type I interferon (IFN) is a family of anti-viral immune cytokines and known to be prominent among immune pathways intrinsically elevated in aged brain. However, the precise cellular and molecular impact of IFN on brain aging is unclear. By examining the transcriptomes of cortex tissues of young and old mice, we detected an aging-associated increase in inflammation, including prevalent IFN-mediated defense response pathways, and simultaneous diminution of various key neuronal processes. Histologically, we observed increased microgliosis in multiple aged brain regions, including hippocampal subregions, cortex, and thalamus, as well as in the corpus callosum. Using a fluorescent fate-mapping reporter which tracks accrued IFN signaling, we uncovered numerous GFP+ cells of many types, including microglia, astrocytes, blood vessels, and neurons, across regions including both gray and white matter compartments, as well as the borders of the aging brain. Selective ablation of Ifnar1 in microglia not only dampened the expression of IFN-induced genes but also restored pathways related to protein homeostasis in the aged cortex. In summary, our study revealed a widespread IFN signaling that affects all cell types and regions during normal brain aging, which seems largely governed by the IFN receptor-mediated response from microglia.

Funding: NIH grants AG057587, AG074283, DK122708-03S1; BrightFocus ADR A20183775; Brown Foundation 2020 Healthy Aging Initiative; COI: None

Poster # 19: SPHINGOSINE KINASE 2 REGULATES PROTEIN UBIQUITINATION IN NEURONS

Presenting author: Ricardo Valencia Jr., BS (UT Health Houston)

Background Two sphingosine kinase isoforms, sphingosine kinase 1 (SPHK1) and sphingosine kinase 2 (SPHK2), synthesize the bioactive lipid sphingosine-1-phosphate (S1P) by phosphorylating sphingosine. SPHK1 is a cytoplasmic kinase and SPHK2 is localized to the nucleus and other organelles. In the cytoplasm, the SPHK1/S1P pathway modulates autophagy and protein ubiquitination, among other processes. In the nucleus, the SPHK2/S1P pathway regulates transcription. Here, we hypothesized that the SPHK2/S1P pathway governs protein ubiquitination in neurons. Methods: We used cultured primary mouse neurons as a model system to study mechanisms associated with the SPHK2/S1P pathway. We overexpressed SPHK2 in these cultures as well as treated these cultures with a specific inhibitor of SPHK2, and performed mass spectrometry and mRNA sequencing to identify the molecular targets of SPHK2. Results: We found that ectopic expression of SPHK2 increases the levels of ubiquitinated substrates in cultured neurons and pharmacologically inhibiting SPHK2 decreases protein ubiquitination. With mass spectrometry, we discovered that inhibiting SPHK2 affects lipid and synaptic protein networks as well as a ubiquitin-dependent protein network. Several ubiquitin-conjugating and hydrolyzing proteins such as the E3 ubiquitin-protein ligases HUWE1 and TRIP12, the E2 ubiquitin conjugating enzyme UBE2Z, and the ubiquitin-specific proteases USP15 and USP30 were downregulated by SPHK2 inhibition. Using RNAs sequencing, we found that inhibiting SPHK2 altered lipid and neuron-specific gene networks, among many others. Genes that encode the corresponding proteins from the ubiquitin-dependent protein network that we discovered with mass spectrometry were not affected by inhibiting SPHK2, indicating that the SPHK2/S1P pathway regulates ubiquitination at the protein level. Conclusion: Our results identify SPHK2/S1P as a novel regulator of protein ubiquitination in neurons and provide a new target for developing therapies for neurodegenerative diseases.

Funding: This work was supported by the National Institute of Neurological Disorders and Stroke [R01NS115886] (A.S.T.), the National Institute on Aging [R21AG083962] (A.S.T. and S.Y.J.), and Hereditary Disease Foundation (J.F.M.M). The Leica DMi8 confocal microscope is supported in part by the Huffington Foundation; COI: The authors declare that there is no conflict of interest.

Poster # 20: STABILIZING G-QUADRUPLEXES INDUCES PIRH2-DEPENDENT DNA DAMAGE IN NEURONS

Presenting author: Rocio Diaz Escarcega, PhD (UT Health Houston)

Background: Non-canonical base pairing between four guanines (G) within single-stranded G-rich sequences leads to the formation of a G-quartet. Self-stacking of G-quartets results in the formation of a columnar four-stranded DNA structure known as the G-quadruplex (G4 or G4-DNA). In cancer cells, G4-DNA regulates a broad variety of DNA-dependent processes including transcription, replication, and telomere function. How G4s function in neurons is poorly understood. Method: We performed a genome-wide gene expression analysis (RNAseq) to identify genes modulated by a G4-DNA ligand, pyridostatin (PDS), in primary cultured neurons. PDS promotes the stabilization of G4 structures, thus allowing us to define genes directly or indirectly responsive to G4 regulation. Result: Our results demonstrate that 901 genes are differentially expressed in neurons treated with PDS out of a total of 18,745 genes with measured expression. 505 genes are downregulated and 396 genes are upregulated, involving networks of genes regulating p53 signaling, immune response, learning and memory, and cellular senescence. Within the p53 network, we discovered that the E3 ubiquitin ligase Pirh2 (Rchy1), a modulator of DNA damage responses, is upregulated by PDS. Ectopically overexpressing Pirh2 promotes the formation of DNA double-stand breaks, suggesting a new DNA damage mechanism in neurons that depends on G4 stabilization. Intriguingly, Pirh2 downregulates DDX21, an RNA helicase that unfolds G4-RNA and R-loops, suggesting that accumulation of R-loops may contribute to PDS-mediated DNA damage.

Funding: 1RF1AG068292, AFAR BIG21042; COI: none

Poster # 21: MAPK-DLK SIGNALING COUPLED WITH DNA DAMAGE PROMOTES INTRINSIC NEUROTOXICITY ASSOCIATED WITH NON-MUTATED TAU

Presenting author: Sanming Li (UT Health Houston)

Alzheimer's disease (AD) is the most prevalent form of neurodegeneration. Despite the well-established link between tau aggregation and clinical progression, the major pathways driven by this protein to intrinsically damage neurons are incompletely understood. To model AD-relevant neurodegeneration driven by tau, we overexpressed non-mutated human tau in primary mouse neurons and observed substantial axonal degeneration and cell death, a process accompanied by activated caspase 3. Mechanistically, we detected deformation of the nuclear envelope and increased DNA damage response in tau-expressing neurons. Gene profiling analysis further revealed significant alterations in the mitogen-activated protein kinase (MAPK) pathway; moreover, inhibitors of dual leucine zipper kinase (DLK) and c-Jun N-terminal kinase (JNK) were effective in alleviating wild-type human tau-induced neurodegeneration. In contrast, mutant P301L human tau was less toxic to neurons, despite causing comparable DNA damage. Axonal DLK activation induced by wild-type tau potentiated the impact of DNA damage response, resulting in overt neurotoxicity. In summary, we have established a cellular tauopathy model highly relevant to AD and identified a functional synergy between the MAPK-DLK axis and DNA damage response in the neuronal degenerative process.

Funding: NIH grants AG057587, AG074283, DK122708-03S1, BrightFocus ADR A20183775, and Brown Foundation 2020 Healthy Aging Initiative (W.C.); COI: none

Poster # 22: THE ROLE OF G-QUADRUPLEX HELICASE DDX5 IN ASTROCYTIC SENESCENCE

Presenting author: Vijay Kumar M J, PhD (UT Health Houston)

Background: Guanine-rich DNA and RNA can fold into non-canonical four-stranded structures called G-quadruplexes (G4s, G4-DNA, G4-RNA). G4-DNA plays, among others, critical roles in replication and transcription while G4-RNA regulates the functions of both coding and non-coding RNAs. Stabilized G4-DNA induces genomic instability,

whereas stabilized G4-RNA disrupts RNA-dependent processes, leading to senescence. Cellular senescence, characterized by chromatin remodeling, transcriptional dysregulation and metabolic reprogramming, plays a key role in aging and age-related neurological disorders such as Alzheimer's disease (AD) and AD-related attention-deficit/hyperactivity disorders (ADHDs). Despite extensive research, it remains elusive how different brain cells respond to metabolic changes and undergo senescence and whether and how G4-DNA and G4-associated proteins and helicases contribute to senescence and aging. Our study aims to identify G4-dependent molecular pathways linked to age-related neurological disorders such as AD and ADHDs. Methods: We used cultured primary human astrocytes as a model system to study mechanisms and pathways associated with senescence, aging and age-related neurological disorders. We used the G4 specific fluorescence probe N-TASQ to detect G4 structures and antibodies raised against senescence markers and DDX5 for immunocytochemistry (ICC). We infected G4 helicase DDX5 tagged to mScarlet in human astrocytes and performed mRNA sequencing (mRNA-seq) to identify the molecular and cellular targets of DDX5 linked to senescence and aging. Results: We discovered that aged human astrocytes contain more G4 structures compared to young ones, making them interesting markers of aging. We also found that DDX5 expression is reduced in aged human astrocytes, providing a possible explanation for the increase in G4s with age. DDX5 regulates the transcription of genes essential for chromatin organization and cell survival; by mRNA-seq, we found that in human astrocytes, DDX5 regulates genes linked to cell cycle, p53 signaling pathways and cellular senescence. Conclusion: Our study demonstrates that G4 homeostasis is imbalanced in aged human astrocytes. Our RNA-seq data provide evidence that DDX5 regulates pathways related to senescence and aging. Our study will create a strong foundation to decode vital functions of G4s and DDX5 in regulating genes related to senescence, and also to delineate molecular pathological mechanisms of age-related neurological disorders such as AD and ADHDs.

Funding: American Federation for Aging Research and Glenn Foundation for Medical Research Breakthroughs in Gerontology (BIG) Award, #BIG21042; COI: None

Poster # 23: ELEVATED CCL23 AND ALTERED MICROBIOME AMONG POST-COVID-19 PATIENTS - A CROSS-SECTIONAL STUDY

Presenting author: Vijayasree Vayalanellore Giridharan, PhD (UT Health Houston)

Background: Dysfunctions in the immune system and alterations in the microbiome following SARS-CoV-2 infection contribute to persistent neurological issues observed in long COVID survivors. Beyond initial respiratory symptoms, a considerable number of COVID-19 patients experience neuropsychiatric manifestations. Our hypothesis posits that imbalances in inflammatory signals and shifts in the gut microbiome status after COVID-19 may be crucial factors contributing to neuropsychiatric disturbances in individuals dealing with the prolonged effects of the disease. Methods: This cross-sectional study included age and sex-matched individuals with post-COVID-19 (n = 26) and healthy controls (n = 62) individuals. We aimed to comprehensively investigate neuropsychiatric symptoms, lipid profile, oxidative stress markers, gut microbiome status, inflammatory signals, and Alzheimer's disease (AD) markers in post-COVID patients' plasma samples. Depressive and anxiety symptoms were assessed using the Hamilton Rating Scale, and cognitive performance was evaluated through standardized measures. We utilized 16S rRNA sequencing to elucidate the intricate details of gut microbiome status. Results: The study revealed no statistically significant differences in depression, anxiety, or cognitive status between the post-COVID-19 and healthy subjects. Similarly, AD markers (Aβ42, Aβ40, t-tau, and p-tau) and oxidative stress markers exhibited no discernible distinctions between the groups. Noteworthy findings include a significant increase in CCL23, the macrophage inhibitory protein-3, among COVID-19 patients. CCL23, implicated in inflammation and host defense, has recently been associated with neuroinflammation in the early stages of AD. Also, apoptosis markers, Caspase-3 and -8 are significantly elevated in COVID-19 patients. Moreover, significantly elevated triglyceride levels were observed in post-COVID-19 individuals. While α-diversity in the gut microbiome showed no significant differences, β-diversity demonstrated a notable distinction between the control and post-COVID-19 groups. Additionally, post-COVID-19 individuals exhibited a decreased abundance of phylum Verrucomicrobia and genus Akkermansia, a short-chain fatty acid producer and microbial group significantly associated with intestinal barrier permeability and cognitive improvement. Conclusion: Although longitudinal studies are imperative to comprehensively explore the behavioral trajectory of COVID-19 individuals, the present findings suggest that CCL23 levels and altered microbiome status may serve as early indicators of post-COVID neurological outcomes.

Funding: NIH (RF1AG072491 to RM and TB) and the Texas Alzheimer's Research and Care Consortium (AGT009122 to RM and TB); COI: Nothing to disclose

Poster # 24: MICROGLIAL ENDOCYTOSIS OF TAU AGGREGATES IS DEPENDENT ON ACTIN, DYNAMIN, AND HEPARAN SULFATE PROTEOGLYCANS

Presenting author: Kristian F. Falkon (Odfalk), BS (UT Health San Antonio)

Background: Tauopathy is a class of neurodegenerative disease characterized by aggregates of aberrantly phosphorylated, misfolded microtubule-associated protein tau (hereafter: Tau). Microglia, the brain resident macrophages, have been shown to internalize and degrade Tau aggregates. However, the exact endocytic mechanism for Tau aggregate endocytosis is still poorly understood. In neurons, heparan sulfate proteoglycan (HSPG) and low-density lipoprotein receptor-related protein 1 (LRP1) bind Tau aggregates and internalize them via macropinocytosis and clathrin-mediated endocytosis (CME), respectively. We hypothesize that antagonism of HSPG/LRP1 and inhibition of macropinocytosis/CME would reduce Tau aggregate endocytosis in microglia. Methods: We studied human recombinant P301S mutant Tau aggregate endocytosis in vitro using BV2 and adult primary microglia. To target HSPG macropinocytosis, we employed heparin (antagonist of HSPGs), cytochalasin D (inhibitor of actin polymerization), wortmannin (inhibitor of phosphoinositide 3-kinase; PI3K), phorbol 12-myristate 13-acetate (PMA; activator of protein kinase C). To target LRP1 CME we used Stable Receptor Related Protein (RAP; antagonist of LRP1) and Dyngo 4a (inhibitor of dynamin). After drug pretreatment, we co-incubated them with these treatments/controls together with fluorescently labeled Tau aggregates. Then, we measured intracellular fluorescence of these aggregates with confocal fluorescence microscopy and flow cytometry. Results: In both BV2 and adult primary microglia, Dyngo 4a robustly inhibited Tau aggregate endocytosis, while heparin, cytochalasin D, and wortmannin only modestly reduced it. Meanwhile, PMA had no effect on Tau aggregate endocytosis in both types of microglia. RAP (only tested in BV2 microglia) had no effect. Conclusions: Thus far, our data suggest that HSPG macropinocytosis which is sensitive to heparin, cytochalasin D, and wortmannin, partially contributes to Tau aggregate endocytosis in microglia, but the lack of any effect of PMA suggests that stimulation of macropinocytosis does not enhance its uptake. The near complete blockade of Tau aggregate uptake by Dyngo 4a might suggest a key involvement of CME in the mechanism. However, dynamin, the target of Dyngo 4a, also plays a role in other types of endocytosis, including macropinocytosis. Future work will focus on elucidating exactly what dynamin dependent process is necessary for Tau aggregate endocytosis in microglia.

Funding: KFO was supported by funding from the National Institutes of Health [T32 NS082145]. SCH is supported by the National Institutes of Health [K01AG066747, R21AG072423], the Alzheimer's Association [AARG-21-846012], CurePSP [679-2021-12] and the Dan & Kelley McNamara Alzheimer's Research Fund; COI: none

Poster # 25: UNIQUE PROTEIN INTERACTORS OF BRAIN-DERIVED TAU OLIGOMERS MAY UNDERLIE DIFFERENTIAL CLINICAL MANIFESTATIONS OF THREE TAUOPATHIES

Presenting author: Danielle Jamison, BS (UT Medical Branch at Galveston)

Background: Tauopathies are a heterogeneous subset of neurodegenerative diseases characterized by abnormal tau aggregation. These diseases are associated with unique tau oligomer polymorphs that may drive diverse clinical manifestations. This is supported by three vastly different tauopathies. Primary age-related tauopathy (PART) is associated with mild amnestic changes despite moderate tau pathology localized to the hippocampus. Alzheimer's disease (AD) is the most devastating neurodegenerative disease, and non-demented with Alzheimer's disease (NDAN) individuals exhibit an asymptomatic tauopathy as they share comparable tau pathology burden with AD patients without cognitive decline or memory deficits. Thus, on the premises that such clinical diversity may be driven in part by different resident protein interactions with tau oligomer polymorphs, the goal of this work was to evaluate whether the unique features of these distinct tauopathies were due to unique brain-derived tau oligomer (BDTO) interactomes. Methods: BDTOs were isolated from PART patients (n = 2, 1M, 1F), AD patients (n = 4, 3M, 1F), and NDAN

individuals (n = 4, 3M, 1F) using immunoprecipitation. Each BDTO and its interactome was submitted to the UTMB Mass Spectrometry Core to undergo liquid chromatography-mass spectrometry/mass spectrometry and label-free quantification. Results: Mass spectrometry identified a subset of proteins that were co-immunoprecipitated with all three BDTOs. On the other hand, fewer BDTO-interacting proteins were found to be uniquely shared by PART and AD as well as PART and NDAN, whereas AD and NDAN shared a majority of their BDTO interactomes. Lastly, each condition also had proteins exclusively associated with the corresponding BDTO. Conclusions: Our results indicate that BDTO from tauopathies with different clinical presentations have unique as well as shared interactomes. Notably, PART (a primary tauopathy) shared a majority of its BDTO interactome with AD and NDAN (secondary tauopathies). However, the reverse was not true as AD and NDAN only shared a fraction of their BDTO interactomes with PART. Further investigation of the similarities and differences between these three diverse tauopathies may highlight novel pathways for neurodegeneration and resilience, and therefore, novel treatments.

Funding: UTMB Presidential Scholars Program, Zelda Zinn Casper Scholar Endowment (DJa); NIA 1R01 AG073133 (GT); COI: No real or perceived conflicts of interest

Poster Theme Group B1. Biomarkers (non-neuroimaging)

Poster # 26: CAN A PICTURE DESCRIPTION DIFFERENTIATE THE NONFLUENT/AGRAMMATIC AND LOGOPENIC VARIANTS OF PRIMARY PROGRESSIVE APHASIA?: EVIDENCE FROM CATALAN-SPANISH BILINGUALS

Presenting author: Lokesh Pugalenthi, BS (Rice University)

Background: Primary progressive aphasia (PPA) is a neurodegenerative syndrome characterized by gradual erosion of speech and/or language. Clinicians often report difficulty differentiating between the logopenic (lv) and nonfluent/agrammatic (nfv) subtypes, as both variants present with disruptions to "fluency" yet for different underlying reasons. In English, acoustic and linguistic markers from connected speech samples have shown promise in machine learning (ML)-based differentiation of nfv from lv. To our knowledge, this approach has not been evaluated in other languages nor in the context of bilingualism. Method: Twenty-four Spanish-Catalan bilingual patients (lv=15, nfv=9) were asked to describe a picture (WAB Picnic Scene) in both their dominant and non-dominant language. From the participant's recorded response, 10 acoustic features were derived with PRAAT and 15 linguistic features were derived with the Natural Language Processing (NLP) tools SpaCy and CLAN. A similarity score between the image and the patient's transcription was derived with the Vision-Language model CLIP. The acoustic features, linguistic features, and CLIP scores, were separately fed into ML classification algorithms for differentiating nfv from lv in participants' dominant and non-dominant samples. Result: The acoustic-based classifiers achieved classification accuracy (F1 score) of 59% in the dominant and 86% in the non-dominant language, respectively. The linguistic-based classifiers achieved F1 scores of 73% in the dominant and 77% in the non-dominant language, respectively. The CLIP-based classifier achieved F1 scores of 82% in the dominant and 82% in the nondominant language, respectively. The acoustic and linguistic classifier performed 25% ($p=0.077$) and 4% ($p=0.18$) better given only non-dominant samples compared to only dominant samples. Conclusion: Taking advantage of recent advances in multilingual NLP, we achieved promising and effective differentiation of nfv from lv for Spanish-Catalan bilingual patients using a nearly automated pipeline. Interestingly, our acoustic and linguistic-based classifiers performed better given responses from a patient's non-dominant language, and the acoustic feature set was more accurate in discriminating between nfv and lv compared to the linguistic model. Future directions include examining patterns in a larger sample size and comparison of performance on different types of connected speech tasks.

Funding: R01AG080470 (NIA/NIH); COI: None

Poster # 27: METHYLATION OF IL-6 & TNF-α ASSOCIATED GENES IN COGNITIVE IMPAIRMENT: A TEXAS ALZHEIMER'S RESEARCH & CARE CONSORTIUM (TARCC) STUDY

Presenting author: Justin De Leon, BS (UNT Health Science Center)

Background: The Mexican American (MA) population poses one of the highest risk groups for the development of Alzheimer's Disease (AD). Inflammatory biomarkers, such as IL-6 and TNF-a, have been associated with cognitive decline but most only in non-Hispanic Whites (NHWs). Epigenetic DNA methylation of CpG islands associated with inflammatory markers (IL-6 and TNF-a) have been studied and identified in other diseases but literature for its effects on cognitive impairment (CI), especially in MAs, is quite sparse. This study aims to determine if DNA methylation of CpG islands for IL-6 and TNF-a are associated with CI in a MA and NHW cohort. Methods: Utilizing the TARCC cohort (N = 551), participants within ethnic groups (N = 299 MAs, N = 252 NHWs) were stratified by cognitive status (normal cognition (NC) or CI). Methylation data at CpG sites were measured as beta values by array probes using the Illumina EPIC array. Linear regression analysis was performed in R comparing the beta value and cognitive diagnosis (NC or CI) for MA and NHW. Covariates include age, sex, education, CD8T cells, CD4T cells, B cells, monocytes, neutrophils, and the APOE gene. Result: The methylation sites cg04381957 and cg04583842 (both associated with IL-6) were significant within MAs. Those sites suggest hypomethylation and hypermethylation, respectively, in CI compared to the NC. Methylation site cg16411857 (associated with TNF-a) was not significant with CI in either MAs or NHWs. Conclusion: There was a stronger association with IL-6 related CpG sites and CI especially in MA at cg04381957 ($p = 0.0035$) within the RFTN1 gene. Future research plans to include inflammatory syndromes, such as diabetes, which could be a potential confounding variable affecting levels of IL-6 or TNF-a.

Funding: HABS-HD Award Numbers: R01AG054073 and R01AG058533, P41EB015922 and U19AG078109. Texas Alzheimer's Research and Care Consortium by the Darrell K Royal Texas Alzheimer's Initiative

Poster # 28: LONGITUDINAL MICRORNA PROFILING OF NEURON-ENRICHED EXOSOMES ASSOCIATED WITH COGNITIVE FUNCTION AND DECLINE

Presenting author: Kumudu Subasinghe, MS (UNT Health Science Center)

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder that disproportionately affects several racial/ethnic groups, including Mexican Americans (MAs). Evidence suggests that early alterations in the AD brain can propagate to local and distal cells through small biological packages called exosomes. Exosomes secreted by neurons are capable of mediating cell-to-cell communication through their bioactive cargo, leading to metabolic and epigenetic reprogramming in target cells. Exosomes derived from neurons have been detected in plasma and isolated from other subpopulations using the neural cell adhesion molecule, CD171. These neuronal-enriched exosomes (NEEs) cross the blood-brain barrier and thus represent an easily accessible derivative of otherwise inaccessible brain tissue in living humans. Small, non-coding RNAs called microRNAs (miRNA) are transcribed from nuclear DNA and function as strong intracellular expression regulators. Transported by the exosomes, miRNAs are believed to significantly alter the expression patterns of their target cells. This project aims to identify the aberrant miRNAs profiles that correlate with disease progression and key comorbidities (e.g., T2D, hyperlipidemia, hypertension) in NEEs of plasma from Mexican Americans and Non-Hispanic Whites. We hypothesize that population-specific differences in NEE miRNA cargo will reflect cognitive function and decline. Methods: Longitudinal plasma samples (two time points, 2 years apart) received from the Texas Alzheimer's Research and Care Consortium (TARCC) were processed using a two-step method that involves precipitation of total exosomes followed by NEE capture with a biotinylated antibody against the neuronal surface marker, CD171. RNA was isolated from NEEs and profiled via next-generation sequencing and analyzed for differential miRNA expression in individuals with cognitive impairment compared to the normal control group. Results: Our preliminary quality control and sequencing data confirmed the successful isolation of the miRNA from NEEs. We identified specific miRNA candidates differentially expressed in cognitively impaired subject's NEEs compared to healthy controls. These miRNAs target gene networks that have been implicated in AD pathophysiology. Conclusion: This innovative workflow along with the unique sample type provides novel insight into the role of exosomal miRNA cargo in AD pathogenesis, identifying novel, population-specific targets for biomarker/diagnosis as well as therapeutic design.

Poster # 29: A STUDY ON THE UTILITY OF BLOOD-BASED BIOMARKERS FOR ALZHEIMER'S DISEASE IN PREDICTING CEREBRAL AMYLOID AMONG INDIVIDUALS WITH DOWN SYNDROME

Presenting author: Shubhangi Awasthi (UNT Health Science Center)

Background: Down Syndrome (DS) is one of the most common genetic disorders. Individuals with DS show Alzheimer's Disease (AD)-related neuropathology at a younger age, placing them at an increased risk for developing dementia. Limited research has explored the relationship between blood-based biomarkers and cerebral amyloid positivity. Our study examines the association between blood-based biomarkers and the presence of cerebral amyloid detected by PET scans in participants with DS. Methods: Data were analyzed on a cohort of n=368 participants with DS aged 30 and above. Proteomic assays of amyloid beta 40 (Aβ40) and 42 (Aβ42), total tau, neurofilament light (NfL), and phosphorylated tau181 (pTau181) were performed on plasma samples using Single Molecule Array (Simoa). Cerebral amyloid levels were obtained through PET Amyloid imaging. Covariates included age, gender, and presence of at least one APOε4 allele. Correlations were run using R statistical software. Random Forest analyses were conducted to examine the link between the select biomarkers and cerebral amyloid SUVR levels. Logistic regressions were also used in examining the utility of AD biomarkers in detecting cerebral amyloid positivity. Significance was set at $p<0.05$. Results: The biomarkers that significantly correlated with cerebral amyloid SUVR levels were Aβ42 ($p=0.020$), total tau ($p<0.001$), NfL ($p<0.001$), and pTau181 ($p<0.001$). There was no significant correlation between Aβ40 ($p=0.888$) and levels of cerebral amyloid. Regression analysis demonstrated a high correlation ($R2 = 0.956$) between the biomarkers and cerebral amyloid positivity. Our profile was accurate in detecting the presence of cerebral amyloid, yielding an area under the curve (AUC) of 0.9984, a positive predictive value (PPV/Precision) of 0.9571, sensitivity of 0.9853, and specificity of 0.9404. Conclusion: Our findings demonstrate that our proteomic profile consisting of the biomarkers Aβ40, Aβ42, total tau, NfL, and pTau181, and select demographics was highly accurate in predicting the presence of cerebral amyloid in our cohort. Having a less invasive and less costly screening tool, such as a blood-based biomarker profile, will allow for earlier detection of dementia in individuals who are at risk. Future research should explore these findings in the context of a larger cohort for increased generalizability.

Funding: NIH/NIA U19AG068054; COI: No conflicts of interest

Poster # 30: NEURONAL SIGNATURES OF OXIDATIVE STRESS VIA EXOSOMAL MIRNA PROFILING

Presenting author: Morad Marikh (UT Arlington)

Background: Alzheimer's disease (AD) progression is insidious with the earliest clinical symptoms appearing decades after key neuropathological changes have occurred. Accurate diagnosis during the transitional period between disease onset & clinical manifestation could provide critical insight into AD pathogenesis & enable development of effective therapeutic strategies to prevent irreversible neuronal death. Evidence suggests that early alterations in the AD brain (e.g., oxidative stress, neuroinflammation, aberrant gene expression) can propagate to local & distal cells through the biological packages secreted by neurons. Circulating exosomes shed from neurons of the CNS may contain cargo that can serve as an easily accessible, early indicator of the forthcoming neuropathological changes in the AD brain, namely oxidative stress. Here, we investigate neuronal exosomal miRNAs released under oxidative stress to identify candidate peripheral biomarkers. Methods: Neuronal exosomes were isolated from SK-N-MC cell culture supernatants. miRNA sequence data was generated from both the exosomal RNAs as well as the neuronal cells themselves. Sequencing data were analyzed with the Qiagen RNA-seq Analysis Portal (v4.0) to identify differentially expressed (DE) between the cellular miRNAs (isolated from the neurons) and miRNAs sequenced from the EVs isolated from the supernatants. We identified miRNAs that exhibited dose-dependent-like increases in exosomes with increasing hydrogen peroxide treatment. Using Target Finder (IPA), we generated a gene list and conducted a Core Analysis, including canonical pathway enrichment analysis (upper bubble plot) and network analysis (lower plots). Results: Many miRNAs are over-represented in exosomes compared to their cells-of-origin; this number increases with H2O2 treatment. Six candidate miRNAs emerged with a stark increase in exosomal cargo in response to H2O2 treatment. The six candidate miRNAs target 980 unique genes. This gene set is enriched for many metabolic pathways and implicates several functional networks, including many AD-relevant pathways (e.g., NFkB). Conclusion: Exosomal miRNAs shed from oxidatively stressed neurons may serve as an early indicator of AD-relevant pathology;

further, our results indicate that these aberrantly expressed miRNAs may regulate gene expression in target cells in a manner that exacerbates pathology.

Funding: This project was supported by the Texas Alzheimer's Research and Care Consortium under the direction of the Texas Council on AD and Related Disorders as well as the Neurobiology of Aging and Alzheimer's Disease Training Grant (NIH–-T32 AG 020494). Protocol and conceptual schematics were created using BioRender. PRISM v.10 was used to generate the fold change line graphs. We also acknowledge Alysia Sebastian, Amaya Green, and Melanie Solis (SRIP students, 2023) for assisting with cell culture work.

Poster # 31: LONGITUDINAL DATA COLLECTED FROM FITNESS TRACKERS PREDICT MILD COGNITIVE IMPAIRMENT

Presenting author: Assaf Gottlieb (UT Health Houston)

Background: Early signs of Alzheimer's disease (AD) are difficult to detect, causing diagnoses to be significantly delayed to time points when brain damage has already occurred and current experimental treatments have little effect on slowing disease progression. Early detection of AD, and tracking of cognitive decline at early stages, are critical tasks, as they allow patients to make lifestyle changes and consider new and experimental therapies. Furthermore, recent clinical trials suggest that therapeutics work best if started at early stages, emphasizing the importance of these tasks for halting cognitive decline and delaying the onset of AD. Although much current research focuses on identifying biomarkers for early detection of AD, none has been validated. Frequently-studied biomarkers such as beta-amyloid and tau levels in cerebrospinal fluid, or brain changes detectable by imaging are invasive and costly, and do not predict conversion from normal to mild cognitive impairment (MCI) or to early AD. Unobtrusive, continuous and passive capture of digital data markers may provide a new direction for detecting early stages of Alzheimer's and pose a significant advantage for elderly patients. Method: We collected sleep, physical activity and heart rate data captured by fitness trackers (Fitbit) over a month from 20 participants (twelve MCI and eight age-matched controls) in a cross-sectional study and constructed a machine learning model to predict MCI status. Result: We tested the use of aggregated vs. daily data across different data modalities. Our computational model obtained good performance on all three types of data modalities (sleep, physical activity and heart rate), ranging between AUC=0.76 using only physical activities to a perfect separation between MCI and controls (AUC=1.0) when all three modalities were combined. Deep sleep length, light physical activity length and different heart rate zones were among the top model features. Conclusion: Our results pave the way to our ultimate goal: detecting cognitive decline and conversion to Alzheimer's Disease in a longitudinal study. By recording digital data over time, we intend to predict the progression from MCI to AD, and identify individuals at risk of developing MCI early, supporting future interventions for slowing or halting the progression.

Funding: Alzheimer's Association award (AARG-NTF-21-847409); COI: None

Poster # 32: PATTERN DYNAMICS OF BRAIN WAVES AFFECTED BY ALZHEIMER'S DISEASE

Presenting author: Clarissa Hoffman, BS (UT Health Houston)

Background: Alzheimer's Disease (AD) is a complex neurodegenerative condition that manifests at all levels, from cellular to cognitive. Here, we investigate the impact of AD pathology on neurocircuits and study changes in spiking activity and synchronized extracellular fields. While most studies are based on analyzing instantaneous or time-averaged characteristics of neuronal activity, we focus on intermediate timescales-patterns of spike trains and waveforms of oscillatory potentials recorded from the hippocampal CA1 area in mice engaged in spatial navigation. Methods: We propose an alternative approach that focuses on the morphologies of waveforms-the patterns of the brain waves over finite timescales-and patterns of neuronal spike trains. Specifically, we use two independent methods for quantifying the structural regularity and irregularity of brain waves and correlate the resulting "stochasticity scores" with behavior. The first quantifies the "randomness" or "haphazardness" of patterns through their deviation from an expected mean trend. The second provides an alternative measure of stochasticity that emphasizes patterns' orderliness. Results: We demonstrate that, in healthy mice, the patterning of neural activity, both

spikes and local field potentials, is coupled to the animal's location, speed, and acceleration. In contrast, in AD mice, the coupling of brainwave rhythmicity with speed deteriorates, spatial selectivity of waveforms is lost, and the statistics of spike patterns are blurred. Furthermore, these differences accumulate with age, manifesting much stronger in older AD mice, thus showing that neurodegeneration disrupts the hippocampal circuit's involvement in spatial navigation. Conclusions: Remarkably, despite the differences in spatiotemporal scales, mechanisms and implementations, patterns of neural activity follow the same universal statistics. In other words, the mathematical laws governing the probability of patterns' appearance override the exhaustive physiological details. At the basic level, differences between AD and WT neural activity can be summarized as follows: healthy mice exhibit well-tuned, purposeful, behavior-coupled LFP rhythmicity and spike patterns, whereas neural activity in AD mice shows weak general dissociation from cognitive and motor activity. These differences can be used to better understand and potentially detect circuit-level pathologies in AD, offering a novel perspective on studying the structure, dynamics, and functionality of the brain at a neurocircuit level.

Funding: NIH R01NS110806-01A1, NSF 1901338, NIH R01NS097764; COI: None

Poster # 33: NEUROCOGNITIVE DISORDER ON LONG COVID

Presenting author: MARIA PAULA MAZIERO, MD (UT Health Houston)

Long-COVID or Post-acute sequelae of SARS-CoV-2 infection (PASC) is a condition where COVID-19 survivors experience persistent symptoms even after recovery. Recent evidence suggests that COVID-19 survivors, regardless of the severity, may experience acute and long-term neurological effects such as fatigue, anxiety, sleep disturbance, myalgia, and memory impairment. It is believed that older COVID-19 survivors are at higher risk of long-term cognitive dysfunction, including cognitive decline, due to overlapping pathologies. To investigate this, our team has conducted cognitive assessments and evaluated biomarkers of neuronal distress at 3/6 months and 12 months post-hospitalization from participants in our COVID-19 biorepository. Our preliminary data of this longitudinal study shows that 30% of the participants exhibited cognitive decline one year after hospitalization. We have established three trajectories for cognitive change in our COVID-19 biorepository participants: Improvers, Stable, and Decliners. Improvers are those whose Briancheck score improved by 6 points or more from 3/6 months to 12 months. Stable are those whose Briancheck score did not change by 5 points or more from 3/6 months to 12 months. Decliners are those whose Briancheck score decreased by 6 points or more from 3/6 months to 12 months. Our study found that cognitive impairment was significantly more significant in subjects older than 50 at 3/6 months post-hospitalization. 52 out of 110 participants were impaired at 3/6 months ($p<0.04$, Fisher's exact test), and 37 out of 86 participants were impaired at 12 months. Our group will monitor these patients for over four years to evaluate the progression of their cognitive decline. Our research aims to investigate the potential link between long COVID-related cognitive decline and the development of neurodegenerative disorders such as Alzheimer's Disease and other forms of dementia. To achieve this, we will analyze the biomarkers associated with these diseases and assess whether individuals who have experienced long COVID-related cognitive decline are more susceptible to developing them. Our hope is that this study will provide valuable insights into the long-term effects of COVID-19 on brain health and inform new approaches to managing and treating these debilitating conditions.

Poster # 34: EXPERIMENTAL BIOMARKER RESULTS FROM A PHASE 1 FEASIBILITY TRIAL OF SENOLYTICS FOR ALZHEIMER'S DISEASE

Presenting author: Valentina R. Garbarino, PhD (UT Health San Antonio)

Background: Accumulation of senescent cells contributes to progression of age-related disorders including Alzheimer's disease. Senolytic drugs are able to specifically target and clear senescent cells, offering a unique therapeutic opportunity for neurodegeneration, which is now being evaluated in clinical trials. Our group recently conducted the first open-label trial aimed at modulating the progression of Alzheimer's disease with a senolytic therapy made up of combined dasatinib plus quercetin provided to an early-Alzheimer's disease patient population. We reported blood-brain barrier penetrance of dasatinib, safety and tolerability of the intervention, and biofluid measures of amyloid beta and tau using commercially available assays. Herein, we report additional exploratory

biofluid outcomes which include a more comprehensive profile of amyloid beta and tau measured by mass spectrometry, additional plasma, cerebrospinal fluid and urine cytokine and chemokine analysis, urine metabolites, and significant transcriptomic changes relevant to chronic stress, after the three-month intermittent treatment period with dasatinib plus quercetin. Methods: Open-label intermittent oral administration of dasatinib + quercetin was provided to five participants with early Alzheimer's disease for three months. Pre- and post-treatment assessments were made utilizing plasma, peripheral blood mononuclear cells, cerebrospinal fluid, and/or urine samples collected at baseline and post-treatment study visits. Result: Baseline vs. post-treatment measures of CSF amyloid-beta and tau proteins were unchanged and nearly identical across multiple measures of Alzheimer's disease amyloid plaque and tau tangle biomarkers. Measures of cytokines in plasma, cerebrospinal fluid, and urine, as well as urine metabolites, were unchanged between baseline and post-treatment measures. In contrast, our transcriptomic biofluid marker measures indicate target engagement of dasatinib and quercetin and may suggest modest improvements in gene expression measures of seven genes relevant to inflammation. Conclusion: These biofluid analyses provide further preliminary evidence into the broad treatment effects of senolytics, and supply foundational evidence for the development of biomarker panels associated with senescent cell clearance that may be utilized in future studies.

Funding: South Texas Alzheimer's Disease Research Center (P30AG066546); Alzheimer's Drug Discovery Foundation (GC-201908-2019443); Coordinating Center for Claude D. Pepper Older Americans Independence Centers (U24AG059624); Institute for Integration of Medicine & Science; Center for Biomedical Neurosciences at UT Health San Antonio; Tracy Family Stable Isotope Labeling Quantitation Center at Washington Univeristy in St. Louis; T32GG021890 and TR002647.

COI: T.T. has a patent for Killing Senescent Cells and Treating Senescence-Associated Conditions Using an SRC Inhibitor and a Flavonoid with royalties paid to Mayo Clinic by Unity Biotechnologies and a patent for Treating Cognitive Decline and Other Neurodegenerative Conditions by Selectively Removing Senescent Cells from Neurological Tissue with Royalties pair to Mayo Clinic by Unity Biotechnologies;R.J.B. co-founded C2N Diagnostics. Washington University and has equity ownership interest in C2N Diagnostics and receive royalty income based on technology (stable isotope labeling kinetics, blood plasma assay, and methods of diagnosing AD with phosphorylation changes) licensed by Washington University to C2N Diagnostics. R.J.B. receives income from C2N Diagnostics for serving on the scientific advisory board. R.J.B. has received research funding from Avid Radiopharmaceuticals, Janssen, Roche/Genentech, Eli Lilly, Eisai, Biogen, AbbVie, Bristol Myers Squibb, and Novartis. M.M.G. reports personal stock in Abbvie. M.E.O. has a patent Biosignature and Therapeutic Approach for Neuronal Senescence pending

Poster # 35: CHANGES OF TRNA-DERIVED FRAGMENTS BY ALZHEIMER'S DISEASE IN BLOOD SERUM

Presenting author: Ernesto G. Miranda-Morales, PhD (UT Medical Branch at Galveston)

Background: Alzheimer's disease (AD) is the most common type of dementia, affecting individuals over 65. AD is also a multifactorial disease, with disease mechanisms incompletely characterized, and disease-modifying therapies are marginally effective. Biomarker signatures may shed light on the diagnosis, disease mechanisms, and the development of therapeutic targets. tRNA-derived RNA fragments (tRFs), a family of recently discovered small non-coding RNAs, have been found to be significantly enhanced in human AD hippocampus tissues. However, whether tRFs change in more easily obtained body fluids such as peripheral blood serum is unknown. Therefore, we investigated whether tRFs in peripheral blood serum are impacted by AD. Method: We first used T4 polynucleotide kinase-RNA-seq, a modified next-generation sequencing technique, to identify detectable tRFs in human cerebrospinal fluid and serum samples obtained from the Texas Alzheimer's Research and Care Consortium (TARCC) biorepository of blood specimens. The detectable tRFs were then compared between serum from control, AD, and mild cognitive impairment (MCI) patients using tRF qRT-PCR. The stability of tRFs in serum was also investigated by checking the change in tRFs in response to protein digestion or exosome lysis. Result: Among various tRFs, tRF5-ProAGG seemed to be impacted by AD in serum. In addition, AD impacted serum tRF5-ProAGG showed a correlation with the AD stage. Putative targets of tRF5-ProAGG in the hippocampus were also predicted by a computational algorithm, with some targets being validated experimentally and one of them being in a negative

correlation with tRF5-ProAGG even using a small size of samples. Conclusion: tRF5-ProAGG showed the potential as an AD biomarker and may play a role in disease regulation and progression of the disease.

Funding: This work was supported by grants from the US National Institute of Health (NIH) R21 AI66543 and R21AG069226 to Xiaoyong Bao, R61 AG075725 and TARCC Investigator-Initiated Research Award 952272 to Xiaoyong Bao and Xiang Fang, R21 AG066060 to Xiang Fang; COI: No conflict to report

Poster # 36: BRAIN-DERIVED TAU OLIGOMERIC CONFORMERS IN BRAIN-DERIVED EXTRACELLULAR VESICLES ISOLATED FROM PLASMA LONGITUDINALLY COLLECTED FROM TEXAS ALZHEIMER'S RESEARCH AND CARE CONSORTIUM

Presenting author: Michela Marcatti (UT Medical Branch at Galveston)

Alzheimer's disease (AD) represents a pressing global healthcare issue, and thus establishing reliable predictive biomarkers becomes critical to identify individuals at a high risk of developing AD, enabling the potential initiation of treatments during the preclinical stage. Recent investigations have focused on blood-based biomarkers, such as plasma brain-derived extracellular vesicles (pl-BDEVs) content, to detect alterations within the central nervous system (CNS). While blood-based biomarkers for amyloid proteins (Aβ42/Aβ40 peptide, tau, and phosphorylated tau) demonstrate promising diagnostic accuracy and correlation with cerebrospinal fluid (CSF) and neuroimaging biomarkers in AD, the urgency of identifying predictive biomarkers remains an absolute imperative. Blood total-tau primarily originates from non-brain sources, underscoring the importance of analyzing brain-derived tau (BDT) in pl-BDEVs as an AD and other neurodegenerative diseases biomarker. Longitudinal studies, which involve collecting repeated samples from a single patient over time, possess the potential to identify specific biomarker patterns during the preclinical stage of individuals who may develop AD. However, investigations have yet to focus on the role of oligomers, the most toxic species in AD. In this study, we enriched pl-BDEVs from CNS cell types (neurons, microglia, astrocytes, oligodendrocytes) from plasma samples longitudinally collected from participants enrolled in the Texas Alzheimer's Research and Care Consortium (TARCC), who were initially cognitively normal or displayed mild cognitive impairment (MCI), and later either progressed to AD (termed "converters") or remained cognitively normal/MCI (termed "non-converters"). We evaluated the isolated pl-BDEVs by nanoparticle tracking analysis (size, number, and distribution), and western blot (expression of extracellular vesicles markers: CD63, CD9, CD81). Moreover, we demonstrated the successful detection of brain-derived toxic tau oligomers (BDTOs) conformers in pl-BDEVs derived from MCI plasma samples and showed differences between converters and non-converters. This study addresses the need for predictive AD biomarkers by exploring previously unexplored BDTOs conformers in pl-BDEVs. Discovering distinct BDTOs conformers in peripheral brain derived extracellular vesicles could enable preclinical forecasting and advance early-stage AD treatments.

Funding: NIH

Poster # 37: BLOOD BIOMARKER FOR ALZHEIMER'S DISEASE: METABOLOMICS

Presenting author: Dwight German, PhD (UT Southwestern Medical Center)

Alzheimer's Disease (AD) and Parkinson's Disease (PD) are the two most common neurodegenerative disorders. Metabolomics offer insights into possible disease pathways and can provide potential biomarkers for early detection. In this study, both combined and individual effects of key metabolite alterations contributing to accurate diagnosis of AD and PD were captured using untargeted metabolomics of blood plasma. We used high-resolution LC-MS Q-TOF mass spectrometry to acquire metabolome profiles of blood plasma extracts from PD (1868 metabolites) and AD (1875 metabolites) cohorts, comprising 100 PD (14 drug-naïve, 86 medicated), 100 AD, and 125 Normal Control (NC) subjects. Both multianalyte (XGBoost) and unianalyte (de-sparsified lasso regression) methods were used to independently quantify the predictive value of metabolite concentrations and clinical features for the diagnosis of PD and AD. The XGBoost model achieved high accuracy in discriminating both drug-naïve PD subjects (AUROC = 0.960, balanced accuracy = 92.4%) and medicated PD subjects (AUROC = 0.971, balanced accuracy = 93.6%) from normal controls. A simplified XGBoost model restricted to 20 metabolites also achieved high accuracy in

differentiating drug-naïve PD subjects (AUROC = 0.931, balanced accuracy = 83.3%) and medicated PD subjects (AUROC = 0.918, balanced accuracy = 86.4%) from normal controls. For AD, a balanced accuracy of 80.0% and AUROC of 0.862 was achieved using the multianalyte XGBoost model. This study demonstrates the clinical potential of metabolomic biomarkers, particularly in early drug-naïve PD subjects, supporting their use in accurate diagnosis and novel biomarker discovery.

Funding: TARCC, NIH (RF1AG059288), Lyda Hill Fnd; COI: none

Poster Theme Group B2. Neuroimaging

Poster # 38: BUILDING INTERPRETABLE MACHINE LEARNING FOR ADVANCED DEMENTIA (ALZHEIMER'S DISEASE)

Presenting authors: Eeshan Joshi, BA & Arpan Patel, BSA (UNT Health Science Center)

Background: This study addresses a significant gap in Alzheimer's disease (AD) research by leveraging cutting-edge Artificial Intelligence (AI) and Machine Learning (ML) methodologies. Employing a retrospective cohort design, the investigation encompasses 1643 participants, including 356 with mild cognitive impairment (MCI) or advanced dementia. The dataset incorporates a diverse set of variables, ranging from demographic factors such as Gender, Age, Ethnicity, and Years of Education to an extensive array of neuroimaging data acquired through Diffusion Tensor Imaging (DTI). Methods: At the core of the analytical approach is the ML algorithm Random Forest. This algorithm is utilized for a nuanced examination of imaging biomarkers, deploying techniques like Feature Importance, Permutation Importance, and SHAP Values. Through this multifaceted analysis, the study aims to uncover subtle patterns that traditional methods may overlook. Results: The findings illuminate specific variables with pronounced associations to MCI/AD states. Notably, Right Entorhinal Thickness emerges as a focal point, carrying a relative importance of +0.027, indicating its heightened significance in discerning cognitive impairment. Similarly, the Axial Diffusivity of the Body of the Left Corpus Callosum, with a relative importance of +0.0012, and the Thickness of CA2, CA3 (Hippocampal subregions), and Left Dentate Gyrus, with a relative importance of +0.013, stand out as pivotal indicators of pathological cognitive decline. Validation involves rigorous assessments, including Confusion Matrices and a 70/30 Training/Testing set division, to evaluate the predictive accuracy of the AI model. The model achieves a 77% accuracy in predicting normal cognitive states based on the identified biomarkers. This underscores the potential clinical utility of the ML model as a diagnostic tool. Conclusion: This study advocates for the expansion of similar research initiatives and emphasizes the need for continuous refinement of AI models. These efforts aim to enhance predictive accuracy and understand the intricate interplay between specific neuroimaging markers and cognitive states. The adoption of ML methodologies represents a transformative shift, enabling a comprehensive exploration of vast datasets, real-time predictive modeling, and enhanced generalizability, all while mitigating inherent biases. The findings collectively underscore the transformative potential of AI and ML in advancing our comprehension of the intricate landscape of AD and associated cognitive disorders.

Funding: Research reported in this presentation was supported by the National Institute on Aging of the National Institutes of Health under Award Numbers R01AG054073 and R01AG058533, P41EB015922 and U19AG078109. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors would like to thank the Health and Aging Brain Study: Health Disparities (HABS-HD) research team and participants; COI: N/A

Poster # 39: REMODELING OF VASCULAR BASEMENT MEMBRANES IN THE LEPTOMENINGEAL BLOOD VESSEL IN ALZHEIMER'S DISEASE

Presenting author: Kiersten Scott, BS (UT Health Houston)

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disease that leads to cognitive impairment. More than 80% of patients with AD develop cerebral amyloid angiopathy (CAA) leading to vascular inflammation,

microbleeds, and lobar intracerebral hemorrhage. However, the mechanism by which amyloid-beta preferentially aggregates in CAA has been understudied. Recent literature suggests that the secreted osteopontin (OPN) aids the formation of amyloid-beta plaques in the brain parenchyma. Thus, we explored the potential role of pro-fibrotic OPN on the remodeling of vascular extracellular matrix (ECM) and the sequestration of amyloid-beta in CAA. Methods: To study OPN-mediated remodeling of the perivascular ECM, we performed single-cell RNA sequencing (scRNAseq) in blood vessel-enriched preparations of whole brains in young (6 months) and aged (18 months) Tg2576 and age-matched wild-type littermate mice. Furthermore, we analyzed public scRNAseq data from patients with AD to assess potential role of OPN in ECM remodeling. We conducted two-photon imaging to determine the structural changes of perivascular fibrotic collagen layers in the leptomeningeal blood vessels in Tg2576 mice. Results: We found that OPN signaling was significantly upregulated in the brains of young Tg2576 mice and that this upregulation was predominantly seen in central nervous system (CNS) fibroblasts. In AD patient brains, the interaction network of microglia-to-fibroblasts predicted dysregulated OPN signaling and tumor growth factor beta (TGFB1) interacted with fibroblast integrin genes ITGA9, ITGAB1, ITGAV, and TGFB3. Cell-cell interaction networks between fibroblasts and astrocytes predicted that dysregulated fibroblast ECM components, including collagens, laminins, and fibronectins interacted with dysregulated astrocyte integrins and OPN receptor (CD44) genes. These results suggest that regulation of the vascular basement membrane through OPN signaling is multimodal, requiring the interplay of perivascular microglia, fibroblasts, and astrocytes within the perivascular space. These results were supported by second-harmonic generation imaging by two-photon microscopy which revealed increased fibrotic collagen layers and abnormal structural organization of the perivascular space in aged Tg2576 mice. Conclusion: The present study suggests that the upregulation of OPN signaling in AD leads to pathological vascular ECM remodeling and CAA.

Funding: GSBS Dean's Excellence Scholarship, NIA, NIH

Poster # 40: DISSOCIATION OF STRUCTURAL AND FUNCTIONAL CHANGES IN ALZHEIMER'S DISEASE AND MILD COGNITIVE IMPAIRMENT

Presenting author: Annie Dang, MS (UT Health San Antonio)

Background: The Amyloid-Tau-Neurodegeneration (ATN) biomarker framework for Alzheimer's disease (AD) indicates binary (positive/negative) designations for each type of pathology, without regard for anatomical distribution. Neurodegeneration is designated as positive if atrophy or hypometabolism are found on imaging. However, Clifford Jack et al., 2016 noted that atrophy and hypometabolism were differently distributed and referenced each to different co-localized pathologies. Thus, there exists a need to further characterize atrophy and hypometabolic changes in AD, with the goal of advancing the application of anatomically-based biomarkers in the ATN framework. Methods: Query of the BrainMap databases of published, group-wise neuroimaging, case-control contrasts was used to identify AD and mild cognitive impairment (MCI) studies for meta-analysis. The voxel-based morphometry (VBM) and voxel-based physiology (VBP) databases were used to identify studies involving atrophy and hypometabolism respectively. 157 VBM contrasts (110 AD, 47 MCI) and 146 VBP contrasts (88 AD, 58 MCI) were identified. Activation likelihood estimation coordinate-based meta-analysis was performed separately for VBM and VBP, to identify cross-study convergence of brain alteration patterns. Mango was then used to visualize results and quantify spatial overlap between VBM and VBP. Results: Structural (atrophy) and functional (hypophysiology) neurodegenerations in AD/MCI exhibit markedly different neuroanatomical distributions. Structural abnormalities chiefly involve the bilateral hippocampus and bilateral temporal lobes; functional abnormalities chiefly involve the bilateral parietal lobes and posterior cingulate. There is a small overlap (2184 mm3) between VBM and VBP, accounting for 10.1% of VBM and 7.1% of VBP. Conclusion: VBM and VBP patterns of alteration appear distinct, aligning with the anterior and posterior default mode network respectively. This dissociation may reflect distinct underlying neuropathologies. We suggest that this knowledge can be used to advance the application of anatomically-based biomarkers in the ATN framework. Network modeling of VBM and VBP data is currently ongoing.

Funding: NIH T32 AG082661; T32 GM145432; MH R0107445-15; COI: None

Poster # 41: QUANTIFICATION OF CSVD LESIONS USING EX-VIVO MRI IN ALZHEIMER'S DISEASE AND RELATED DEMENTIAS

Presenting author: Mariam Mojtabai, MS (UT Health San Antonio)

Background: This study provides feasibility data and a methodological approach for manual segmentation of cerebral small vessel disease (CSVD) lesions in magnetic resonance imaging (MRI) of postmortem brains for use in the application of machine learning-based quantification methods. The goal is to develop an automated image processing pipeline to identify and localize lesions, as well as to investigate the relationship between CSVD and dementia and to use CSVD as a predictor of severity in Alzheimer's Disease (AD) and other forms of dementia. Methods: From 2019 to 2023, 207 hemispheres of participants (110 female, 99 male) were scanned. These include 95 with AD, 20 with Lewy body dementia, 17 with vascular dementia, 13 with frontotemporal dementia, 11 with Parkinson's Disease, 6 with Parkinsonian syndrome, 1 with Creutzfeldt-Jakob disease, 1 with Huntington's disease, 2 with multiple sclerosis, 1 with amyotrophic lateral sclerosis, 23 with unspecified dementia, and 12 with unknown diagnosis. Of these, 19 had multiple diagnoses. The hemispheres were fixed and submerged in formalin and scanned with a 3T Siemens TIM Trio scanner with an 8-channel knee transmit/receive coil. The scans included T1- and T2-weighted images, susceptibility weighted images, and diffusion tensor images. Results: Visual examination of the AD-diagnosed hemispheres revealed numerous white matter hyperintensities (WMH), enlarged perivascular spaces (ePVS), and infarctions. Through expert annotation of 38 hemispheres, we found that, per participant, the average WMH volume was (± standard error) 13,772±2,046 mm3. The average number and volume of infarctions were 4.91±0.79 and 312±177 mm3, respectively. There were 81±22 ePVS lesions with a mean total volume of 95±161 mm3. Conclusion: CSVD, prevalent with aging, has been associated with vascular risk factors of cognitive impairment such as hypertension and diabetes mellitus. We are in the process of creating additional expert-labelled data, which is vital to produce robust and accurate machine learning models.

Funding: 5R01AG080821, P30AG066546-01A1

Poster # 42: MILD COGNITIVE IMPAIRMENT IMPACTS HIGHER-ORDER SOMATOSENSORY INHIBITION

Presenting author: Mahak Virlley, BS (UT Southwestern Medical Center)

Background: Somatosensory gating (SG) is a neurophysiological phenomenon in which the brain responds dynamically less to redundant somatic or tactile information, reflecting a neural inhibitory mechanism. Prior studies have reported aberrant SG in the primary somatosensory cortex of patients with mild cognitive impairment (MCI) and Alzheimer's disease using a region-of-interest approach, as well as age-related SG declines in the dorsolateral prefrontal cortex (DLPFC) in other clinical populations with cognitive impairment (HIV-associated neurocognitive disorder) using a whole-brain approach. However, similar whole-brain analyses have not been applied in the context of MCI. We hypothesize that individuals with MCI will demonstrate perturbed SG within the DLPFC with advancing age. Method: We acquired magnetoencephalography (MEG) brain imaging on 46 cognitively healthy (CH) adults (M age = 59, 27 female) and 30 adults with MCI (M age = 63, 20 female) during a somatosensory paired-pulse paradigm. Cognitive status was determined by consensus amongst two board-certified neuropsychologists. All MEG data underwent standard preprocessing and significant neural oscillatory responses relative to baseline were imaged using a beamformer. The resulting whole brain maps were used to create gating difference (GD = Stim1-Stim2) maps per subject. Whole brain GD maps were regressed on age, cognitive group (CH, MCI), and their interaction term while controlling for sex, education, and attention metrics (Trail Making A and Digit Coding), and results were corrected for multiple comparisons. Result: A significant age by group interaction on gating in ipsilateral secondary somatosensory cortex was observed, such that gating increased with age in MCI patients. A significant interaction on gating in ipsilateral DLPFC also emerged, such that gating decreased with age in MCI patients, while in CH adults gating increased with age. All p's < .05, corrected. Conclusion: In CH adults, increases in SG in ipsilateral DLPFC might reflect a necessary compensatory inhibition mechanism for healthy aging. However, in older MCI adults, there is a decline in DLPFC SG and increased gating of SII which might reflect a novel compensatory mechanism guiding somatosensory inhibition in older individuals with MCI.

COI: n/a

Poster # 43: ALTERED NEURAL DYNAMICS SUPPORTING WORKING MEMORY ENCODING IN INDIVIDUALS WITH MCI

Presenting author: Megan White, MS (UT Southwestern Medical Center)

Background: In cognitively healthy (CH) adults, the neural oscillatory dynamics underlying verbal working memory (VWM) performance have been well characterized, but how mild cognitive impairment (MCI) impacts these oscillatory dynamics is less clearly understood. We utilized the spatiotemporal precision of magnetoencephalographic brain imaging (MEG) to characterize changes in the neural dynamics supporting the encoding phase of VWM between CH adults and adults with MCI. In congruence with the compensation-related utilization of neural circuits hypothesis (CRUNCH), we hypothesized that individuals with MCI would recruit greater neural resources during VWM encoding. Methods: Fifty-nine CH adults (32 females, M age: 59.1) and 29 adults with MCI (20 females, M age: 63.9) completed a modified Sternberg-type VWM task during MEG. Cognitive status was determined by consensus between two board-certified neuropsychologists. Only clean, correct trials were analyzed, and the average number of correct trials included in analysis did not significantly differ between groups. All MEG data were preprocessed using a standard pipeline, were transformed into the time-frequency domain, and significant neural oscillatory responses relative to baseline were imaged using a beamformer. The resulting whole-brain maps were entered into a full factorial design to determine the neural oscillatory differences between groups (CH vs. MCI), with age and education included as covariates, and results were corrected for multiple comparisons. Results: During the latter portion of encoding (850-2050 ms), significant group differences in theta (4-6 Hz) oscillatory activity were observed. Both groups exhibited increased theta activity in the left dorsolateral prefrontal cortex (dlPFC) relative to baseline; however, participants with MCI demonstrated significantly stronger theta activity in this region compared to CH participants. All p's < .05, corrected. Conclusion: While both groups recruited the left dlPFC during VWM encoding, individuals with MCI recruited this region more strongly. In line with the CRUNCH hypothesis, this result suggests that individuals with MCI may recruit greater neural resources during VWM performance as a compensatory mechanism. Future analyses should incorporate behavioral performance to support or refute this interpretation.

Funding: The Dallas Hearts and Minds Study; COI: N/A

Poster Theme Group C1. Neuropsychiatry and Behavioral Neurology

Poster # 44: COGNITIVE DEFICITS IN THE 5XFAD MOUSE MODEL OF ALZHEIMER'S DISEASE: INSIGHTS FROM CORTICOSTRIATAL HYPERACTIVITY AND REDUCED CHOLINERGIC FUNCTION

Presenting author: Ruifeng Chen (Texas A&M University)

The deposition of Aβ and cognitive inflexibility characterizes Alzheimer's disease. However, the link between Aβ deposition and cognitive deficits remains elusive. In this study, we conducted experiments to elucidate the mechanisms by which Aβ deposition impacts cognitive function. We utilized 5xFAD mice as an Alzheimer's disease model. Behavioral investigations revealed deficits in reversal flexibility during instrumental learning tasks. Histological analyses revealed increased recruitment of cortical and striatal neurons during reversal learning. Furthermore, physiological studies confirmed cortical neuron hyperactivity and hyperactivity in striatal direct-pathway medium spiny neurons (dMSNs) in 5xFAD mice. Cholinergic neuron activity in the striatum and basal forebrain declined. Ex-vivo confocal imaging, employing genetically encoded sensors, revealed decreased acetylcholine release in 5xFAD mice. Ultimately, sustained inhibition of cortical neurons normalized glutamatergic transmission, reduced Aβ accumulation, elevated striatal Ach release levels, and improved cognition in 5xFAD mice. In summary, these findings propose that the Aβ-induced hyperactive corticostriatal pathway contributes to declined cholinergic activity and impaired cognitive function. This study provides novel insights into the neurobiological alterations associated with the cognitive deficits observed in Alzheimer's disease.

Poster # 45: DYSLIPIDEMIA IN HISPANIC PREDIABETICS WITH MILD COGNITIVE IMPAIRMENT

Presenting author: Paul Koester, MS (UNT Health Science Center)

Background: Prediabetes or impaired glucose tolerance affects an estimated 96 million adults in the United States and may be a modifiable risk factor for cognitive impairment. Several studies have shown that prediabetics experience poorer longitudinal cognitive outcomes compared to non-diabetics; however, the exact mechanism is still a matter of debate. Furthermore, prediabetic patients often experience metabolic syndrome-related comorbidities like dyslipidemia that may be related to in the development and progression of cognitive impairment in prediabetic patient populations. The aim of this study was to examine the relationship between lipid levels between ethnic groups in prediabetic, mildly cognitively impaired, Hispanics, Non-Hispanic Whites, and African Americans. Methods: Data from 144 mildly cognitively impaired prediabetic participants (Hispanics, Non-Hispanic Whites, and African Americans) was collected and analyzed from the Health and Aging Brain Study: Health Disparities (HABS-HD), a community-based epidemiological study of aging. Participants of the study undergo cognitive and functional testing, as well as brain imaging (MRI and PET). Basic demographic information is also collected, and blood samples are used to determine HbA1c, fasting blood glucose, and lipid profiles. One-way ANOVAs examined differences in total cholesterol, triglyceride, and LDL measurements based on ethnicity. Results: Results showed significant differences in total cholesterol levels between the Hispanic (M = 193.98, SD = 38.17), non-Hispanic white (M = 169.54, SD = 37.26), and African American (M = 170.41, SD = 35.52) populations ($F = 7.20$, $p < 0.001$), triglyceride levels between the Hispanic (M = 154.25, SD = 80.47), non-Hispanic white (M = 124.62, SD = 50.81), and African American (M = 95.17, SD - 57.77) populations ($F = 10.96$, $p<0.000$), and LDL levels between the Hispanic (M = 111.86, SD = 31.88), non-Hispanic white (M = 95.62, SD = 29.91), and African American (M = 94.77, SD = 27.38) populations ($F = 5.37$, $p<0.006$). Conclusion: Prediabetic Hispanic participants in the study with MCI were shown to have higher lipid profiles (triglycerides, LDL, and total cholesterol) as compared to non-Hispanic white and African American participants. Future studies should further examine the relationship between prediabetes and dyslipidemia, including clinical outcomes regarding the treatment of elevated lipids.

Funding: National Institute of Aging Grant; COI: None

Poster # 46: UNRAVELING THE IMPACT OF LONG COVID-19: COGNITIVE, EMOTIONAL, AND FUNCTIONAL INSIGHTS IN AN ELDERLY COHORT

Presenting author: Lucineia Gainski Danielski, PhD (UT Health Houston)

Long COVID-19, affecting up to 30% of those who have recovered from acute cases, results in symptoms like depression, anxiety, cognitive dysfunction, memory issues, and fatigue. Natural aging is already associated with cognitive decline. Therefore, the objective was to assess cognitive performance, anxiety, and depression in older adults who have experienced COVID-19. We assessed cognitive and functional capacity, depression, anxiety, and instrumental activities of daily living in an Elderly Patient Cohort. A group of 151 elderly individuals, comprising 66 males and 85 females, were evaluated through score assessments. Out of the 151 participants, 72 tested positive for COVID-19 while 79 were control subjects without COVID-19. The average age of the participants was found to be 68.6 (± 6.9) years. Patients with COVID-19 exhibited a significantly higher prevalence of heart disease/infarction ($p=0.024$) and rheumatic-autoimmune diseases ($p=0.043$). Furthermore, they reported experiencing more difficulty in recalling information about people, events, or situations from the past 30 days ($p=0.003$) and were more likely to report memory loss ($p=0.007$). Notably, this same also displayed a greater presence of depressive and anxiety symptoms ($p<0.05$). Among the patients with COVID-19 who exhibited some level of functional dependence, those who were older had a higher representation ($p=0.013$). When considering a multivariate model, age and marital status remained significantly associated with functional dependence in the IADLs among patients with COVID-19. Specifically, for each year increase in age, there was an average 13% rise in the prevalence of functional dependence ($PR=1.13$; 95% CI: 1.03-1.25; $p=0.009$). Moreover, single, or divorced/separated patients demonstrated approximately 3.5 ($PR=3.47$; 95% CI: 1.22 - 9.89; $p=0.020$) or 10 ($PR=10.2$; 95% CI: 1.64 - 63.7; $p=0.013$) times higher prevalence of functional dependence compared to those who were married or in a union. In conclusion, elder

patients with COVID-19 exhibited a higher prevalence of heart disease/infarction and rheumatic-autoimmune diseases. They reported increased difficulty in recalling recent information and were more likely to experience memory loss, as well as higher rates of depressive and anxiety symptoms. Older age and marital status were identified as significant factors associated with functional dependence in IADLs among patients with COVID-19.

COI: Authors declare no conflict of interest

Poster # 47: SINGLE-ITEM SCREENING FOR DEPRESSION IN ADULTS (50+) WITH HISTORY OF TRAUMATIC BRAIN INJURY

Presenting author: Shannon Lavigne, PhD (UT Health San Antonio)

Background: Depression is common after traumatic brain injury (TBI). Single-item screening for depression has shown utility in research using young adults. Less work has focused on individuals 50 and older for whom depression might complicate diagnosis of neurodegenerative conditions. We examined the utility of single-item depression screening in adults 50 and older with a history of TBI one year after injury. Method: This project involved secondary analysis of deidentified data obtained from the Federal Interagency Traumatic Brain Injury Research (FITBIR) Informatics System. Data were collected in the Transforming Research and Clinical Knowledge in Traumatic Brain Injury study. The initial dataset included observations from 2,657 participants. Participants 50 years old with complete demographic and outcome data were included. Participants with questionable symptom validity (n=24) were excluded. The final sample (N=508) included 61 control participants and 447 cases grouped by severity into mild (n=169), complicated-mild (n=217), and moderate-severe TBI (n=61). Outcome measures included the Brief Symptom Inventory-18 depression scale (BSI-D) and Patient Health Questionnaire-9 (PHQ-9). Depression was determined psychometrically by BSI-D (≥63 T) and PHQ-9 (≥9) if either score was above the cutoff. The Rivermead Postconcussion Symptoms Questionnaire depression item (RPQ-D) was used in logistic regression (LR) and receiver operating characteristic (ROC) analyses to predict depression. Results: PHQ-9 and BSI-D scores were not significantly different between case and control participants or by TBI severity. Age (r=-.20) and education (r=-.12) were associated with PHQ-9; age(r=-15) was associated with BSI-D. Depression was observed in 16.1% of cases and 6.6% of control participants (p=.05) with non-significant variability across TBI severity (12.9-18.3%; p=.17). The LR model with depression outcome and age, education, TBI severity, and RPQ-D as predictors was significant with age and RPQ-D as significant predictors. The model classified 87.9% of participants correctly. The area under the ROC curve was .86 with classification accuracy optimized (86.8%) by RPQ-D≥3 and sensitivity maximized (90.3%) by RPQ-D≥1. Conclusion: Single-item screening for depression is a suitable approach in adults 50 and older with a history of TBI. Employing a brief instrument like the RPQ in this manner can identify cases in need of further evaluation for possible depression.

Funding: n/a; COI: None

Poster Theme Group C2. Neuropsychology

Poster # 48: REPORT OF DISINHIBITION AND GLOBAL COGNITIVE FUNCTIONING SCORES AS PREDICTORS FOR INCIDENT DEMENTIA IN A MULTI-ETHNIC SAMPLE

Presenting author: Shannon Lavigne (UT Health San Antonio)

Background: Previous work has demonstrated that Mild Behavior Impairment (MBI) with apathy is a strong risk factor for developing dementia. When exploring the relationship between apathy and cortical atrophy in European American and Hispanic American older adults, higher cortical volumes in the orbital frontal cortex were found in the Hispanic American group. Given the importance of the orbital frontal cortex for inhibitory control, we calculated the predictive power of disinhibition and global neuropsychological functioning for eventual diagnosis of dementia in Hispanic Americans and non-Hispanic white participants. Method: Data from a total of 13,061 adults 65 and older from the NACC database were selected for analyses if they were classified as either having normal cognition or MCI

at the time of their first visit, completed more than one visit, and identified as either Hispanic or non-Hispanic and White. Neuropsychological testing and neuropsychiatric inventory data were gathered from the initial visit. Data were analyzed using Cox proportional hazards ratios. Results: When looking at the hazard ratios for developing a dementia, report of disinhibition at the time of the first visit is associated with about a 2-3-times greater risk for developing dementia after controlling for age, sex, and education (Hispanic HR = 3.10; 95% CI 1.07,8.98; non-Hispanic HR = 2.42; 95% CI 1.82,3.22). Global composite neuropsychological scores (Dodge et al, 2020) were not associated with an increased risk in a model controlling for age, sex, education, and report of disinhibition (Hispanic HR = 0.07; CI 0.02,0.24; non-Hispanic HR = 0.19; CI 0.16, 0.22). Conclusion: Report of changes in disinhibition is associated with a greater risk for incident dementia in both ethnic groups. These results indicate that reports of disinhibition alone could necessitate additional neurological monitoring for incident dementia, likely regardless of global neuropsychological functioning.

COI: none to report

Poster # 49: INVESTIGATION OF INFLAMMATION AND CHRONIC PAIN ON COGNITIVE DECLINE IN RURAL TEXAS: A PROJECT FRONTIER STUDY

Presenting author: Lauren Chrzanowski, BS (Texas Tech University)

Introduction: Chronic pain is becoming increasingly prevalent in older adults. Recent literature has proposed a link between chronic pain and neurocognitive decline in aging; however, the mechanism driving this relationship is unknown. This study hypothesized that chronic pain leads to an increase in inflammation, which leads to neurocognitive decline. However, no existing studies have examined this relationship in rural populations. Methods: This study included 1864 participants (561 men, 1295 women; Mage = 59.68 years) 40 and over, living in rural West Texas. Cognitive functioning was measured using the RBANS, TRAILS, and CLOX. We used CRP levels to measure inflammation, which were dichotomized ("standard" below 3mg/L and "high" at or above 3mg/L) to represent inflammation. Chronic pain conditions were reported during a medical examination (1414 no chronic pain; 446 with chronic pain). Results: A MANCOVA was performed to determine the effects of inflammation and chronic pain on cognitive function. CRP values significantly predicted cognitive functioning when controlling for age and gender ($F(1,973) = 3.67$, $p = .006$), such that those with high CRP (M=82.03, SD = 14.72) had significantly lower overall cognitive functioning ($F(1,1079) = 11.04$, $p < .001$, $\eta p2 = .13$) compared to those with lower CRP (M=85.89, SD =16.10). Also, TRAILS delta (i.e., processing speed; ($F(1, 973)=4.54$, $p = .03$, $\eta p2 = .09$) has the same results, as high CRP (M=78.33, SD =65.31) resulted in significantly slower processing speed than the low CRP group (M=66.84, SD = 54.20). However, the interaction between chronic pain and CRP was not significant ($F(1,973) = .86$, $p = .49$). Conclusion: These results suggest that there is no interaction between inflammation and chronic pain on cognitive decline in rural populations. However, it appears inflammation markers, specifically, CRP, is a significant predictor of neurocognitive functioning in this rural population. This provides further evidence that rural populations are epidemiologically unique and an indication that inflammation may not be the mechanism by which chronic pain may lead to cognitive decline. Additionally, these results direct future studies to investigate comorbidity and risk factors for cognitive decline other than chronic pain.

Funding: Private foundation grants; COI: None

Poster # 50: PSYCHIATRIC DISTRESS PREDICTS COGNITIVE AND FUNCTIONAL STATUS IN INDIVIDUALS WITH SUBJECTIVE COGNITIVE COMPLAINTS.

Presenting author: Anika Bhatia, BS (UT Austin)

Background: In previous studies, we show that both subjective cognitive complaints (SCC) and intraindividual variability (IIV) in cognitive performance are associated with greater psychiatric distress and increased risk for cognitive decline. The purpose of the present study was to identify predictors of cognitive (MMSE) and functional (IADLS) status in cognitively normal older adults with (SCC+) and without (SCC-) SCC. Based on our prior findings that SCC+ individuals have higher levels of psychiatric distress associated with greater cognitive IIV, we

hypothesized that these variables would be predictive of MMSE and IADLS scores in SCC+ and not SCC- individuals. Methods: The sample included baseline data from 1034 cognitively normal older adults (SCC+ = 248; SCC- = 786) enrolled in the Texas Alzheimer's Research and Care Consortium (TARCC). Hierarchical linear regression analyses predicting cognitive (MMSE) and functional (IADLS) status were conducted separately in both groups, with demographics (age, education, ethnicity), psychiatric symptoms (NPI-Q: apathy, anxiety, dysphoria, and disinhibition), health comorbidities (pulse pressure, cardiovascular risk factors, and genetic [APOE] risk), and IIV metrics (IIV-Across tests and IIV-Between traditional cognitive domains) entered in separate blocks. Results: Statistically significant models ($p<0.01$) emerged for each analysis conducted, but this combination of variables only accounted for 5-9% of the variance in the outcome measures for the SCC- group versus 42-52% of the variance explained for the SCC+ group. In the SCC- group, only education and ethnicity emerged as significant predictors of MMSE scores, while age and education were the only significant predictors of IADLS scores. In the SCC+ group, greater psychiatric symptoms and genetic risk were predictive of MMSE scores, while greater psychiatric symptoms and IIV-Across tests predicted IADLS scores. Conclusions: Findings suggest that psychiatric distress is the strongest predictor of cognitive and functional status in cognitively normal older adults with SCC, while demographics remain the strongest predictors in those without SCC. These data highlight the prominent role of psychiatric distress in the day-to-day lives of cognitively normal individuals undergoing dementia evaluations and warrant further investigation to elucidate the etiological underpinnings.

Funding: the Texas Alzheimer's Research and Care Consortium and The Alzheimer's Association; COI: N/A

Poster # 51: DIGITAL VS. ANALOG APPROACHES FOR PERFORMING DAILY ACTIVITIES IN OLDER ADULTS: IS TECH USE ASSOCIATED WITH MORE ERRORS?

Presenting author: Rachel E. Mis, PhD (UT Austin Dell Medical School)

BACKGROUND: Technology is increasingly critical for daily activities, with prior studies suggesting technology may be harder for older adults to use, especially for those with cognitive weaknesses. Limited work has examined whether digital approaches to daily tasks amplify errors in daily activities. The purpose of this study was to characterize older adults' use of digital vs. analog approaches to daily activities and determine whether a digital approach was associated with more errors in performing daily activities. METHOD: Sixty older adults (mean age: 62.98±8.44 years) without neurocognitive disorders were recruited from the community. Participants completed a questionnaire on frequency of using digital and analog approaches to nine daily activities as well as perceived errors for each task. A digital preference score was calculated, with higher values indicating greater digital preference. Demographic characteristics and telephone-administered neuropsychological tests were also collected. Pearson correlations and hierarchical linear modeling explored the relations between digital preference, perceived daily errors, cognition, and demographic factors. RESULT: Overall, 80% of older adults endorsed greater digital vs. analog approaches to daily activities (mean digital preference: 15.65±26.98; range: -50-66.67). Digital preference was not associated with greater perceived errors ($r=.06$, $p=.65$). In hierarchical linear regression, the model of demographics and global cognition to predict perceived daily errors was statistically significant, $R2=.18$, $F(5, 54)=2.44$, $p=.05$; adjusted $R2=.11$, with better cognition associated with fewer errors, $p=.006$. The addition of digital preference did not improve model fit, $F(1, 53)=1.87$, $p=.18$, suggesting a digital approach to daily activities does not necessarily increase risk of perceived errors. CONCLUSION: In our sample, older adults frequently use digital approaches for daily activities, with over 80% favoring digital approaches. Contrary to the notion that technology is too difficult for older adults, there was no pattern of increased errors with technology use. This finding held even after adjusting for global cognition. Our results are consistent with the technological reserve hypothesis, wherein digital technologies are hypothesized to provide a scaffold for daily tasks, even in the face of cognitive weaknesses. Future work should continue to explore technological methods to support daily functioning in older adults, with limitations and future directions discussed.

Funding: Texas Alzheimer's Research and Care Consortium (TARCC; 202200035); University of Houston Start-up Fund; COI: None

Poster # 52: EDUCATION LEVEL AND ESTIMATED IQ EFFECTS BETWEEN MEXICAN AMERICANS AND NON-HISPANIC WHITES WITH MCI AND DEMENTIA ON BOSTON NAMING TEST

Presenting author: Paulina Vanessa Devora, MS (UT Dallas)

Background: Confrontational naming (CN) assessments are commonly used in both clinical and research settings for diagnosing MCI and dementia. Deficits on CN tasks are reported to occur early during dementia, with dementia severity strongly correlating with degree of anomia. Given the importance of properly assessing these deficits during cognitive evaluations, the effects of individual demographic factors (such as education level and IQ) should be properly considered when interpreting CN scores between different ethnicities, as these can have varying effects on performance. Factors underlying discrepancies in CN tasks between different ethnic groups have been somewhat explored in cognitively intact samples, but further investigation is needed in the populations of MCI and dementia. The current study examines data from Mexican Americans (MA) and Non-Hispanic White (NHW) older adults with MCI and dementia from the TARCC Hispanic Cohort database. Methods: Correlation analyses were used to examine the strength of associations between BNT scores and years of education, estimated IQ, age, and sex. Hierarchical regression analyses were used to examine the individual contributing effects of education level and estimated IQ, along with the interaction effects of Education x Ethnicity and Estimated IQ x Ethnicity. Results: Across ethnic and diagnostic subgroups, BNT, education, and estimated IQ were all moderately to strongly correlated with each other, except for education and BNT for both AD subgroups. A one-way ANOVA revealed a significant three-level interaction effect between ethnicity, diagnosis, and education level. Follow up tests revealed a significant interaction effect between ethnicity and education for the MCI only, not AD. Further, regression analyses revealed significant relationships between education and BNT for both the ethnic MCI groups, with a stronger relationship for MA's than for NHW's. Conclusions: Results suggest an ethnicity effect between education level and BNT performance at the MCI diagnostic stage, but not at the AD diagnostic stage. Properly controlling for these effects when interpreting CN performance for determining cognitive status is of utmost importance when evaluating patients of different ethnicities. Considering the different ways demographic factors such as education contribute to patterns of performance on CN tasks can help reduce misdiagnoses across Hispanic ethnic groups.

Poster # 53: ASSOCIATION OF BRAIN-BASED BIOMARKERS WITH SUBJECTIVE AND OBJECTIVE COGNITIVE FUNCTIONING IN A DIVERSE SAMPLE

Presenting author: Alyssa Kaser, BA (UT Southwestern Medical Center)

Objective: Individuals with subjective cognitive complaints (SCCs) and brain-based biomarkers [reduced hippocampal volumes (HV) and greater white matter hyperintensities (WMH)] may be at increased risk of future cognitive decline, though findings have been mixed. The current study explores the association of HV and WMH with SCCs and objective cognitive performance in a diverse sample. Method: Participants in a population-based cardiovascular risk study (N=1291; MAge=58.9, 58% Female, 52% Black, 11% Hispanic) responded to three subjective cognitive functioning questions prior to completing the Montreal Cognitive Assessment (MoCA): 1) Do you have consistent memory problems, 2) If YES, do they interfere with everyday activities, and 3) do you have trouble figuring things out/solving problems. Brain volumetrics were derived from a 3-tesla MRI and normalized using total intracranial volume. Partial correlations examined associations between HV, WMH, MoCA scores, and SCCs, while one-way ANCOVA compared HV and WMH by SCC endorsement pattern, controlling for demographics. Results: Findings revealed smaller HV in those who endorsed all SCC questions ($p=.004$, $\eta 2=.013$) and significantly less WMH in those with no SCCs compared to those endorsing memory complaint with problem-solving difficulties ($p=.004$, $\eta 2=.017$). HV were not correlated with SCCs ($r=-.06$, $p=.10$) or cognitive performance ($r=.01$, $p=.75$), though SCCs had a small correlation with MoCA scores ($r=-.18$, $p<.001$) and WMH ($r=-0.79$, $p<.01$). Conclusions: Subjective cognitive functioning was minimally associated with brain-based biomarkers and cognitive performance in this sample, suggesting that SCCs and brain-based biomarkers should not be used in isolation to identify possible cognitive decline. Unclear significance of SCCs in this study may be related to midlife, diverse sample, nonspecific SCC items, or self-only report. Further research is needed to understand the possible

neuroanatomical correlates of SCCs, sensitivity and specificity of SCC questions, and their predictive ability in the early identification of cognitive decline.

Poster # 54: PERCEIVED PSYCHOSOCIAL DISADVANTAGE PREDICTS COGNITIVE IMPAIRMENT IN A PRELIMINARY 10-YEAR FOLLOW-UP TO THE DALLAS HEART STUDY

Presenting author: Anthony Joseph Longoria, MS (UT Southwestern Medical Center)

Background: While extensive research has evidenced the impact of objective socioeconomic status (SES) and socioeconomic disadvantage on cognitive impairment, subjective elements have been relatively understudied. Using preliminary data from a diverse probability-based community sample of adults, the aim of this study was to investigate the influence of perceived psychosocial disadvantage compared to traditional proxies of SES and cardiovascular risk in predicting cognitive impairment approximately ten years later. Methods: Five hundred sixty-four participants [Age$\bar{X}$=62, Female=60%, Black=34%; Hispanic/Latinx=10.4%] completed both Phase 2 of the Dallas Heart Study (DHS-2; Time 1) and Phase 3 [Dallas Hearts and Minds Study (Time 2)] ten years later. Participants rated their perception of neighborhood quality, cohesion, and exposure to violence in addition to their ability to pay for basic needs and healthcare at Time 1. At Time 2, participants completed a brief neuropsychological battery and received a consensus diagnosis of Cognitively Impaired or Non-Impaired. A logistic regression examined whether perceived neighborhood quality at Time 1 predicted cognitive impairment at Time 2, controlling for demographics (age, sex, race/ethnicity), objective proxies for SES (income, years of education), and cardiovascular risk score. Results: The overall model was significant ($p<.001$, $R2=0.18$). Perceptions of neighborhood quality ($p<0.001$), exposure to violence ($p=.02$), ability to pay for healthcare ($p<0.02$), and black race ($p=0.01$) were significant in predicting the odds of an individual being classified as 'impaired.' Specifically, the likelihood of receiving an impaired diagnosis increased with lower reported neighborhood satisfaction (OR=0.63), higher neighborhood violence (OR=1.39), and lower ability to pay for healthcare (OR= 0.66). Individuals identified as black were more likely to be classified as 'impaired' (OR=1.87) compared with their white counterparts controlling for demographics, objective proxies for SES, and cardiovascular risk score. Conclusions: Results extend prior research that has found associations between neighborhood disadvantage and cognition across the lifespan, showing these factors are associated with cognitive impairment approximately ten years later. Given the risks of perceived psychosocial disadvantage on cognition over time, efforts to address root causes of these concerns while considering the disproportionate impact on individuals from marginalized populations has the potential to affect long-term cognitive outcomes and inform public health policy.

Funding: Moss Heart Trust; COI: N/A

Poster # 55: THE UTILITY OF MONTREAL COGNITIVE ASSESSMENT SCORES IN PREDICTING ALZHEIMER'S DISEASE DEMENTIA PROGRESSION AMONG INDIVIDUALS WITH AMNESTIC MILD COGNITIVE IMPAIRMENT

Presenting author: Oscar Kronenberger, BA (UT Southwestern Medical Center)

Background: Predicting progression from amnestic mild cognitive impairment (aMCI) to Alzheimer's disease (AD) remains vital for determining treatment and prognosis. The Montreal Cognitive Assessment (MoCA) is a widely used screening tool, with a Memory Index Score (MIS) that can be derived from delayed recall items (15 total points; 3 points for free recall, 2 points for category cues, and 1 point for multiple choice cues). We evaluated whether different MoCA and MoCA-MIS scores predicted conversion from aMCI to AD dementia. Methods: Data from individuals with aMCI aged >=50 years (M = 75.35, SD = 7.92) with at least 7 visits (n=356) were obtained from the National Alzheimer's Coordinating Center. Participants were educated (M=16.37 years, SD=5.21), and mostly male (n=207, 58%), with 190 (53%) converting to AD dementia over the next 6 visits. Stepwise logistic regressions controlling for demographics and apolipoprotein E4 status examined risk of AD conversion based on MoCA-Total (Range 6-30, M=22.3, SD=3.3), MoCA delayed recall score (Range 0-5, M=1.3, SD=1.5), MoCA-MIS (Range 0-15, M=7.7, SD=3.6), and added MIS points (i.e., MIS category and multiple choice points minus MIS delayed recall points;

Range 0-10, M=3.9, SD=2.1) over the next 6 visits. Results: In separate models, MoCA-Total Score (OR=0.786, Nagelkerke R2=0.22, Classification accuracy=70.5%), MoCA delayed recall score (OR=0.624, Nagelkerke R2=0.22, Classification accuracy=67.4%), MoCA-MIS Score (OR=0.823, Nagelkerke R2=0.22, Classification accuracy=67.4 %), and added MoCA-MIS points (OR=1.123, Nagelkerke R2=0.12, Classification accuracy=61.2%), all predicted dementia conversion (p's < .001). Conclusion: Total MoCA scores, delayed recall scores, and total MIS scores were generally similar in terms of classification accuracy and odds ratios to predict conversion to AD. Unlike the other MoCA and MoCA-MIS scores, points added from categorical/multiple choice cues after accounting for delayed recall points actually increased risk of conversion by ~12% for each additional point, perhaps due to the inverse relationship with missed delayed free recall items. As such, clinicians are cautioned against using categorical cues and multiple-choice performance to predict dementia risk from aMCI. Future research efforts may explore if applications of the MoCA-MIS have clinical value (e.g., patterns of MoCA-MIS in separating AD from non-AD dementias).

Funding: N/A; COI: N/A

Poster Theme Group D1. Dementia Care Research (nonpharmacological) & Poster Theme Group G3. Prevention (nonpharmacological)

Poster # 56: THE IMPACT OF IMMERSIVE VIRTUAL REALITY MEDITATION ON MENTAL HEALTH AMONG PEOPLE LIVING WITH DEMENTIA

Presenting author: Junhyoung Kim, PhD (Texas A&M University Health Science Center)

Background: Non-immersive, technology-based mindfulness meditation programs have been shown to effectively reduce stress and improve the mental health of users. Still, little research has been conducted to assess the health benefits of an immersive virtual reality meditation (IVRM) program among persons living with dementia (PLWD). The current pilot study investigates the impact of the IVRM on depression and anxiety among PLWD. Among the innovations of this study is its assessment of a physiological measure of emotional health. Methods: This pilot study is based on a single-arm, longitudinal design. PLWD (N=8) received six sessions (three times a week for 2 weeks) of an IVRM program lasting 30-40 minutes each. The IVRM program is used as an individualized, customized meditation tool within the context of VR that provides more than 300 audio tracks, meditation process monitoring, and a selection of meditation environments. We used electrocardiography to measure coherence achievement score (CAS), the Rating Anxiety in Dementia (RAID) scale to measure anxiety, and the Cornell Scale for Depression in Dementia Short Form to measure depression. The Generalized Estimated Equation (GEE) was used in this study. Results: The descriptive baseline data for study variables anxiety and depression were (M = 12.83, SD = 3.51) and (M = 7.88, SD = 1.95) respectively, and CAS gap between before and after six sessions of IVRM (M = 81.68, SD = 24.21). The participants showed lower anxiety and depression levels by achieving a large CAS gap after the use of IVRM. Age was a significant parameter of depression (B = 0.01, 95% CI, 1.00 - 1.04), indicating that participant depression levels were age-dependent. Conclusion: This pilot study provides suggestive evidence that the IVRM program led to the improvement in CAS, which is associated with a reduction in depression and anxiety. Findings suggest that the IVRM program can be instrumental in reducing depression and anxiety among PLWD. It is recommended that activity professionals, caregivers, and therapists who work with PLWD learn more about IVRM programs and how they might be integrated into their services to improve the emotional health and well-being of their clients.

COI: None

Poster # 57: THE LONGITUDINAL RISK OF ALZHEIMER'S DISEASE AND OTHER DEMENTIAS FOLLOWING PARTICIPATION IN COGNITIVELY STIMULATING LEISURE ACTIVITIES AMONG MCI AND NON-MCI

Presenting author: Junhyoung Kim, PhD (Texas A&M University Health Science Center)

Background: There is growing interest in identifying interventions that can slow the onset and progression of Alzheimer's Disease and Related Dementia (ADRD). This study investigated the longitudinal relationship between participation in Cognitively Stimulating Leisure Activities (CSLAs) and the risk of ADRD among older adults with and without mild cognitive impairment (MCI). Methods: This study analyzed data from the Health and Retirement Study from 2012 to 2020. Older adults with MCI (n = 14,280); and without MCI (n = 13,695) were identified for comparison purposes. Generalized Estimated Equation (GEE) was used to investigate the longitudinal relationship between CSLA and the risk of AD/ADRD assess differences. The GEE-based logistic regression model was used to calculate the probability of disease between 0 and 1 (coded as 1 for diagnosed, 0 for non-diagnosed) during the given period. We compared the odds ratio of AD/ADRD following a level of CSLA participation between the MCI group and the non-MCI group. Results: We see that the probability of AD/ADRD decreased by 71% when respondent CSLA engagement reached a score of 44 or higher and increased by 2% per year of advancing age among participants with MCI. In addition, for participants without MCI, the probability of developing AD/ADRD decreased by 67% when the respondent CSLA engagement was measured at a score of 37 and increased by 1% per year of advancing age. The results show that CSLAs are associated with a reduced probability of reporting the presence of ADRD in both groups over an eight-year timeframe. Conclusions: This finding suggests that CSLAs may serve as an effective intervention to reduce the risk of developing ADRD. The stronger association among older adults with MCI, compared to those without MCI, suggests priority target populations for CSLA intervention. Thus, therapists and healthcare providers can use the new knowledge generated in this study to design and implement effective CSLA-based dementia prevention interventions for older adults with different levels of cognitive impairment.

COI: None

Poster Theme Group D1. Dementia Care Research (nonpharmacological)

Poster # 58: DEVELOPMENT AND PRELIMINARY EVALUATION OF THE OLERA.CARE: A NOVEL DIGITAL CAREGIVING ASSISTANCE PLATFORM FOR DEMENTIA CAREGIVERS

Presenting author: Logan DuBose, MBA, MD (Texas A&M University Health Science Center)

Background: With the escalating prevalence of Alzheimer's disease (AD) and related dementia (ADRD) in the United States, there is an urgent need for innovative solutions for caregivers. A web-based care planning tool, Olera.care, was designed and developed as a digital aid for caregivers managing dementia-related challenges. This study aims to preliminarily evaluate the quality and usability of the Olera.care platform. Methods: Participants were engaged in two rounds of interviews to understand their caregiving needs, engage with the platform, and complete the modified Mobile Application Rating Scale (MARS) via a Qualtrics online survey. The survey also included the sociodemographic characteristics and caregiving experiences. Descriptive statistics were used to describe the quality and usability of the platform and characteristics of the participants. Two-sample t-tests were conducted to examine the differences in the major MARS evaluation scores by caregiver characteristics. Results: The evaluation engaged 30 adult caregivers in Texas, predominantly over 50, female, White, financially stable, and primary caregivers with an average caregiving duration of 5.45 years. The Olera.care platform received high overall satisfaction (4.57/5) and scored favorably across all caregiver demographics in engagement, functionality, aesthetics, and information quality (scores ranging 4.10-4.76). A statistically significant difference (P=0.021) was observed in functionality evaluation scores by duration of caregiving, with caregivers dedicating more hours to care rating it higher than those providing less care (4.6 vs 4.2). Additionally, caregivers with less caregiving experience reported significantly higher evaluation scores (Ps<0.05) for aesthetics (4.7 vs 4.3) and information (4.8 vs 4.6) compared to those with longer years of caregiving. All participants expressed a willingness to recommend the platform, with 90.0% giving it an overall positive rating. Conclusion: The preliminary assessment of Olera.care indicates its potential as an efficacious, user-friendly, and informative digital resource for dementia caregivers. Further development and expansive research are recommended to optimize the platform and validate its utility across a more diverse caregiver cohort.

Funding: NIA SBIR 1R44AG074116-01; solicitation AG21-025; COI: None

Poster # 59: EXPLORING ELDER CARE NEEDS OF TEXAS-BASED FAMILY CAREGIVERS FOR PEOPLE LIVING WITH DEMENTIA: A MIXED-METHODS NEEDS ASSESSMENT STUDY

Presenting author: Minh-Nguyet Hoang, MBA (Texas A&M University Health Science Center)

Background: Family caregivers, especially those caring for people living with dementia (PLwD), often have neglected needs and expectations. This study aims to investigate the elder care needs and preferences for a digital health platform among these family caregivers for PLwD. Methods: Using a purposeful sampling approach, adult family caregivers in Texas involved in dementia care were recruited from January to May 2022. Participants engaged in two rounds of Zoom interviews to express their caregiving needs and completed a survey via Qualtrics. Thematic analysis was utilized to analyze qualitative data, focusing on caregivers' financial, legal, and functional needs and their desired features of a digital health platform. Descriptive analysis of the survey data examined the most used and needed elder care services and communication preferences. Data triangulation was implemented to determine most sought-after features and needs for a digital health platform to support caregiving. Results: Thirty caregivers (mean age: 61.57±2.23 years; 76.7% female; 83% White; 10% Hispanic; 53.3% employed) participated in both the interviews and surveys. The most frequently utilized elder care services included home health (63.3%), hospice (33.3%), and certified financial planners (30.0%). Thematic analysis revealed challenges in functional care and financial and legal aspects of caregiving. Participants expressed a need for an integrative digital platform that offers educational resources, community support, and information sharing to enhance care quality and reduce caregiver burden. Key needs identified included caregiver support groups (80.0%), medical providers (76.7%), and memory care providers (63.3%). A preference for anonymous initial interactions and the use of computer browsers over mobile apps was noted. Conclusion: The study highlighted the elder care needs of family caregivers for people with dementia in Texas, underscoring the need for a web-based digital health platform that caters to caregiver support, medical assistance, and memory care services.

Funding: NIA SBIR 1R44AG074116-01; solicitation AG21-025; COI: None

Poster # 60: THE IMPACT OF THE JIGSAWDIO PROGRAM ON COGNITIVE FUNCTION AND MENTAL HEALTH AMONG PEOPLE LIVING WITH DEMENTIA

Presenting author: Yongseop Kim, PhD (Texas A&M University Health Science Center)

Background: There is recent interest in creating novel interventions that improve the cognitive abilities and mental health of PLwD. This qualitative study was also employed to elicit perceptions of the benefits and challenges associated with using the Jigsawdio program, an innovative application of an audiovisual jigsaw puzzle, which creates meaningful moments for PLwD from multiple stakeholders including PLwD, caregivers, and facility staff. As a pilot study, the main purpose of this study was to provide the foundation for designing a follow-up experimental study to further explore the benefits of Jigsawdio program. Methods: The qualitative study was designed to capture the benefits and challenges associated with the use of the Jigsawdio program among PLwD (N=12), caregivers (N=6), and facility staff (N=1). This device is designed to provide the PLwD with customized, individualized puzzles involving a personalized, low-tech, easy-to-use, and mentally stimulating tablet interface. Photos, stories, and music are used to manufacture functional puzzles capable of replaying audio recordings. Using a purposeful criterion sampling strategy, semi-structured in-depth interviews were conducted with 19 participants. Data were qualitatively analyzed using the constant comparative method. Result: Based on the participant statements and experiences about their Jigsawdio experience and the caregiver and trained staff observations, two major themes were reported as health outcomes by participants as further described below: (a) enhanced cognitive function and (b) improved emotional health. This finding suggests that the Jigsawdio program can be beneficial for the cognitive and emotional functioning of participants. Conclusion: The findings present evidence that PLwD participants who engaged with Jigsawdio experienced enjoyment and a sense of achievement, positive experiences that can be effective in reducing depression levels. Also, caregivers and facility staff provided evidence of the impact of Jigsawdio on emotional health, indicating that Jigsawdio improved the enjoyment of PLwD participants based on their observations. This preliminary evidence provides implications for future researchers who wish to investigate the effect of Jigsawdio program use on the

emotional health of PLwD. Thus, the finding of our study suggest that Jigsawdio can be used as a mechanism to increase cognitive function and emotional health by enabling PLwD to explore meaningful event.

Funding: NIH; COI: None

Poster # 61: EXAMINING THE EFFECTS OF AN INTERVENTION FOR PERSONS WITH DEMENTIA AND THEIR FAMILY CAREGIVERS ON NEUROCOGNITIVE OUTCOMES: A PILOT STUDY

Presenting author: Sydnie Schneider, BS (Texas Tech University)

Background: Alzheimer's Disease and Alzheimer's Disease Related Dementias (AD/ADRD) will affect approximately 13 million individuals by 2050. As AD/ADRD progresses, individuals become increasingly reliant on family caregivers, who have a higher risk for negative health outcomes, including neurocognitive decline. However, research has shown an interdependence on outcomes between the person with AD/ADRD and their family caregivers. Though respite services have been shown to be beneficial for family caregivers and recreational-based activities beneficial to persons with AD/ADRD, current interventions have failed to examine effects on both individuals. This preliminary investigation examines the effect of a recreational-based intervention for the person with AD/ADRD and respite for the family caregiver on overall neurocognitive functioning. Method: Participants were persons with AD/ADRD and their family caregivers (6 dyads; N=12). AD/ADRD participants attended 12 once-weekly, 3-hour recreational-based intervention sessions that includes activities (i.e., sensory, fine motor, physical, visual/auditory activities), which provides 3 hours of respite to family caregivers. Neurocognitive functioning was measured at baseline and 12-weeks using the RBANS. Results: Average overall neurocognitive functioning scores improved in family caregivers between baseline (M = 108.0, SD = 6.4) and the 12-week follow-up (M = 111.3, SD = 7.3). The average overall neurocognitive functioning scores for the person with AD/ADRD remained the same at baseline (M = 51.8, SD = 15.4) and the 12-week follow-up (M = 51.8, SD = 16.3). There also appeared to be some indication of interdependence between the dyad. More specifically, two dyads showed a direct interdependence as both increased in neurocognitive functioning. The other four went in a similar direction as either one of the members of the dyad showed no change in their scores while the other improved. Conclusion: This pilot study suggests this dyadic intervention, respite and recreational intervention, positively effects neurocognitive functioning in both the person with AD/ADRD and the family caregiver. More specifically, it appears our hypothesized mechanism of reducing stress (through respite), has a positive effect on the family caregiver's neurocognitive functioning. Further, only 1 of the 6 persons with AD/ADRD showed decline in neurocognitive functioning where others improved or remained stable following the intervention.

Funding: Private funding; COI: No conflicts of interest to disclose

Poster # 62: FACTOR STRUCTURE OF THE INSTRUMENTAL ACTIVITIES OF DAILY LIVING SCALE VARIES BY ETHNOLINGUISTIC GROUP

Presenting author: Bonnie Scott, PhD (UT Austin Dell Medical School)

Background: In our prior work (Scott, under review), we found collateral informant ratings of functional impairment (FI: Instrumental Activities of Daily Living Scale [IADLS]) were influenced by the interaction of gender with ethnicity and language dominance. Here, we sought to compare the underlying factor structure of the IADLS in cognitively normal older adults from different ethnic (Hispanic vs. Non-Hispanic) and linguistic (English vs. Spanish dominant) groups. Methods: Baseline data from 1060 cognitively normal older adults [Non-Hispanic English-speakers (NE) = 597; Hispanic English-speakers (HE) = 249; Hispanic Spanish-speakers (HS) = 214] between 50-90 years of age enrolled in the Texas Alzheimer's Research and Care Consortium (TARCC) Longitudinal Hispanic Cohort Study were analyzed by means of exploratory factor analysis (Promax rotation) performed separately in each ethnolinguistic group. Results: Indicators of factorability were good in each group and the cumulative variance explained ranged from 58.3% to 62.5%. Across groups, the first three items (Telephone, Shopping, Food Preparation) loaded strongly on to Factor 1 (F1), which did not include Finances and Medications (F2). However, only 2-factors

were identified in the NH group, while a slightly different 3-factor solution emerged in both the HE and HS groups. In the NH group, F1 also included Housekeeping and Laundry, while Transportation loaded onto F2. All three of these items loaded onto a third factor (F3) in the HS group, while Housekeeping loaded onto F1 and Laundry and Transportation onto F3 in the HE group. The amount of variance in each item explained by the analysis was in an acceptable range (>0.5) except for Transportation (0.19) and Medications (0.36) in the NH group and Transportation (0.45) and Finances (0.34) in the HS group. Conclusions: Obtained findings suggest that specific IADLS items may function differently in cognitively normal older adults from different ethnic and linguistic backgrounds. Altogether with our previous work, these data highlight a lack of equivalence in the construct validity of a common psychometric tool used to assess FI in dementia evaluations.

Funding: Texas Alzheimer's Research and Care Consortium and Alzheimer's Association; COI: None

Poster # 63: CALCIUM-PERMEABLE AMPA RECEPTOR ELECTROPHYSIOLOGICAL RESPONSES IN INDIVIDUALS RESILIENT TO ALZHEIMER'S DISEASE NEUROPATHOLOGY

Presenting author: Berenice Adriana Gutierrez Grebenkova, MD, PhD (UT Medical Branch at Galveston)

Alzheimer's disease (AD) is a prevalent form of dementia characterized by the accumulation of amyloid beta and pTau proteins in the brain. Interestingly, there are individuals without dementia symptoms but with high AD pathology, known as resilient individuals. Calcium-permeable AMPA receptors (CP-AMPARs) have been implicated in the calcium dyshomeostasis of AD, however their electrophysiological properties in resilient individuals are still unknown. To investigate this, we examined the synaptic responses of CP-AMPARs in a cohort of 30 individuals, including control (3M,4F; non-demented/no neuropathology), AD age-matched to control (2M, 5F), resilient (2M, 6F; non-demented with AD neuropathology), and AD age-matched to resilient (2M, 5F). We isolated and transplanted synaptic membranes from the parietal cortex of each group into Xenopus laevis oocytes. By activating and subsequently inhibiting AMPARs, we determined the contribution of CP-AMPARs to the overall response, revealing differences in the responses of CP-AMPARs in resilient individuals. Further investigations are needed to fully understand the mechanisms underlying these alterations and their implications for the progression of AD.

Funding: AG070255 to AL; COI: No conflicts of interest

Poster # 64: FAMILY CAREGIVERS' USE OF GAMEPLAN4CARE, AN EVIDENCE-BASED, ONLINE APPROACH TO DEMENTIA CARE

Presenting author: Marcia Ory, PhD (Texas A&M University Health Science Center)

Background: There is a need to translate dementia caregiving interventions into acceptable online websites for family caregivers. GamePlan4Care (GP4C) translated one of the leading evidence-based dementia caregiving interventions, Resources for Enhancing Alzheimer's Caregiver Health II (REACH II), into an online, interactive system. GP4C includes the full breadth of REACH II education and skill-building materials, delivered within an automated, online platform with integrated support from a Dementia Care Specialist via telephone/video conferencing. The earlier TARCC-funded Texas Cares initiative helped lead to funding from the National Institute of Aging (NIA) to further develop the specific computer programming for GamePlan4Care decision algorithms and to conduct a randomized clinical trial of its effectiveness. Methods: The GP4C online system was provided to 120 family caregivers of persons living with dementia as part of an NIA-funded study (R01 AG061973). This poster presentation will focus on caregivers' use of the system and on feedback collected in a formal questionnaire completed by caregivers after 6 months of use of the GP4C online system. The therapeutic content included 7 domains: Safety, Stress, Health, Emotions, Care Services, Support, and Behaviors. Caregivers were involved in the creation of the system and will be engaged in its refinement. Results: 93 family caregivers (77.5%) successfully accessed the system. The average amount of time that caregivers used the system was about 6 hours. On average, users logged into the system an average of 14 times. Of the seven content domains represented in the system, Safety and Stress were the two most visited domains in the system. Social Support and Health were the two least visited domains by caregivers. Overall, caregivers reported benefiting from GP4C. Conclusion: This study provided insights into intervention

implementation. Overall use of the GP4C online system was less than expected. Caregivers reported several "usability" issues with the system and that the content was more appropriate for those new to the role of dementia care. Modifications to the content and functionality of the GP4C system are ongoing and will be evaluated in future studies.

Funding: Funding by NIH/NIA: R01AG061973, A. Stevens, Principal Investigator (PI), TARCC Texas Cares; COI: None

Poster Theme Group D2. Psychosocial Factors and Environmental Design

Poster # 65: KEY FACILITATORS TO AGING-IN-PLACE FOR OLDER ADULTS WITH DEMENTIA: GLOBAL PERSPECTIVES ON ACHIEVING A DEMENTIA-FRIENDLY GLOBAL COMMUNITY

Presenting author: Marcia Ory, PhD (Texas A&M University Health Science Center)

Introduction: Alzheimer's Disease and related dementias (ADRD) are on the rise globally, making investigation into ways to ameliorate these issues a timely and critical pursuit. Methods: An international Delphi survey was conducted to gather information from experts in: 1) Aging Services, 2) Built Environments, and 3) Health Care; with n~50 overall, with ~15 in each of these 3 areas of expertise. Experts answered, What are the major facilitators that already exist or that could be implemented for those with dementia that could help in safely navigating the community?; with emphasis on modifiable items that can make it easier for older adults with dementia to safely navigate their community. Results: Experts identified several major facilitators: community resources including financial assistance; informal caregiving resources (non-professional); formal caregiving resources (professional and/or paid); informal social support (non-caregiving); dementia-specific training (not caregiver related); dementia-specific training (caregivers); interagency alignment/integration/multi-sectorial approaches; programs/services; community awareness about dementia needs; housing design; community design; wayfinding; transportation/ transportation planning technology; policy/advocacy/gov. Among those items identified as factors that could help implementation of the above mentioned facilitators (if not already implemented or not implemented widely) experts identified several items including, but not limited to: improved federal and state funding; policy changes to provide funding for construction; the Alzheimer's Association; increased grant funding for fall-specific evidence-based programs; caregiver programs; respite programs; grant funding in smaller rural communities; providing incentives to businesses/organizations to get involved; building landmarks (for wayfinding); clearly identifying different municipal agencies and the specific actions they will perform towards improving community navigation; funding for transportation services; national campaigns for dementia-friendly communities; more education offerings across all areas of social and health services; and improved social interaction. Conclusions: Identifying strategies to help enable individuals with ADRD to age-in-place is critical, especially with insights from multiple areas of expertise with global insights.

Funding: Support/Funding Source: NIH 1R01CA197761-01; COI: None

Poster Theme Group D2. Psychosocial Factors and Environmental Design
& Poster Theme Group D1. Dementia Care Research (nonpharmacological)

Poster # 66: EFFECTIVENESS OF A BILINGUAL PROBLEM-SOLVING TRAINING FOR CARE PARTNERS OF ADULTS WITH DEMENTIA

Presenting author: Matthew Lee Smith, PhD, MPH, CHES (Texas A&M University Health Science Center)

Background: Care partners (i.e., informal caregivers) of individuals with Alzheimer's disease and related dementias (AD/ADRD) are essential, but often underserved, members of the healthcare team. This is especially true among those with fewer resources and the large and rapidly growing Hispanic population. Care partners often experience debilitating caregiver burden and emotional distress. Though Problem-Solving Training (PST) is known to effectively improve burden and distress, less is known about the intervention dose necessary to evoke and maintain PST benefits

(e.g., number of PST sessions, post-training "boosters"). Methods: We conducted a factorial-design randomized optimization trial of remotely delivered PST (or the Spanish language version: DSJ) sessions to care partners of those with AD/ADRD. The purpose was to compare the efficacy and feasibility of 3 vs. 6 PST/DSJ sessions + booster sessions to decrease care partner burden and depression. Caregiver burden was measured with the Zarit Burden Interview. Depression was measured with the eight-item version of the Patient Health Questionnaire (PHQ-8). Burden and depression were assessed at baseline, 1-month after intervention completion (i.e., prior to boosters), and 6-months after intervention completion (i.e., after the time window for boosters). Results: Ninety-seven care partners participated in the study. Participants' median age was 61 years and 85% were women. For caregiver burden, all intervention groups improved significantly over time (p=.004), with no difference by group in burden or change in burden over time. Women overall reported higher caregiver burden than men (p=.004) across time points. For depression, though all groups improved over time, those receiving 6 sessions showed greater improvement over time (p=.07) than those receiving 3 sessions, regardless of boosters. Conclusion: PST/DSJ was effective for improving caregiver burden and depression in as few as three sessions, though six sessions may have an even greater benefit for improving depression among care partners. These results will help us establish guidelines to implement an evidence-based, culturally adapted problem-solving intervention to reduce stress and burden and improve health and well-being among diverse dementia care partners.

Funding: Study funded by TARCC; COI: The authors have nothing to disclose.

Poster # 67: ASSESSING SOCIAL-EMOTIONAL RISK AMONG OLDER ADULTS WITH VARYING COGNITION LEVELS

Presenting author: Matthew Lee Smith, PhD, MPH, CHES (Texas A&M University Health Science Center)

Background: Health assessments among persons with cognitive impairment often focus on task performance and activities of daily living. Unfortunately, social and emotional health are less frequently assessed, which limits opportunities for intervention. The purpose of this study was to assess social-emotional risk among older adults with varying levels of cognition. Methods: Neurocognitive and self-reported data were collected from 89 adults in a clinical setting. The Saint Louis University Mental Status (SLUMS) Examination was administered to assess cognition among participants. Participants also completed a survey to identify their self-reported levels of depression (i.e., measured with the Patient Health Questionnaire [PHQ-9]), anxiety (i.e., measured with the Digital Choice Anxiety Survey [DCAS-7]), social disconnectedness (i.e., measured with the Upstream Social Interaction Risk Scale [U-SIRS-13]), and loneliness (i.e., measured with the UCLA-3). Internal consistency reliability coefficients (i.e., Cronbach's alpha) were calculated for all scales. Relationships between measures were assessed using Pearson's r correlations. Scale reliability and relationships were assessed for consistency within each SLUMS category: Regular Cognitive Function (28.1%); Mild Cognitive Impairment (46.1%); and Dementia (25.8%). Results: On average, participants were age 74.2±6.3 (range: 65-93 years) and 62% were female. Internal consistency reliability coefficients were strong for the PHQ-9 (alpha=0.833), DCAS-7 (alpha=0.751), U-SIRS-13 (alpha=0.777), and UCLA-3 (alpha=0.791). SLUMS scores (i.e., higher indicates better cognition) were negatively associated with depression (r=-0.25, P=0.020), social disconnectedness (r=-0.22, P=0.047), and anxiety (r=-0.24, P=0.025). Significant positive associations were observed between depression, anxiety, social disconnectedness, and loneliness, respectively (P<0.001). The relationships between depression and social disconnectedness remained statistically significant within each SLUMS category (P<0.01). All scale reliability coefficients remained strong among older adults with Mild Cognitive Impairment; however, only the correlation between SLUMS scores and social disconnectedness remained statistically significant (r=-0.37, P=0.036). Conclusion: Findings suggest that persons with more cognitive impairment have more social-emotional risk indicators. While larger samples are needed to confirm these relationships, results indicate the utility of robust measures to identify social-emotional risk factors. Efforts are needed to identify social-emotional risk profiles among persons living with cognitive impairment and link them to cognitively-appropriate programs and services to reduce symptomatology and avoid negative consequences.

COI: The authors have no conflicts to disclose.

Poster Theme Group D2. Psychosocial Factors and Environmental Design

Poster # 68: LIVING IN A NEIGHBORHOOD WITH DIVERSE WALKABLE DESTINATIONS CAN HELP MAINTAIN PHYSICAL ACTIVITY IN OLDER ADULTS DURING COVID-19 PANDEMIC

Presenting author: Xi Chen, PhD (Texas A&M University Health Science Center)

Background: Physical activity decreased significantly during COVID-19 due to the public health mandates implemented to reduce the spread of disease. Such measures may also contribute to inadvertently expediting the progression of cognitive decline and future risk of dementia in older adults. The positive roles of the diversity of neighborhood walkable destinations (NWD) on physical activity in community-dwelling older adults have been well studied, but limited studies were conducted on people with memory problems (PwMP) and little is known about whether the mechanisms may vary between before and since COVID-19. This study, focusing on PwMP living in communities aims to investigate their changes in moderate to strenuous exercise (MSE) and recreational walking before and since COVID-19 and to what extent the diversity of NWD can help explicate any changes. Methods: We used retrospective caregiver-report online survey data from 77 caregivers for community-dwelling PwMP aged 50 or older living in Texas. Presence of NWD characteristics (e.g. stores, services, parks and recreational facilities, public buildings, places for social interactions) in the neighborhood where PwMP were living were reported by their caregivers considering the conditions immediately before COVID-19. Difference-in-difference (DID) estimations based on zero-inflated negative binomial regression models were performed to examine the differences in recreational walking and MSE before and since COVID-19 and if the differences vary by diversity of NWD. Results: In the total sample, there was a significant reduction in both recreational walking (Δ change=-45.16 min/week, S.E.=11.48) and MSE (Δ change=-36.64 min/week, S.E.=15.99) since COVID-19 compared to before COVID-19. COVID-19 impact on MSE varied by diversity of NWD (DID=0.83, p=0.025), with greater decrease in MSE being observed among people living in neighborhoods with low diversity of NWD. Conclusion: The findings of this study suggest that the variation in MSE change since COVID-19 can be partially explained by the diversity of the NWD. Post-pandemic planning policies and design guidelines need to consider enriching the NWD and services that can maximize the potential of PwMP to engage in physical activity even during stay-at home-pandemics like COVID-19.

Funding: National Institute on Aging; COI: None

Poster # 69: DESIGN FOR DEMENTIA-FRIENDLY LONG-TERM CARE: IMPACTS OF MULTI-LEVEL FACTORS ON RESIDENTS' SOCIAL ACTIVITIES

Presenting author: Xuemei Zhu, PhD (Texas A&M University Health Science Center)

BACKGROUND: About one in ten older adults are living with Alzheimer's' disease in the U.S., and this rate is even higher in long-term care facilities (LCFs). Social isolation is a growing public health challenge that has been declared a global epidemic for older adults. It may be more difficult to address social isolation when older adults move into LCFs, becoming more dependent on care and having less intimate social relationships. This study examines the impacts of LCF environments on social interactions among cognitively impaired residents and explores relevant, evidence-based design solutions. METHOD: A multi-state survey was conducted with LCF managers to collect information about their residents' social interactions and desired environmental improvements. With 228 completed surveys, we will continue collecting responses until January 2024. Preliminary analyses used ordinal logit models to predict the frequency of social interactions of residents with moderate or severe cognitive impairment, using facility and resident characteristics, physical environment, and social environment. RESULT: The top locations for social interactions in LCFs were central dining areas, covered outdoor seating areas, activity rooms, lounge areas, and main lobbies. Having memory care services in the LCF and more residents who were able to walk without assistance or who rolled wheelchairs for exercise increased social interactions for cognitively impaired residents. Among physical environmental factors, having lounge areas throughout the building and covered outdoor areas without seating improved their social interactions. The number of types of outdoor spaces reduced such social interactions, which is unexpected and possibly because the complexity of outdoor spaces made it more challenging to navigate for cognitively impaired residents. Among program offerings, card and game programs significantly increased social interactions for cognitively impaired residents. Music and art programs, however, reduce their social interactions. We

posit it may be due to the different focus of music and art programs and their varying impacts on the social interactions of people with dementia as suggested by previous research. CONCLUSION: Future design of LCFs should consider lounge areas throughout the building and covered outdoor areas as potential strategies to increase social interaction for residents with cognitive impairment.

Funding: This study is supported by the Innovation[X] grant from Texas A&M University; COI: None

Poster # 70: THE ASSOCIATION OF SUBJECTIVE COGNITIVE DECLINE AND DEMOGRAPHIC, SOCIAL, CLINICAL, AND NEUROPSYCHOLOGICAL FACTORS IN THE HABS-HD COHORT

Presenting author: Darrian Johnson (UNT Health Science Center)

Background: Mexican Americans experience an earlier onset of Alzheimer's disease, but research shows that the illness is diagnosed much later in their lives. Sociodemographic projections predict a larger percentage of Hispanics with subjective cognitive decline (SCD) in the future. SCD is related to cognitive decline and dementia risk. This study will explore how SCD is associated with sociodemographic and clinical factors along with cognitive performance amongst Mexican Americans (MA) and non-Hispanic white (NHW) participants of the Health and Aging Brain - Health Disparities Study (HABS -HD). Methods: In this longitudinal study, a cross-sectional analysis of cognitively normal participants was performed. The cohort underwent clinical interviews, neurocognitive and functional examinations, brain imaging, and biomarker review. Neighborhood socioeconomic status (NSES) was measured using the national area deprivation index (ADI) percentile ranking. Statistical analysis was based on binary logistic regression using SCD as the dependent variable and was stratified by ethnicity with sex, age, education, and BMI (body mass index) as co-variants. Results: SCD was present in 49% of the sample. MA were younger, less educated, more likely to live in the most deprived neighborhoods, and had less social support. In addition, they were more likely to be depressed and diabetic with higher BMIs and experiencing more SCD than NHW. MMSE scores were lower in MA. Logistic regression models showed an association of SCD with age and GDS scores in NHW and MA. After adjustment for cognitive scores, only GDS remained significant in both races. MA living in the most deprived neighborhoods had a 2.45 more chance to present with SCD than those living in the least deprived neighborhoods. There was no difference in NHW. Conclusion: Our study showed that individuals with a higher degree of SCD were more likely to live in high ADI neighborhoods. The idea of SCD as a proxy for objective memory impairment and AD faces many barriers in minorities. However, while chronic stress and depression burden vulnerable communities, it is possible that SCD may serve as an indicator for future cognitive impairment and prompt the establishment of strategies to address these issues in neighborhoods influenced by inequitable circumstances.

Funding: National Institutes of Health under Award Numbers R01AG054073 and R01AG058533, P41EB015922 and U19AG078109; COI: N/A

Poster # 71: EVALUATION OF CHATGPT RESPONSES TO QUESTIONS POSED BY DEMENTIA CAREGIVERS

Presenting author: Alyssa Aguirre, LCSW (UT Austin)

Background: Large-language models such as ChatGPT hold great promise to improve dementia caregivers' quality of life by providing high-quality responses to meet their information needs. Studies have examined ChatGPT responses to patients' questions about other health conditions, but to our knowledge, none have examined responses to topics relevant to dementia care. To date, evidence on the quality of ChatGPT responses is limited, and there remain no standardized methods for rating the quality of responses. In this study, 3 interdisciplinary dementia clinicians used a modified rating scale to examine the quality of ChatGPT responses to commonly asked questions of dementia caregivers. Method: 60 posts by dementia caregivers were selected from the social media platform, Reddit. Posts were verified by 3 dementia clinicians as representing dementia caregivers' wants and needs for information in the areas of memory loss and confusion, driving, and aggression. To evaluate the quality of ChatGPT responses, a 5-point rating scale was used. Responses received 1 point for each of the following characteristics: factuality; interpretation; application; synthesis; and comprehensiveness, with a possible total score of 0-5 for each response; higher scores

indicate higher quality. Results: ChatGPT quality scores ranged from 3 to 5 (highest quality); 26 (43%) of the 60 responses received 5 points; 21 (35%), 4 points; and 13 (21.7%), 3 points, suggesting that ChatGPT provided high-quality responses to complex questions posted by dementia caregivers. However, it did have limitations: 1) Being unable to anticipate future problems that a human professional might recognize and address in a clinical encounter; 2) Recommending strategies that caregivers have already explicitly tried; 3) Missing nuances, such as understanding that moving a relative to a 'home' meant residential care setting. Conclusion: This study suggests the potential of ChatGPT to provide high-quality information to enhance dementia care and patient-caregiver education in tandem with information provided by health professionals. Evaluating the quality of responses is necessary to ensure that adults can make informed decisions. ChatGPT has the potential to transform the field of medicine by shaping how caregivers receive health information, however, limitations such as the lack of transparency, potential bias, and inconsistency remain.

Funding: NIH R56 AG075770-01; COI: No conflicts of interest to disclose

Poster # 72: HARMONY IN NUMBERS: UNRAVELING THE TAPESTRY OF SOCIAL BONDS THROUGH AN INNOVATIVE MODEL OF INTERACTION

Presenting author: Ismael Perez (UT Health Rio Grande Valley)

Background: Social interaction is fundamental to the functioning of everyday life in both animals and humans. For instance, research on social interaction has revealed that a lack of it can lead to the development of altered behavioral effects such as depression, aggression, and anxiety (Andrade et al., 2023). Some datasets provide data on how much people interact with one another; however, the National Alzheimer's Coordinating Center (NACC) does not have this explicit metric included. To circumvent this limitation within the NACC dataset, the current study proposes the use of a latent variable for the measurement of social interaction. Method: The current study will utilize data from +47,000 individuals in the NACC dataset to develop a latent variable model that assesses social interaction. The latent variable will consist of four questions from the NACC dataset which are: living situation, level of independence, type of residence, and ability to shop alone. A structural equation model was conducted to determine whether the model has a proper index of fit. The latent variable was compared to the observed variable of dependability using items from the Functional Assessment Scale. Result: A chi-square analysis revealed high correlation between the variables (X^2 (63, 128098 = 191601, $p < 0.001$). Additional fit indices revealed that the model was as a latent variable of social interaction (CFI=0.919, TLI=0.900, and RMSEA=0.154, $p < 0.001$). Conclusion: The NACC dataset provides valuable information of health outcomes of older adults in the United States of America; however, the dataset lacks an important component which is measurement of social interaction. To our knowledge, the current study was the first that has attempted to create a direct way of measuring social interaction within the NACC dataset.

Funding: N/A; COI: None

Poster Theme Group E1. Dementia Care Practice (descriptive research)

Poster # 73: ADAPTATION OF GAMEPLAN4CARE FOR HOSPITAL CARE AND CARE TRANSITIONS

Presenting author: Molly Horstman, MD, MS (Baylor College of Medicine)

Background: Adults with dementia rely on family caregivers after hospital discharge. The increase in caregiving demands and caregiver stress following discharge may lead to worse outcomes for caregivers and adults with dementia. Our aim was to adapt GamePlan4Care, a community-based caregiver support intervention, to support caregivers of hospitalized Veterans with dementia at the Michael E. DeBakey VA Medical Center. Methods: GamePlan4Care combines online, self-directed skills training with four phone calls from a dementia care specialist. Using a planned adaptation approach, potential adaptations were identified through a review of the literature and semi-structured interviews with health professionals and caregivers. Prototypes of adaptations were created and

presented to three caregiving researcher consultants, a stakeholder panel that included a caregiver and health professionals, and individuals who implemented GamePlan4Care in the community. All adaptations were reviewed with the GamePlane4Care developer to assess whether adaptations preserved the core elements of the intervention. We used the Framework for Modification and Adaptations (FRAME) to record and describe the final adaptations. Results: All adaptations were planned and made during the pre-implementation stage. Content and context adaptations included: 1) adding training content for care transitions, 2) modifying existing content to improve caregiver engagement, and 3) modifying intervention delivery. Five training topics were added: completing a medication review, identifying red flags, identifying and addressing delirium, addressing functional decline, and learning new medical tasks. To provide VA-specific information about home and community services, a handbook was added to the intervention. To increase caregiver engagement, we reduced and simplified text throughout the intervention and removed repetitive portions of training videos. To ensure timely support, the intervention was redesigned to start while Veterans are in the hospital and the timing of phone calls with the dementia care specialist was changed to 2-, 7, 21-, and 90-days following discharge. All adaptations preserved the core elements of GamePlan4Care. Conclusions: Evidence-based interventions designed for outpatient and community settings need to be adapted before they can be implemented as part of hospital care. Using insights from multiple sources, we developed HospitalGamePlan4Care, a new intervention that combines care transitions training with an evidence-based dementia caregiver support intervention.

Funding: National Institute on Aging, VA Health Services Research and Development; COI: None

Poster # 74: DEMENTIA CARE MHEALTH APPLICATIONS FOR INFORMAL CAREGIVERS' INFORMATION NEEDS: A SYSTEMATIC EXAMINATION

Presenting author: Bo Xie, PhD (UT Austin)

Background: Informal caregivers of people with dementia (PwD) are using mobile health (mHealth) technologies, particularly mHealth applications (apps), as a cost-effective and convenient source for dementia care information. Some mobile apps for dementia caregivers are available to support caregivers. However, little is known about the types and quality of dementia care information within the apps, and if and how existing apps provide tailored information to dementia caregivers. This study aimed to address these gaps. Methods: 35 eligible mobile apps that provide support for informal caregivers' care for PwD were selected in August 2023 through a multi-stage process. Three frameworks were used to evaluate the selected apps: (1) types of dementia care information offered were assessed using a 3-item evidence-based ADRD daily care strategy framework, adapted from our own prior work; (2) quality of dementia care related information provided in the apps was assessed using the 11-item guidelines recommended by the National Library of Medicine of the National Institutes of Health; and (3) tailoring of care information were assessed using a 3-item framework adapted from the literature. Results: Results suggest that educational information was the most prevalent content in the apps (28 out of 35, 80%), followed by tangible actions (e.g., redirection, reassurance; 20/35, 54.3%) and referrals (e.g., consult with physician, contact community organization; 13/35, 28.6%). The most common indicators of dementia care information quality included content that avoided making unrealistic or emotional assertions (33/35, 94.3%) and clearly stated the apps' objectives (30/35, 85.7%), but few had content generated or reviewed by experts (8/35, 22.9%). Although many apps (19/35, 54.3%) collected personal health data, only a few (3/35, 8.6%) provided individualized content and feedback that match with caregivers' inputs, such as tailored to the relationship to the PwD or recommendations for the specific type of dementia. Conclusions: The results indicated that existing dementia care apps are insufficient in providing comprehensive, high-quality information tailored to informal caregivers' information needs. Informal caregivers of PwD should exercise caution when using existing dementia care apps. Findings from the investigation can inform future dementia care app developments to better support caregivers.

Funding: National Institute On Aging of the National Institutes of Health under Award Number R56AG075770; COI: No Conflict of Interest

Poster # 75: BARRIERS AND FACILITATORS: PROVIDERS' EXPERIENCES IMPLEMENTING COGNITIVE CARE PLANNING

Presenting author: Katherine Carroll Britt, PhD, MSN, RN (UT Austin)

Background: Cognitive care planning-the process of regularly and systematically assessing patient needs and documenting recommendations to address them-improves health and quality of life among patients with cognitive impairments, like Alzheimer's disease and related dementias (ADRD)1. A cognitive care plan may promote physical exercise, social engagement, healthier eating, medication recommendations, and overall improvement in care management (e.g., advance care planning), which translates to lower health facility use and better quality of life2. As dementia is progressive, even short-term improvements in quality of life, emotional health, and resource use can significantly alleviate the disease burden. With limited pharmaceutical treatments, cognitive care planning is likely to remain one of the most effective ways to promote care among patients with ADRD. Despite significant potential benefits for patients and caregivers, formal and individualized cognitive care planning remains underutilized. Methods: We conducted a qualitative study exploring providers' perceptions and experiences implementing cognitive care planning in their practice. A purposive sample of 8 primary care providers actively caring for older adults including patients with ADRD participated in semi-structured teleconference interviews. Iterative inductive content analysis was used to analyze data. Results: Our preliminary results indicate several barriers and facilitators for implementing cognitive care planning into practice by providers. Providers reported some familiarity with general cognitive care and assessment but lacked a clear systematic approach and thorough understanding of the cognitive care planning process and steps. Across patient- and caregiver-related, organization-related, clinical care team-related, and provider-related focused areas, we identified five categories: (1) perceptions (buy-in or reluctance), (2) family presence (context, support, communication, provider-patient relationship), (3) logistics and priorities (time, schedule, staffing, priorities), (4) structure/systemized approach (standardization, templates, clear roles, referrals), and (5) experience and training (confidence or unfamiliarity). Conclusion: Providers expressed the value of a structured approach for successfully implementing cognitive care planning. Buy-in at multiple levels (patient, caregiver, organization, and clinical team) may prompt prioritizing this care approach in practice to restructure the assessment process for older adults. In addition, caregiver and family accompaniment to patient visits can increase contextual knowledge and provider communication for tailoring cognitive care plans.

Funding: This study is supported by the National Institute On Aging of the National Institutes of Health under Award Number R44AG078006. Author KCB is supported by the National Institutes of Health, National Institute on Nursing Research (T32NR009356); COI: All authors have reported personal fees from BrainCheck, and KS and BH report receiving stock options from BrainCheck.

Poster Theme Group F1. Human

Poster # 76: UNRAVELING THE IMPACT OF LIFESTYLE AND BIOLOGICAL FACTORS ON COGNITIVELY HEALTHY SUPERIOR AGERS IN RURAL WEST TEXAS

Presenting author: Ujala Sehar, PhD (Texas Tech University Health Sciences Center)

Background and Purpose: Alzheimer's disease (AD) is a worldwide pandemic that affects the elderly, causing devastating consequences without a cure. Dementia's contributing factors include lifestyle choices, genetics, epigenetics, and socio-economic circumstances. In rural West Texas, cognitive health varies among those aged 60-90, some experience no impairments, and age gracefully while others face progressive decline with age. The underlying factors for these differences are not clearly understood. Our study examines the lifestyle and biological factors associated with successful cognitive aging in this region. Methods: Our longitudinal cohort study investigates factors impacting cognitive status in individuals aged 60-90. We aim to enroll 4000 cognitively healthy participants and 500 with MCI and AD/ADRD. The objective is to identify factors that contribute to delayed aging by exploring genetics, epigenetics, ethnicity, biology, culture, and lifestyle. To gather relevant data, we will assess participants' cognitive abilities using the Montreal Cognitive Assessment (MoCA), record anthropometric measurements, analyze blood profiles, and administer socio-demographic and behavioral questionnaires. Results and Discussion: At present, our study is in its first year and has successfully recruited 25 cognitively healthy individuals and 5 patients with AD. Through the assessment of bloodwork and questionnaires, we have observed that the cognitively healthy population

exhibits higher levels of physical and mental well-being. Additionally, we have identified a correlation between a healthy lifestyle, including factors such as sleep, diet, and exercise, and successful aging in the cognitively healthy group. Conclusion: Our current data indicate a clear association between scores on the MoCA test, blood biomarkers, and psychosocial parameters. The findings of the study are highlighting the pivotal significance of sufficient nutrition and lifestyle factors in preserving cognitive well-being and mitigating the risk of cognitive decline and its progression to dementia. These findings are significant and contribute to our understanding of healthy aging in the rural West Texas population. The outcomes of our study are anticipated to provide fresh and valuable insights into the factors influencing successful aging in this specific region.

Poster Theme Group G1. Epidemiology

Poster # 77: POTENTIAL BIOLOGICAL MECHANISMS UNDERLYING THE PROTECTIVE ASSOCIATION BETWEEN VACCINATIONS AND ALZHEIMER'S DISEASE: A LITERATURE REVIEW OF MOUSE MODEL STUDIES

Presenting author: Kristofer Harris, MPH, RN (UT Health Houston)

Background: Several epidemiological studies demonstrate a protective association between vaccinations and Alzheimer's disease (AD) and Alzheimer's disease and related dementias (ADRD). We, for example, have published studies illustrating the protective effects of influenza, Tdap/Td, shingles, and pneumococcal vaccinations on AD risk. We now propose to explore the mechanisms underlying this apparent protective effect. A number of theorized pathways have been proposed, including reduction of infection-mediated neuroinflammation and enhancement of the immune response to AD pathology (more efficient clearance, less collateral neurotoxicity to healthy parenchyma). We conducted a literature review of mouse model studies of pathogen-specific vaccinations (as opposed to vaccines specifically designed to elicit an immune response against AD pathology) and AD. Methods: A literature review was conducted on November 30, 2023 in PubMed using the terms: ("mouse" OR "mice") AND "alzheimer*" AND ("vaccin*" OR "immunization*"), along with the CDC's recommended adult immunizations for persons >65 years old and based on previous epidemiological data: "influenza", "respiratory syncytial virus", "tetanus", "diphtheria", "pertussis", ("shingles" OR "herpes zoster"), "pneumo*", "polio*", "hepatitis A", "hepatitis B", "typhoid", "rabies", "yellow fever", "cholera", ("meningitis" OR "meningococcal"), and ("bcg" OR "Bacille Calmette-Guérin"). Results: Overall, 50 manuscripts were identified. Four met criteria for this review. All studies used APP/PS1 transgenic mice. One study inoculated mice with an inactivated influenza vaccine, and three used BCG vaccinations. Age at vaccination ranged from 3-9 months, representing both pre-pathological and pathological stages of disease. Using the Morris Water Maze test, three studies measured spatial learning and memory and found that vaccinated mice outperformed controls. Influenza vaccination, but not BCG vaccination, was associated with a reduction in cerebral Aβ plaque burden; however, BCG vaccination was associated with reduced vascular amyloid deposition. There was an increase in pro- and anti-inflammatory cytokines for the influenza vaccine. BCG was found to increase anti-inflammatory and decrease pro-inflammatory cytokines. Conclusion: In humans, vaccines appear to influence AD pathobiology. In a mice model for AD the pathology improved through diverse mechanisms after immunization. Further research is needed comparing different vaccine technologies (adjuvanted, recombinant, mRNA, etc.) and vaccines targeting other diseases, such as pneumococcus, on AD pathobiology.

Funding: No funding to disclose; COI: Paul E. Schulz is funded by the McCord Family Professorship in Neurology, the Umphrey Family Professorship in Neurodegenerative Disorders, multiple NIH grants, several foundation grants, and contracts with multiple pharmaceutical companies related to the performance of clinical trials. He serves as a consultant and speaker for Eli Lilly, Biogen, and Acadia Pharmaceuticals. Xiaoqian Jiang is funded by Christopher Sarofim Family Professorship, the CPRIT RR180012 award, UT Stars award, and NIH grants R01GM114612 and U01TR002062.

Poster # 78: INTERACTION OF SOCIAL DETERMINANTS AND VITAMIN D3 LEVELS ON COGNITIVE TEST SCORES IN OLDER ADULTS FROM NHANES 2011-2014

Presenting author: Juan Carlos Lopez-Alvarenga, MD, DSc (UT Health Rio Grande Valley)

Introduction: Cognition, a complex combination of memory, executive function, reasoning, attention, and visuospatial skills, evolves dynamically with age. Cognitive assessments serve both diagnostic and exploratory purposes, influenced by factors like age, education, and income. The global surge in obesity and metabolic disorders raises concerns about cognitive function. This study delves into the combined impact of vitamin D levels, education, and household income on cognitive test scores in adults aged 60 and above, using NHANES data and the Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Methods: A cross-sectional analysis of NHANES 2011-2014 data included participants aged 60 and above who underwent Verbal Fluency, Word List Learning, and Digit Symbol Substitution Test. Structural equation modeling, adjusting for covariates, was executed with Stata release 18. Results: Involving 2,635 participants (mean age 69.4, BMI 29.1), education, household income, and vitamin D3 levels significantly correlated ($p<0.001$), forming a latent Factor1 explaining 49% of their total variance. Age, sex, and BMI remained observed exogenous variables. Cognitive tests correlated between 0.34 to 0.73 (all $p<0.001$), their combination explained 58% of variance. Factor1 had a significant impact on test scores ($b=0.46$). White and Asian ethnic groups scored higher on Factor1 and exhibited higher test scores. Conclusion: Economic household income and education, coupled with vitamin D3 levels, significantly influence cognitive test scores in older adults. Notably, these impacts are more pronounced in Hispanic groups and African Americans, highlighting disparities in cognitive outcomes. This study underscores the interconnected influence of social determinants and vitamin D on cognitive health in the aging population.

Funding: KL2; COI: N/A

Poster # 79: GAIT SPEED AND COGNITION IN THE COMPADRE-CART LONGITUDINAL HISPANIC/LATINO COHORT

Presenting author: Luis Serrano-Rubio, BS (UT Health San Antonio)

Background: The COMPADRE-CART study is a longitudinal 3-year study examining risk and resilience factors for cognitive decline in Mexican-American older adults, a population with 1.5 higher risk of dementia compared to non-Hispanic white adults. A gap in knowledge regarding how physical activity affects cognitive health exists. Measurement of gait speed has become a promising marker for early detection of cognitive impairment. In this preliminary analysis, we examined cross-sectional associations between gait speed and cognition in Hispanic/Latino participants in the COMPADRE study. Methods: Participants completed the NIH Toolbox 4-meter walk gait test and the Uniform Data Set (UDS) version 3, which includes clinical and cognitive assessments. Gait speed was measured by having participants walk back and forth over a 4-meter distance twice. The average speed in meters per second over the two trials was calculated. Linear regression models were used to analyze associations between gait speed and cognition, adjusting for age, sex, education, and BMI. Results: A total of 83 participants (mean age = 70, SD = 5; female 74%) were included in this preliminary analysis. Longer gait test times were associated with decreased MoCA scores ($p=0.04$). Non-significant associations were observed with Craft Story Immediate ($p=0.8$) and Delayed recall ($p=0.8$), Benson Immediate ($p=0.9$) and Delayed ($p=0.6$), Multilingual Naming Test (MINT; $p=0.7$), Category Fluency ($p=0.13$) and Trails B ($p=0.2$). Increasing Trails A scores were found to be marginally associated with longer gait test times ($p = 0.045$). Conclusion/Future Directions: This preliminary analysis found that faster baseline gait speed was significantly associated with better global cognition in Hispanic/Latino adults. Future longitudinal studies will be necessary to evaluate if gait speed can serve as an accessible, non-invasive biomarker for cognitive decline that could be leveraged to advance early diagnosis and intervention planning in at-risk populations.

Funding: R01AG077472, P30AG066546; COI: none

Poster Theme Group G3. Prevention (nonpharmacological)

Poster # 80: REDUCED HEALTH CARE ACCESSIBILITY INCREASES RISK OF VITAMIN D DEFICIENCY/INSUFFICIENCY: A PROJECT FRONTIER STUDY

Presenting author: Claudia Morris, BSA (Texas Tech University Health Sciences Center)

Background: Previously, we described health disparities in Vitamin D (VD) status, depression, and Hispanic ethnicity in an aging West Texas population from Project FRONTIER (Facing Rural Obstacles to Health Care Now Through Intervention, Education, and Research). Using the same sample, we examined relationships between VD status and existing variables that relate to health care access. Methods: Of 299 participants in which serum 25-hydroxyvitamin-D levels were available, we examined relationships between health insurance status, whether, in the past 12 months, cost prohibited a physician visit, and time since last physician visit. Logistic and linear regression analyses were performed on binary and categorical variables, respectively. We utilized the Mann-Whitney test for between-group comparisons. Results: VD levels among participants (n=299; mean age 62.6±11.8) were found to be deficient (□20 ng/ml, 25.17%), insufficient (21-29 ng/ml, 36.58%), sufficient (30-38 ng/ml, 22.15%) or high sufficient (>38 ng/ml, 15.77%). We found that 59/298 reported no health insurance. A significant negative association was found between the probability of health insurance and VD level (p=0.0042). Lower VD levels were observed in uninsured (24.9 ± 1.4 ng/ml) compared to insured (29.4 ± 0.8 ng/ml) participants (p=0.004). We also found a significant negative association between VD levels and the probability of experiencing a time in the past 12 months when needing to see a doctor but could not because of cost (n=294, p<0.0001). Finally, we found a significant negative association between VD level and the length of time it had been since the participant had seen a doctor (p<0.0001). Overall, these observations suggest that reduced accessibility to health care is significantly associated with lower VD levels. Conclusion: Our results reveal that insurance level, access to care, and length of time since seeing a physician likely impact VD status. The data suggest that access to care in rural West Texas participants influences VD levels in this aging population, highlighting areas where healthcare and education need to be improved. VD deficiency has previously been shown to be associated with depression and Alzheimer's disease in the elderly, further underscoring the importance of improving access to healthcare.

Funding: None; COI: None

Poster Theme Group H. Novel Statistical Methods

Poster # 81: PYTHON-BASED MACHINE LEARNING FOR THREE-DIMENSIONAL HUMAN BRAIN MODEL SEGMENTATION AND ANALYSIS

Presenting author: Morgan Mekale Smith, MS (UT Health San Antonio)

Background: Pathology and cell loss in neurodegenerative diseases results in brain atrophy of specific neuroanatomical structures, and is often characterized by subjective, qualitative severity measures. Three-dimensional (3D) imaging and modeling technologies now permit visualization and quantitative analysis approaches, including model mesh segmentation. One such platform for this approach is Python, a coding software containing libraries that facilitate the manipulation, visualization, and analysis of various data forms. We aim to apply these techniques to assess patterns of neurodegeneration in 3D brain surface models. Methods: 3D scanned brain .obj files were imported into Python. These file types function as 3D meshes and can be visualized using Python coding segments (various modules), Blender, and several other software applications. The .obj files of 3D brain models were simplified using Python software mesh decimation. This decimation reduced the number of faces, edges, and vertices and allowed for the manual segmentation of 3D models in Blender. We used the volume, area, number of vertices, edges, and faces to segment the 3D models based on readily identifiable cortical gyri and sulci. Next, we focused on automating segmentation of large, well-defined structures, namely the cerebellum and cerebrum. Segmentation was performed using vertices and texture mapping for comparative analysis. Using the manual mesh segmentation data from these 3D models, Python software machine learning techniques were applied to automate the mesh segmentation of various brain regions based on a healthy brain structure. Results: Using these techniques, we assessed tissue structural and tinctorial properties of the human postmortem autopsied brain to segment 3D models based on neuroanatomical location. We have developed and piloted machine learning techniques within the Blender application, which can be utilized to accurately identify anatomically correct structures of the brain. Conclusions: Our findings provide support for the utilization of machine learning techniques to identify specific areas of the brain using 3D brain models.

Additional research, validating against other imaging modalities including magnetic resonance imaging, is necessary to confirm the consistency surface mesh segmentation (both manual and automated) to other brain atrophy metrics. We believe these tools have broad applicability in practice (including guided tissue sectioning), research and education.

Funding: This work is supported by funding from the National Institute on Aging (P30-AG066546; R01-AG070214), Texas Alzheimer's Research & Care Consortium, Zachry Endowment for Alzheimer Research, Reed Precision Medicine Center, and the J.M.R. Barker Foundation; COI: There are no real or perceived conflicts of interest.