unchanged in animals consuming Mediterranean diets. Taken together, these findings demonstrate that Western diets induce widespread structural shifts which may increase risk of cognitive decline and neuropathology, whereas Mediterranean diets may exert a stabilizing influence on the brain. This study provides important insights about the significance of diet on brain structure and lays the groundwork for future investigations to uncover the molecular underpinnings of diet-induced changes in the brain. Mediterranean diet may protect against structural changes in brain that occur with age in those consuming a Western diet.

OBSTACLE NEGOTIATION IN OLDER ADULTS: PREFRONTAL ACTIVATION INTERPRETED THROUGH CONCEPTUAL MODELS OF BRAIN AGING

David Clark,[1] Sudeshna Chatterjee,[1] Rachael Seidler,[2] Jared Skinner,[3] Dorian Rose,[1] paige Lysne,[4] and Adam Woods,[5] *1. University of Florida, Gainesville, Florida, United States, 2. Applied Physiology and Kinesiology, Gainesville, Florida, United States, 3. Appalachian State University, Boone, North Carolina, United States, 4. Aging and Geriatric Research, Gainesville, Florida, United States, 5. Clinical and Health Psychology, Gainesville, Florida, United States*

Age-related decline in executive function is associated with walking deficits in older adults. The main objective of this study was to better understand the cognitive control of obstacle negotiation in older adults by identifying predictors of prefrontal recruitment during the task. The study also examined the association between prefrontal recruitment and walking performance as well as interpretation of prefrontal activity relative to cognitive models of brain aging. Prefrontal oxygenated hemoglobin concentration (O2Hb) was measured by functional near-infrared spectroscopy during typical walking (Typical) and obstacle negotiation (Obstacles) tasks in older adults. The primary outcome was change in prefrontal recruitment (ΔPFR), measured as Obstacles ΔO2Hb minus Typical ΔO2Hb. Stepwise regression was used to identify potential predictors of ΔPFR. Additional analyses were conducted to further examine the relationship between ΔPFR and the identified predictors. Greater ΔPFR was predicted by lower age, worse executive function, and their interaction ($R2=0.19$, $p=0.02$). Particularly, the effect of executive function on ΔPFR was more pronounced for "early aging" than for "late aging" older adults ($p<0.001$). Greater ΔPFR was significantly associated with a smaller reduction in walking speed during Obstacles compared to Typical. In conclusion, age, executive function, and their interaction predict prefrontal recruitment during obstacle negotiation in older adults. These findings are generally consistent with existing cognitive models of brain aging including neural inefficiency, compensatory overactivation, and capacity-limitation with a recruitment ceiling effect.

P300 AMPLITUDE IN RELATION TO AGE, NEUROPSYCHOLOGICAL PERFORMANCE, AND GENETIC RISK FOR ALZHEIMER'S DISEASE

Julia Sheffler,[1] Greg Hajcak,[2] Cynthia Vied,[2] Melissa Meynadasy,[2] and Russell Mach,[2] *1. Florida State University College of Medicine, Tallahassee, Florida, United States, 2. Florida State University, Tallahassee, Florida, United States*

The P300 event-related potential (ERP) is associated with aging and risk for Alzhiemer's disease (AD) and mild cognitive impairment (MCI). Our study sought to replicate previous findings regarding P300 amplitude, age, and neuropsychological outcomes. We also sought to fill gaps in the literature by assessing associations in a primarily healthy sample of older adults (aged 60-75) and through use of comprehensive assessment procedures for ERPs, neuropsychological outcomes, and a genetic risk score (i.e., BDNF, APOE, and PSEN1 mutations). Approximately 25% of our total sample (N=72) met criteria for possible or probable mild cognitive impairment. We assessed whether the P300 elicited by auditory (oddball) and visual (go/nogo) paradigms were associated with performance across neuropsychological tests commonly used in clinical settings, which include cognitive domains of semantic, episodic, and visual memory, executive functioning, language (confrontation naming), abstract reasoning (visual and verbal), and attention. Further, we examined associations between P300 and multiple genetic risks for AD. Our findings demonstrated differences in outcomes between audio and visual tasks of P300, with visual tasks tending to show stronger relationships with neuropsychological and genetic factors. Neuropsychological measures of memory and executive functioning were most closely related to visual P300 amplitude. P300 amplitude was also significantly associated with a genetic risk score for AD, despite the sample generally performing in the normal range on most neuropsychological tasks. Overall, our study has implications for use of the P300 for early detection of risk for AD and for improving our understanding of the P300 as a cognitive biomarker.

PAINTING BY LESIONS: FUNCTIONAL NETWORKS AFFECTED BY WHITE MATTER LESIONS ARE ASSOCIATED WITH POORER COGNITION

Rachel Crockett,[1] Chun Liang Hsu,[2] Roger Tam,[1] Todd Handy,[1] and Teresa Liu-Ambrose,[1] *1. University of British Columbia, Vancouver, British Columbia, Canada, 2. Harvard Medical School, Boston, Massachusetts, United States*

Cerebrovascular disease (CvD) is the second most common cause of dementia. Its associated pathology, such as white matter lesions (WML), is associated with reduced cognition. Due to the high variability, the relevance of WML location remains unknown. We hypothesised that although the location of WMLs may appear sporadic, they may actually lie within common functional networks. We used novel imaging methods to map the location of WMLs in a clinical sample with the functional connectivity associated with the same location in the human connectome. This identified the functional networks containing the largest WML load (>50%) in older adults with CvD. We then analyzed the association between level of disruption to these networks and measures of global cognition and executive functions. Included in this study were 164 older adults (>55 years old) with CvD. Cognition was assessed using the: 1) Montreal Cognitive Assessment (MoCA); 2) Stroop Colour Word Test; 3) Trail Making Tests; and 4) Digit Symbol Substitution Test. Our results found that the visual network and ventral attention

network (VAN) surpassed the 50% overlap threshold with 85% and 66% overlap respectively. Additionally, after controlling for multiple comparisons and age, the level of disruption to the VAN was significantly associated with poorer global cognition, as measured by the MoCA (p=.001). These novel findings identify the functional networks most affected by the presence of WMLs in older adults with CvD and suggest that the disruption to the VAN caused by WML load may underlie the deficits seen in cognition in this population.

PATTERNS OF WEIGHT CHANGE IN AGING AND DYING

Stephen Thielke, *University of Washington, Seattle, Washington, United States*

Little research has characterized the natural history of weight change in older adults. Different changes may occur during aging and dying. We analyzed 18 years of weight measures from a cohort of 736,361 Veterans, all of whom had died at age 70 or older. We produced summary measures that accounted for both chronological age and number of years before death. Several clear population-level trends appeared. (1) The average weight of the sample declined across all ages at a rate of about 0.18 BMI points per year. (2) Starting about seven years before death, the amount of loss began to accelerate, reaching a decline of 0.75 BMI points in the year before death. (3) Changes in weight relative to years of remaining life were independent of chronologic age. People who died at age 70 experienced, on average, the same type and duration of terminal decline as did those who died at age 95. (4) The dying process involved a cumulative loss of about 1.3 BMI points. (5) The distribution of weights during advancing age both declined and narrowed. (6) Disproportionate deaths occurred at the lower BMI ranges (below a BMI of 24), and especially below 18, regardless of age. (7) The finding in #5 is explained by the entire cohort losing weight, with death of the thinnest members. These findings argue for examining survival time in studies of weight change. They indicate that weight loss may be a natural part of dying, rather than a risk factor for it.

RESTRICTED MEAN SURVIVAL TIME IN ACTION TO CONTROL CARDIOVASCULAR RISK IN DIABETES (ACCORD) BLOOD PRESSURE

Sandra Shi,[1] Lee-Jen Wei,[2] and Dae Kim,[3] *1. Beth Israel Deaconess Medical Center, Boston, Massachusetts, United States, 2. Harvard School of Public Health, Boston, United States, 3. Hebrew SeniorLife, Harvard Medical School, Roslindale, Massachusetts, United States*

Background: Restricted mean survival time (RMST) provides mean time lost or gained by an intervention. This may be a more intuitive way to understand treatment effect. Objective: To determine overall and subgroup treatment effects from blood pressure targets in older adults with diabetes. Methods: We analyzed the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial data. Our outcome was cardiovascular disease free survival. We measured 5-year RMST (days) between standard and intensive blood pressure control, and compared the difference by age (≥70 or <70 years old) and glycemic control (standard vs. intensive). Results: Over 5 years, those with intensive treatment lived, on average, 1716 days compared to 1714 days with standard treatment, with a RMST difference of 1.3 days (95% confidence interval, -22.1, 12.4). Among adults ≥70 years old, compared to standard treatment, intensive treatment resulted in an additional 13.6 (95% CI, -43.2, 70.3) days, where the difference was -0.5 (-20.8, 19.7) days for those aged <70 years old (p-for-interaction=0.673). Compared to standard treatment, intensive treatment resulted in 28.1 (0.4, 55.9) more days for those assigned to standard glycemic control, but it appeared to result in 25.2 fewer days (-52.3, 1.9) for those assigned to intensive glycemic control (p-for-interaction=0.007). Discussion: The benefit of intensive treatment over standard treatment varies by age and glycemic control. RMST difference may allow for more intuitive and personalized weighing of benefits and risks of intensive blood pressure control.

ROLE OF GENETIC INTERACTIONS IN ALZHEIMER'S DISEASE: LESSONS FROM LONG LIFE FAMILY STUDY (LLFS)

Anatoliy Yashin,[1] Dequing Wu,[2] Konstantin Arbeev,[1] Eric Stallard,[3] Qihua Tan,[4] Alexander Kulminski,[1] Mary Feitosa,[5] and Svetlana Ukraintseva,[1] *1. Duke University, Durham, North Carolina, United States, 2. Duke University, Durham, United States, 3. Duke University, Biodemography of Aging Research Unit, Durham, North Carolina, United States, 4. University of Southern Denmark, Odense C, Denmark, 5. Washington University School of Medicine, St Louis, Missouri, United States*

Experimental and clinical studies of Alzheimer's disease (AD) provide plentiful evidence of AD heterogeneity and involvement of many interacting genes and pathways in regulation of AD-related traits. However, detailed mechanisms of genetic interactions (GxG) involved in AD remain largely unknown. Uncovering hidden patterns of such interactions from human data will help better understand the nature of AD heterogeneity and find new targets for AD prevention. In this paper, we applied a newly developed method of evaluating joint GxG effects on AD to analysis of the Long Life Family Study data. The analysis included several steps: (i) selecting candidate genes from stress response pathways that are thought to be involved in AD; (ii) estimating interaction effects of SNP-pairs on AD risk, and selecting the top interacting SNPs; (iii) running GWAS-like interaction analysis for SNP-pairs, with one SNP fixed; (iv) using characteristics of the detected SNP-pairs interactions to construct the SNP-specific Interaction Polygenic Risk Scores (IPRS); and (v) evaluating the effects of IPRSs on AD. We found that SNP-specific IPRS have highly significant effects on AD risk. For most SNPs involved in the significant interaction effects on AD, their individual effects were statistically not significant. Male and female analyses yielded different subsets of the top interacting SNPs. These results support major role of genetic interactions in heterogeneity of AD, and indicate that AD mechanisms can involve different combinations of the interacting genetic variants in males and females, which may point to different pathways of resistance/response to stressors in two genders.

TORQUE AND VELOCITY DEPENDENCE OF MUSCLE FATIGUE IN AGING

Liam Fitzgerald,[1] Anthony Martin,[2] Rajakumar Nagarajan,[3] and Jane Kent,[3] *1. University of*