(p=.025). Compared to non-carriers, carriers had higher levels of NfL (p=.014), lower performance on the MMSE (p<.001) and on the RPM (p=.001). In the whole sample, performance on the RPM was significantly associated with age (r= -.144, p<.001), and MMSE score (r=.198, p<.001). In carriers only, performance on the RPM was negatively associated with NfL levels (r=-.121, p=.009). This association was not significant in non-carriers.
Conclusions: Our findings support the hypothesis that plasma NfL levels may be indicators of disease progression and early cognitive dysfunction in autosomal dominant AD. Future work with NfL, abstract reasoning and memory with larger samples across the preclinical/prodromal spectrum will allow a more comprehensive examination of these associations.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: dementia - Alzheimer's disease
Keyword 2: cognitive functioning
Keyword 3: visuospatial functions
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5 Intraindividual Variability in Processing Speed on Digital Cognitive Assessments Differs by Amyloidosis Status in Cognitively Normal Older Adults

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Objective: Intraindividual variability (IIV) is defined as fluctuations in an individual's cognitive performance over time1. IIV has been identified as a marker of neurobiological disturbance making it a useful method for detecting changes in cognition among cognitively healthy individuals as well as those with prodromal syndromes2. IIV on laboratory-based computerized tasks has been linked with cognitive decline and conversion to mild cognitive impairment (MCI) and/or dementia (Haynes et al., 2017). Associations between IIV and AD risk factors including apolipoprotein (APOE) ε4 carrier status, neurodegeneration seen on brain imaging, and amyloid (Aβ) Positron emission tomography (PET) scan status have also been observed1. Recent studies have demonstrated that evaluating IIV on smartphone-based digital cognitive assessments is feasible, has the capacity to differentiate between cognitively normal (CN) and MCI individuals, and may reduce barriers to cognitive assessment3. This study sought to evaluate whether such differences could be detected in CN participants with and without elevated AD risk.
Participants and Methods: Participants (n=57) were cognitively normal older adults who previously received an Aβ PET scan through the Butler Hospital Memory and Aging Program. The sample consisted of primarily non-Hispanic (n=49, 86.0%), White (n=52, 91.2%), college-educated (M=16.65 years), females (n=39, 68.4%). The average age of the sample was 68 years old. Approximately 42% of the sample (n=24) received a positive PET scan result. Participants completed brief cognitive assessments (i.e., 3-4 minutes) three times per day for eight days (i.e., 24 sessions) using the Mobile Monitoring of Cognitive Change (M2C2) application, a mobile app-based cognitive testing platform developed as part of the National Institute of Aging's Mobile Toolbox initiative (Sliwinski et al., 2018). Participants completed visual working memory, processing speed, and episodic memory tasks on the M2C2 platform. Intraindividual standard deviations (ISDs) across trials were computed for each person at each time point (Hultsch et al., 2000). Higher ISD values indicate more variability in performance. Linear mixed effects models were utilized to examine whether differences in IIV existed based on PET scan status while controlling for age, sex at birth, and years of education.
Results: n interaction between PET status and time was observed on the processing speed task such that Aβ- individuals were less variable over the eight assessment days compared to Aβ

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+ individuals (B= -5.79, SE=2.67, p=.04). No main or interaction effects were observed on the visual working memory task or episodic memory task.
Conclusions: Our finding that Aβ- individuals demonstrate less variability over time on a measure of processing speed is consistent with prior work. No associations were found between IIV in other cognitive domains and PET status. As noted by Allaire and Marsiske (2005), IIV is not a consistent phenomenon across different cognitive domains. Therefore, identifying which tests are the most sensitive to early change is crucial. Additional studies in larger, more diverse samples are needed prior to widespread clinical use for early detection of AD.

Categories: Dementia (Alzheimer's Disease)
Keyword 1: positron emission tomography
Keyword 2: dementia - Alzheimer's disease
Keyword 3: computerized neuropsychological testing
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6 Exercise Induced Growth Factor Increases Directly and Indirectly Reduce Systemic Vascular Risk Parameters: Translational Project Amongst Midlife Human and Animal Models of Preclinical Alzheimer's disease and Vascular Dementia

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Objective: Using a humanized APOE3/4 (Alzheimer's disease genetic risk allele) mouse model we investigated the potential modulating effects of exercise on systemic risk factors and the ability of this mouse model to translate to active or sedentary, midlife, human participants. We present preliminary results of an ongoing, translational pilot study.

Participants and Methods: 26 Midlife individuals, ages 40-65, were recruited from the community and dichotomized into active or sedentary groups following health screening and cognitive assessment. Blood samples were drawn from human participants for lipid assessment and other general health measures as well as peripheral growth factors concentrations (VEGF, BDNF and FGF21). Traditional, transgenic mouse models have helped the scientific community to understand biological mechanisms of Alzheimer's disease (AD), but they do not develop significant neuronal loss, a hallmark of AD pathology. The MODEL-AD consortium has created a new "humanized" APOE4 model that has the human APOE4 allelic sequence in place of the mouse APOE gene; the model has shown known human phenotypes including deficits in cholesterol trafficking, amyloid clearance and BBB integrity. Of upmost importance, this model does not develop a full AD phenotype indicating that additional genetics and/or environmental factors are required as would be seen in human populations. We used males and females of this model to complete identical sedentary and active measures of each APOE genotype.
Results: Lipid and general health marker assessment between mouse and human were similar and reproduced published literature. In both humans and mice we saw increased total cholesterol and HDL in active females and decreased total cholesterol and HDL in active males. We also saw similar relationships between APOE genotype, sex, and activity with regards to triglycerides. Although total cholesterol, HDL and LDL measures are the primary lipids needed to confirm or deny translation, other lipid measurements were not equivalent between the two models.
Growth factor assessment in both species are also similar and reproduce published literature with regards to VEGF and BDNF as we see trending elevated levels in the active group. Less published on is the finding seen between active females and these elevated growth factors levels; our results indicates that although elevated as a result of exercise, this increase may be more prominent in females.
Conclusions: Based on the results found here we conclude that The Jackson Laboratory's humanized APOE3/4 mouse model is a translatable model of vascular dysfunction, dementia and Alzheimer's disease. We also conclude that exercise modulates these aspects by growth factor activation and increases

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