Digit Span subtests from the Wechsler Adult Intelligence Scale, 4th Edition, Trail-Making Test (TMT), Stroop Color Word Test (SCWT), and the Symbol Digit Modalities Test (SDMT). Plasma protein levels were analyzed using the Olink Target 96 Neurology assay (Uppsala, Sweden), selected a priori for the established markers linked to neurobiological processes and diseases. Changes in cognitive measures and protein levels were assessed using pairedsample t-tests, and Pearson's correlations were calculated for significant findings. Results: Participants' cognitive performance significantly improved on the SCWT color trial (t = -2.19, p = 0.042) and SDMT (t = -2.17, p = .043). Significant decreases in plasma proteins levels were found for GDNF family receptor alpha-1 ([GFRA1]: t =2.05, p = 0.055), neuroblastoma suppressor tumorigenicity-1 ([NBL1]: t = 2.13, p= .046), and neuropilin-2 ([NRP2]: t = 2.61 p= 0.017). Correlational analyses showed reductions in NBL1 were significantly associated with changes in both SDMT (r = -.61, p = 0.006) and the color trial of SCWT (r = .48, p = .038), and NRP2 was significantly associated with improvement on the SDMT (r = -.46, p = 0.045). GFRA1 was not significantly associated with change on any cognitive measure.

Conclusions: In a sample of older adults with MCI, participation in high-intensity water-based exercise led to significant improvements in cognitive function as well as changes in neurological plasma proteome. Improved outcomes in processing speed, attention, visuospatial scanning, and working memory were associated with changes in specific plasma protein concentrations. This highlights potential activity-dependent neurobiological mechanisms that may underlie the cognitive benefits derived from physical activity. Future studies should explore these findings in Randomized Control Trials with a comparative condition and larger sample size.

Categories: Aging

Keyword 1: mild cognitive impairment Keyword 2: cognitive functioning Keyword 3: cognitive neuroscience Correspondence: Adriana Savettiere, Palo Alto University, asavettiere@paloaltou.edu Peter Louras, Sierra Pacific Mental Illness Research, Education, and Clinical Center (MIRECC) at VA Palo Alto Health Care System (VAPAHCS); Stanford University School of Medicine, Department of Psychiatry and Behavioral Sciences, peter.louras@va.gov

3 Body Mass Index Partially Mediates Gait Speed and Executive Functioning in Older Adults

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Objective: Gait speed is associated with poorer executive functioning performance in older adults such that individuals with slower gait speed have shown declines in cognitive flexibility and set-shifting. Body mass index (BMI) is associated with sedentary lifestyles and slower gait speed, and has demonstrated negative effects on executive set-shifting in this population. However, the interaction between gait speed, BMI, and executive functioning has yet to be examined. The purpose of this study is to investigate the potential mediating effect of BMI on the negative relationship between gait speed and executive functioning in older adults. Participants and Methods: The sample included 154 community-dwelling older adults drawn from two clinical trials. Participants were recruited from the VA Palo Alto Health Care System and Stanford/VA Alzheimer's Disease Research Center, Gait speed was measured using the six-minute walk test, with longer distances representing faster gait speeds. Weight and height were used to calculate BMI. Each participant completed the Trail Making Test Part B (TMTB), which was used to measure executive functioning. A simple mediation analysis was performed using SPSS PROCESS Macro version 3.5. The outcome variable for the analysis was TMTB completion times. The predictor variable was gait speed, and the mediator variable was BMI. Age was entered as a covariate. We hypothesized that gait speed will negatively predict time to completion on the executive functioning task. We also hypothesized that BMI will mediate this relationship.

Results: The analysis found that gait speed negatively predicted executive functioning scores (b = -.12, p = .02). The overall mediation model was statistically significant (F(3, 150) =9.17. p < .001). Gait speed and age negatively predicted BMI (p < .001). BMI was a significant predictor of executive functioning (p = .001). The direct effect of gait speed on executive functioning remained significant after including BMI in the model (p < .001), which suggests that BMI partially mediated the relationship between gait speed and executive functioning. The indirect effect of the model when including BMI was tested using the bootstrap estimation approach with 5,000 samples, and was found to be significant (95% CI [.03,.11]), indicating that mediation did occur in the analysis. Conclusions: BMI partially mediated the relationship between gait speed and executive set-shifting. Thus, the path by which gait speed predicted executive functioning abilities was partially attributable to BMI, one measure of obesity. This finding suggests that older adults with slower gait speeds may have poorer executive function partially due to greater BMI. Given the importance of executive functions on independence and well-being in older adulthood, management of BMI could lead to improved functioning and quality of life. Interventions to decrease weight in older adults is likely to result in several positive health outcomes, and these results suggest that they may also promote important cognitive processes.

Categories: Aging Keyword 1: executive functions Keyword 2: aging (normal) Keyword 3: movement Correspondence: Aidan Boese, Palo Alto University, aboese@paloaltou.edu

4 The Effect of Age on the Relationship Between Adverse Childhood Experiences and Frailty in Late Life: A Moderation Model

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Objective: Although relationships between Fried frailty criteria (i.e., weakness, slowness, weight loss, exhaustion and low physical activity), cognitive decline, and adverse childhood experiences (ACEs) have been examined (Brigalo et al., 2015, Brown et al., 2022, Fabricio et al., 2020, & Tani et al., 2021), the moderating effect of age on the relationship between ACEs and frailty has yet to be explored. The present study examined whether age moderates the relationship between total number of ACEs and number of frailty criteria in older age. Participants and Methods: 137 older adults were recruited from University of Miami clinics and surrounding community care centers. Collected data included demographic information, number of frailty criteria met, and number of ACEs endorsed. Participants were primarily Hispanic-White (64.2%) and female (56.9%), with a mean age of 73.62 years (SD=6.252). Data were initially analyzed using descriptive statistics. A hierarchical linear regression was run to test the effect of ACE score on number of frailty criteria met. A simple moderation analysis using the PROCESS macro was then performed with total number of medical conditions included as a covariate to address any potentially confounding effects. To avoid multicollinearity issues, number of ACEs endorsed and age were mean centered and an interaction term between the two was produced. Results: Scores on the ACE did substantially effect the total number of frailty criteria met by participants in this study (f=2.37, p=0.028, $\Delta R2=0.023$), independent of number of medical conditions. The overall moderation model was significant (f=2.99, p=0.022, R2=0.103), and the addition of the interaction effect resulted in a statistically significant change to the model (f=4.08, p=0.045, ΔR2=0.035). Taken together, support for a moderating effect was found, specifically within the lower age group (65 -71years), but not older (greater than 72 years) with ACE score positively predicting the number of frailty criteria met (b =0.230, t=2.62, p=0.010). Conclusions: Results largely support the positive effect of ACE endorsement on the number of frailty criteria met in later life. Age acted as a moderating effect, for the younger old population, such that as number of ACEs endorsed increased, so too did the number of frailty criteria met. This finding highlights the importance of early intervention among those in younger late life who have experienced trauma. Given the positive relationship between frailty and cognitive decline in late life (Brigalo et al.,