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22 Cognitive Reserve's Relationship to Brain Burden in Parkinson's Disease Without Dementia

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Objective: Individuals with Parkinson's disease (PD) have varying trajectories of cognitive decline. One reason for this heterogeneity may be "cognitive reserve": where higher education/IQ/current mental engagement compensates for increasing brain burden (Stern et al., 2020). With few exceptions, most studies examining cognitive reserve in PD fail to include brain metrics. This study's goal was to examine whether cognitive reserve moderated the relationship between neuroimaging indices of brain burden (diffusion free water fraction and T2-weighted white matter changes) and two commonly impaired domains in PD: executive function and memory. We hypothesized cognitive reserve would mitigate the relationship between higher brain burden and worse cognitive performance.

Participants and Methods: Participants included 108 individuals with PD without dementia (age mean=67.9±6.3, education mean=16.6±2.5) who were prospectively recruited for two NIH-funded projects at the University of Florida. All received neuropsychological measures of executive function (Trails B, Stroop, Letter Fluency) and memory (delayed recall: Hopkin's Verbal Learning Test-Revised, WMS-III Logical Memory). Domain specific z-score composites were created using data from age/education matched non-PD peer controls (N=62). For the Cognitive Reserve (CR) proxy, a z-score composite included years of education, WASI-II Vocabulary, and Wechsler Test of Adult Reading. At the time of testing, participants completed multiple MRI scans (T1-weighted, diffusion, Fluid Attenuated Inversion Recovery) from which the following were extracted: 1) whole-brain free water within the white matter (a measure of microstructural integrity and neuroinflammation), 2) white matter hyperintensities/white matter total volume (WMH/WMV), and bilaterally-averaged edge weights of white matter connectivity between 3) dorsolateral prefrontal cortex and caudate and 4) entorhinal cortex and hippocampi. Separate linear regressions for each brain metric used executive function and memory composites as dependent variables; predictors were age, CR proxy, respective brain metric, and a residual centered interaction term (brain metric*CR proxy). Identical models were run in dichotomized short and long disease duration groups (median split=6 years).

Results: In all models, a lower CR proxy significantly predicted worse executive function (WMH/WMV: beta=0.49, free water: beta=0.54, frontal edge weight: beta=0.49, p's<0.001) and memory (WMH/WMV: beta=0.42, free water: beta=0.35, temporal edge weight: beta=0.39, p's <0.01). For neuroimaging metrics, higher free water significantly predicted worse executive function (beta=-0.39, p=0.002) but not memory. No other brain metrics were significant predictors of either domain. Accounting for PD duration, higher free water predicted worse executive function for those with both short (beta=-0.49, p=0.04) and long disease duration (beta=-0.48, p=0.02). Specifically in those with long disease duration, higher free water (beta=-0.57 p=0.02) and lower edge weights between entorhinal cortex and hippocampi (beta=0.30, p=0.03) predicted worse memory. Overall, no models contained significant interactions between the CR proxy and any brain metric.

Conclusions: Results replicate previous work showing that a cognitive reserve proxy relates to cognition. However, cognitive reserve did not moderate brain burden's relationship to cognition. Across the sample, greater neuroinflammation was associated with worse executive function. For those with longer disease duration, higher neuroinflammation and lower medial temporal white matter connectivity related to worse memory. Future work should examine other brain burden metrics to determine whether/how cognitive reserve influences the cognitive trajectory of PD.

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23 Musical Training May Not Enhance Cognitive-Motor Integration in Healthy Young Adults.

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Objective: Hand and arm functions have been associated with cognition in healthy young and older adults (Vasylenko et al., 2018) and in patients with Parkinson's disease (Bezdicek et al., 2014). Music training has been proposed to integrate motor and cognitive functions by engaging motoric, sensory, perceptual, and various cognitive domains (Wan & Schlaug, 2010). In this study, we examined if performance on fine and gross motor tasks is predicted by cognitive measures of memory, attention, and executive functions, and whether this relationship varies by the extent of musical training in healthy young participants.

Participants and Methods: Forty five healthy young participants were recruited (*M* = 22.32, *SD* = 4.10; 78% female). Participants completed fine (Grooved pegboard) and gross motor (Box and Blocks) measures as well as cognitive measures (Rey auditory verbal learning test, Stroop, Trail making, and D2 cancellation), and the musical training subscale of the Goldsmith Musical Sophistication Index. Two multiple regression models were conducted assessing cognitive measures as predictors of fine and gross motor functions, with musical training as a covariate in both models.

Results: Musical training was normally distributed across participants (*M* = 23.47, *SD* = 10.28). The results of the first model assessing the role of cognitive measures as predictors of fine motor function indicate a moderate fit ($F(5,36) = 3.32$, $R = 0.55$, explaining .32 of variance, $p < .05$), with memory ($B = 2.75$, $SE = 0.82$, $p < .005$) and sustained attention ($B = 0.09$, $SE = 0.03$, $p < .01$) as moderate predictors. These cognitive measures were also found to predict gross motor function ($F(5,36) = 3.06$, $p < .05$, $R = 0.55$, explaining .30 of the variance), with memory retention ($B = 2.49$, $SE = 0.83$, $p < .001$) and sustained attention ($B = 0.07$, $SE = 0.03$, $p < .05$) as moderate predictors. In both models, musical training was not a significant predictor.

Conclusions: We found that both fine and gross hand motor functions are predicted by cognitive measures of memory retention and sustained attention. Our results support previous findings associating cognition and motor function, with attention being relevant in young adults and memory a predictor in older adults (Vasylenko et al., 2018). We corroborate these findings for hand function, but did not find executive functions to be implicated, which were previously reported as a predictor only for older adults. While musical training has been suggested to enhance the cognitive-motor relationship as it involves motor skills as well as engages various cognitive domains (Wan & Schlaug, 2010), prior musical training was not found to affect this relationship. While music background did not predict better hand motor function, it did account for more interpersonal variance. The results suggest that for most amateur musicians, including those with years of experience, musical training may not affect the association between cognition and both fine and gross hand motor skill. The current findings indicate that while musical training can be an enriching experience, it may not (exclusively) enhance motor-cognitive integration. Different outcomes may be found with more extreme levels of music training, or a different age group.

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24 Functional Distinctions in Metabolic Network Patterns in Parkinson's Disease

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Objective: Cognitive decline is a common non-motor feature of Parkinson's disease (PD). However, the underlying mechanisms of