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during processing [24], support this hypothesis. Working memory has been shown to decrease with age (e.g. [25-27]).Interestingly, Salthouse and Babcock [28] investigated age-related differences of three components of working memory: processing efficiency, storage capacity and coordination effectiveness. Performance declined with increased age; however the impact of age was mediated by processing speed of simple operations. Furthermore, Parkin and Java [29] found that performance on the Symbol Digit Substitution test was a strong predictor of memory performance. Thus there is ample support for the hypothesis that processing speed sub serves higher order cognitive function from the study of working memory.

Similarly, age-related decline in the performance of measures of inhibition have been associated with processing speed as well. Inhibition, or the ability to suppress attention to irrelevant or off goal-path thoughts (e.g. [30]), is important for the efficient operation of selective attention and working memory, limiting the amount of information into working memory that is not along the goal-path [31]. Inhibition is also important during parallel processing, when deficits may result in cross talk, and during language comprehension, suppressing irrelevant meanings of words of phrases [31]. Thus deficits in inhibition increase the contents of working memory with irrelevant information, resulting in competition at retrieval, which leads to poorer memory performance, increased distractibility, increased errors and increased response time. Adolfsdottir et al. [32] recently measured inhibition and switching in a longitudinal study of 123 subjects, with three samples over six years. They found that age contributed to longitudinal models of inhibition and switching as did processing speed, while measures of education and retest effects did not. Similarly, Marco et al. [33] examined inhibition,

- Symbol Digit Modalities Test (SDMT, Oral Version [49]) is a psychometric measure of processing speed and visual tracking. The participant is presented with a coding key containing nine numbers, each corresponding to a different symbol. Below the key, a series of symbols is also presented, and the participant must state the number corresponding to the symbols in order as quickly as possible. Score is the number of items successfully completed in 90 s.

Data Analysis

All statistical analysis was performed using SPSS (version 23; http://www.ibm.com/analytics/us/en/technology/spss/). Between groups comparisons were made using Multivariate Analysis of Variance (MANOVA). Pearson correlation ($p<0.05$) was used to evaluate the linear relationship between processing speed and demographic, cognitive, motor, mood and disease severity measures for participants with PD.

We also performed two mediation analyses to evaluate a presumed mediation effect of processing speed and mood variables on the relationship between age and 1) working memory and 2) inhibition (see http://davidakenny.net/cm/mediate.htm for an overview). We followed the four steps described by Baron and Kenny [50] and others [51,52] to establish mediation. We used hierarchical regression to show that either working memory or inhibition score were correlated with age to establish that there was an effect to be mediated. Second, we used a similar regression model to determine that age was correlated with the possible mediating variables (processing speed, depression and apathy). Third, we determined if the mediator affected the outcome variable (either working memory or inhibition measures) by entering both age and the mediators into a regression model with working memory or inhibition measures as the outcome variable. Further, we used this same model to determine the degree of mediation (complete or partial). The amount of mediation is called the indirect effect or the reduction of the effect of the causal variable (age) on the outcome (working memory or inhibition) due to the mediators. We used bootstrapping to test the indirect effect [53,54]. We resampled with replacement 5000 times to determine a confidence interval and p value. We used the PROCESS SPSS macro provided by Hayes and Preacher to perform this analysis [55].

Results

Group differences

Demographic and descriptive data: The PD and control groups were not significantly different in age ($F(1,129)=3.332$, $p=0.070$), years of education ($F(1,129)=2.169$, $p=0.143$), daytime sleepiness ($F(1,129)=3.545$, $p=0.062$), premorbid IQ ($F(1,129)=0.099$, $p=0.753$) and MMSE score ($F(1,129)=0.459$, $p=0.499$; Table 1). However, the PD group indicated greater symptoms of depression (GDS; $F(1,129)=12.277$, $p<0.001$) and apathy (FLOPS; $F(1,129)=9.159$, $p=0.003$) than the control group. Note that PD participants were at a relatively early disease stage (H&Y scale score, Table 2). Dopamine equivalents are listed in Table 2.

Cognitive measures

For the measure of processing speed, the PD group correctly completed fewer items in 90 s compared to the control group, with a mean difference of 8.3 items (SDMT $F(1, 129)=18.648$, $p<0.001$, Table 3). 75% of PD participants (58/77) had processing speed scores below mean control group performance. For the measure of working memory, while there was no statistically significant difference between groups (Digit Span Backward; $F(1,129)=3.818$, $p=0.053$; Table 3), there poorer performance on measures of working memory and inhibition, increased age and increased reported symptoms of depression and apathy.

subjects. ey found that activation in inferior frontal gyrus, middle frontal gyrus and basal ganglia was modality independent. In fact, mild cognitive impairment, including de cits in working memory and inhibition, has been linked to frontostriatal dopamine modulated function, while dementia in PD, characterized by impairments in verbal uency, verbal and visual memory and visuospatial skills, is associated with more widespread, posterior degeneration [75-77].

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