

Working Memory in Parkinson's Disease

Dissertation submitted by

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Declaration

I declare that this honours dissertation is my own work and has not been submitted in any form for another degree or diploma at any university or other institution of tertiary education. Information derived from the published or unpublished work of others has been acknowledged in the text and a list of references is given.

Andrew Johnson

7th November 2014

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Journal Article

Abstract

Parkinson's disease (PD) is a progressive neurodegenerative disorder associated with impaired spatial and verbal working memory (SWM, VWM). There are two motor subtypes of PD, tremor dominant (TD) and postural instability and gait difficulty (PIGD). This study explored the longitudinal relationship between the two motor subtypes and VWM and SWM assessed at a two year follow up. The study comprised 84 males and 30 females ($N = 114$), aged between 39 and 85 ($M = 64.82$, $SD = 9.23$) with confirmed PD at Time 1. Two structural equation models and two multiple groups confirmatory factor analyses were conducted. No (Bonferroni-corrected) significant relationship was found with either subtype. In the whole sample, a significant relationship was seen between postural/ gait symptoms and SWM ($p = .01$). Within the PIGD subtype, there was a significant relationship between postural/gait symptoms and SWM ($p = .001$) and a trend towards significance in VWM ($p = .02$). Within the TD subtype there were no significant relationships, but the parameter estimates were markedly larger for the postural /gait scores than they were for the tremor. This was assumed to be due to the postural/gait symptoms not being severe enough to be statistically significant. The results suggested that cholinergic denervation impacts WM performance in PD. Future research should look to confirm this initial finding. This relationship could allow for early intervention for WM difficulties, improving the long-term quality of life for individuals with PD.

Parkinson's disease (PD) is a progressive neurodegenerative disorder; the second most common neurological disease in Australia, it affects over 64 000 people, with prevalence rates suggested to increase by 4% per year for the foreseeable future (Access Economics, 2011). PD is associated with a variety of motor and non-motor symptoms. There are three cardinal motor symptoms of PD, including; tremor at rest, slowness/poverty of movement (bradykinesia/akinesia), and rigidity (Dauer & Przedborski, 2003). Individuals with PD can be identified as belonging to a particular motor subtype based on the presentation of these motor symptoms (Jankovic et al., 1990). The 'tremor dominant' (TD) subtype includes individuals who demonstrate significant tremor symptoms but do not exhibit postural difficulties (Jankovic et al., 1990). Conversely, the 'postural instability and gait difficulty' (PIGD) subtype includes those individuals who demonstrate postural symptoms but do not exhibit tremor (Jankovic et al., 1990). The PIGD subtype is reported to be almost twice as prevalent as the TD subtype (Alves, Larsen, Emre, Wentzel-Larsen, & Aarsland, 2006).

There are a range of non-motor symptoms also associated with PD. These include neuropsychiatric disorders and working memory impairments (Martinez-Martin, Rodriguez-Blazquez, Kurtis, & Chaudhuri, 2011). Working memory (WM) is a short-term memory system that allows for the storage and manipulation of information over a short period of time (Baddeley, 2003). Baddeley (2003) proposed two subdivisions specialised for different types of information; verbal working memory (VWM) and spatial working memory (SWM). VWM is responsible for the storage and manipulation of verbal information and SWM is responsible for storing and manipulating visual and spatial information (Baddeley, 2003). Other conceptualisations of WM include those by Cowan (1995) and Ericsson & Kintsch (1995). In these conceptualisations, WM does not have information-specialised subdivisions. In Cowan's (1995) model, WM activates representations of information held in long-term memory (LTM) and then has a limited-capacity attentional component to manipulate and process that information. Similarly, Ericsson and Kintsch (1995) propose that most information is held in LTM and is linked together by complex retrieval structures. The individual need only hold a few concepts in WM at a time, and these activate the relevant retrieval structures to recall the information from LTM as needed (Ericsson & Kintsch, 1995).

The severity of WM impairment demonstrated by an individual is associated with the clinical stage of their PD, as assessed by motor symptom severity (Lewis, Dove, Robbins, Barker, & Owen, 2003). The relationship between individual patterns of motor symptoms and

WM has received limited attention. Identification of the specific motor symptoms which impact WM would allow for the use of targeted interventions as soon as they present. Given the association between WM deficits and poor quality of life in PD (Aarsland et al., 2010), research in this area has the potential to improve health outcomes for individuals.

The primary cause of Parkinsonism is the degeneration of dopaminergic neurons in the pars compacta of the substantia nigra (Dauer & Przedborski, 2003). These dopaminergic neurons primarily project to the putamen and the caudate nucleus in the striatum with the pathway to the putamen demonstrating the most degeneration (Dauer & Przedborski, 2003). This reduces neural dopamine levels, and the neurons that use dopamine to fire can no longer do so (dopaminergic denervation). The primary pharmacological treatment for the motor symptoms of PD is levodopa, a precursor for dopamine which acts to replace the dopamine lost due to the substantia nigra degeneration (Jankovic & Stacy, 2007). Given the responsiveness of its symptoms to levodopa, the tremor dominant (TD) subtype is suggested to be driven by this dopaminergic denervation (Bohnen & Albin, 2011). However, the PIGD symptoms show little response to levodopa, suggesting that the two motor subtypes have differing neuropathologies (Bohnen & Albin, 2011).

The cholinergic system is responsible for the production and transport of the neurotransmitter acetylcholine (Müller & Bohnen, 2013). Like dopamine, acetylcholine plays a large role in motor generation and modulation (Müller & Bohnen, 2013). There are two main cholinergic projections; the nucleus basalis of Meynert and the pedunculopontine nucleus-laterodorsal tegmental complex (Müller & Bohnen, 2013). Similar to the substantia nigra of the dopaminergic system, these cholinergic projections degenerate in PD and it is the resulting acetylcholine denervation that is suggested to underlie the PIGD subtype (Bohnen & Albin, 2011).

The two neurotransmitter systems have a cooperative effect on cognition in PD. The traditional view is that the dopaminergic denervation causes an overactivity of acetylcholine production (Calabresi, Picconi, Parnetti, & Di Filippo, 2006). This overactivity impacts motor abilities and is treated with anticholinergic medications. Anticholinergics, however, have an adverse impact on cognitive function in PD (Calabresi et al., 2006). The physiological processes of synaptic plasticity are heavily influenced by levels of dopamine and acetylcholine (Centonze, Gubellini, Pisani, Bernardi, & Calabresi, 2003). Given this, it has been suggested that imbalance between the two impairs plasticity (Calabresi et al., 2006).

Short-term synaptic facilitation (a form of plasticity) has been proposed to modulate WM (Mongillo, Barak, & Tsodyks, 2008). The influence of a neurotransmitter imbalance is further supported by literature demonstrating the effect of both dopamine (Lewis, Slabosz, Robbins, Barker, & Owen, 2005) and acetylcholine (Seeger, 2004) on WM performance. This indicates that neither neurotransmitter solely impacts WM. For an individual to be subtyped, one of the neurotransmitter systems would likely have degenerated markedly more than the other, such that one motor symptom is more severe. This suggests that WM impairment should be present in one of the subtypes, as an imbalance would be necessary for the subtype to present.

The literature concerning the impact of motor subtype on WM in PD is inconsistent. The PIGD subtype is associated with significantly impaired SWM performance (Domellöf, Elgh, & Forsgren, 2011). Yet, the use of levodopa (treatment used to alleviate TD symptoms) increased SWM performance, albeit with a small sample size ($N = 19$; Costa et al., 2003). This suggests that SWM is not associated with a single subtype. Similar contradictions have been seen with VWM. The PIGD subtype was significantly associated with impaired VWM performance in some studies, but not in others (Lyros, Messinis, & Papathanasopoulos, 2008; Sollinger, Goldstein, Lah, Levey, & Factor, 2010). This suggests that WM would be impacted in both motor subtypes. However, methodological flaws may have influenced the results.

A recurring theme in the exploration of this research area is the use of a cross-sectional design. Given the progressive nature of PD, exploration of cognitive performance at a single time point may not capture deficits that have not yet fully developed, accounting for the inconsistent results of previous studies. Many studies also do not examine VWM and SWM in the same study, meaning that conclusions have to be made across studies. Given established age (Rypma & D'Esposito, 2000) and gender (Speck et al., 2000) differences in WM performance, making conclusions across samples is inappropriate. A major limitation is the use of small sample sizes, limiting the validity of the results.

Research concerning working memory performance in PD is limited, with inconsistent results. Associations between motor subtypes and WM were seen in underpowered, cross-sectional studies that did not look at both VWM and SWM. It is expected that a longitudinal approach with an adequate sample size and concurrent assessment of VWM and SWM will show a clear relationship with one motor subtype. There are two hypotheses of this study. Firstly, after controlling for age and gender, motor subtype

(TD/PIGD) at Time 1 will account for a significant amount of variance in VWM assessed at a two-year follow-up. Secondly, after controlling for age and gender, motor subtype (TD/PIGD) at Time 1 will account for a significant amount of variance in SWM assessed at a two-year follow-up.

Method

Research Design

The study used data from the ongoing longitudinal study: “Cognitive and motor heterogeneity in Idiopathic Parkinson’s Disease”, conducted by the ParkC group at Curtin University. A longitudinal correlational design was used to examine WM performance over time.

The motor subtype of the individual was the predictor variable and had two levels: tremor-dominance, and postural instability and gait difficulty. There were two outcome variables: verbal working memory and spatial working memory. Age and gender were included as potential control variables.

Participants

Local advertising was used to recruit individuals with diagnosed idiopathic PD (Time 1: $N= 254$, Time 2: $N= 148$). Inclusion required a PD diagnosis in accordance with the United Kingdom Brain Bank criteria (Hughes, Daniel, Kilford, & Lees, 1992). The Mini Mental State Examination (MMSE) was used to screen for the presence of dementia (Folstein, Folstein, & McHugh, 1975). Two participants were excluded for falling below the MMSE age and education appropriate cut-off scores provided by Iverson (1998), as proposed by Crum et al. (1993). Two participants were excluded for a confirmed misdiagnosis of PD. One hundred and twenty-four participants were excluded for missing data on at least one full measure. A total sample of 126 participants remained, demographics are reported in Table 1.

Given the non-independence of the two outcome variables, separate regressions were not suitable and structural equation modelling (SEM) was used. Kline (2005) recommends a minimum of 10 participants per free parameter in SEM. There were six free parameters included in the present model, suggesting a minimum of 60 participants were required.

Measures

Motor subtype.

Motor subtype was determined using Parts II and III of the Unified Parkinson's Disease Rating Scale (UPDRS). The UPDRS assesses four different aspects of PD: non-motor experiences of daily living, motor experiences of daily living, a motor assessment, and complications resulting from therapy. The UPDRS was used as it is the 'gold' standard clinical motor assessment for PD (Evans et al., 2011).

Table 1

Sample Characteristics per Subtype at Time 1

	PIGD (n = 51)	TD (n = 63)	Indeterminate (n = 12)	Total (n = 126)
Sex				
Male	33	51	6	90
Female	18	12	6	36
Marital Status				
Single	0	2	0	2
Married/De-Facto	37	51	11	99
Widowed	5	5	1	11
Divorced/Separated	9	5	0	14
Age (years)	64.37 (8.55)	65.17 (9.79)	66.92 (7.17)	65.02 (9.05)
Time Since Diagnosis (years)	7.11 (4.52)	4.09 (3.72)	5.54 (6.63)	5.45 (4.56)

Part II is a self-report section comprising 13 questions about the motor aspects of daily living, such as chewing and walking. The participants rate the severity of their symptoms on a scale from 0 (normal) to 4 (severe). Part III is a physical assessment by a trained clinician of the individual's rigidity, tremor and postural stability, with severity rated on a scale from 0 (normal) to 4 (severe).

Parts II and III demonstrate excellent internal consistency ($\alpha = .92$, $\alpha = .93$; Martinez-Martin et al., 2013). Part II has adequate convergent validity with the Rapid Assessment of Disability Scale ($r = .80$; Martinez-Martin et al., 2013). Part 3 has adequate convergent validity with the Clinical Impression of Severity Index for PD-Motor signs ($r = .73$; Martinez-Martin et al., 2013).

Classification of participants into one of the two motor subtypes was conducted according to established criteria (Jankovic et al., 1990). For the TD classification, items 2.10, 3.15, 3.16, 3.17, and 3.18 were used. These items assess the daily experience and constancy of tremor, and the severity of postural and kinetic tremors. For the PIGD classification, items 2.12, 2.13, 3.10, 3.11 and 3.12 were used; these items assess the daily experience and severity of gait difficulty, freezing, and postural instability. For each individual their mean TD score was divided by their mean PIGD score, resulting in a TD/PIGD ratio which was used to identify subtype inclusion. A score of less than 1 resulted in PIGD classification and a score of 1.5 or more in TD classification. Individuals who scored between 1 and 1.5 were classified as ‘indeterminate subtype’ and were not included in subsequent analyses.

Verbal working memory.

The Hopkins Verbal Learning Test – Revised (HVLT-R) is a brief test of verbal memory comprising a list of 12 words which are read to the participant (Benedict, Schretlen, Groninger, & Brandt, 1998). Immediately after hearing the list, the participant states as many words as they can remember across three consecutive trials. The HVLT-R has adequate test-retest reliability ($r = .73$; Conway Greig, Nicholls, Wexler, & Bell, 2004) and demonstrates good discriminant validity with the Brief Visuospatial Memory Test-Revised ($r = .13$; Woods et al., 2005). The total number of words correctly recalled across all three trials was used as the measure of VWM, with higher scores indicating higher VWM capacity.

Spatial working memory.

The Spatial Working Memory (SWM) measure is part of the Cambridge Neuropsychological Test Automated Battery (CANTAB; Robbins et al., 1994) a standardised neuropsychological assessment tool. The CANTAB is a small touch-screen tablet computer. The SWM task requires individuals to search through a number of squares to find blue tokens. Tokens do not appear in the same square twice, so the individual needs to hold the previous token locations in memory (see Figure 1). The number of squares increases as the task progresses, increasing the strain on SWM. The task progresses from three, to four, to six, and to eight squares. There are four trials at each of these levels. The SWM task has been established as reliable and with adequate construct validity (Cambridge Cognition, 2013). The total number of errors made during the eight squares trials was used as the measure of SWM, with higher scores indicating lower SWM capacity. This level of the task represented

the greatest strain on SWM and it was expected that deficits would more clearly present at this level.

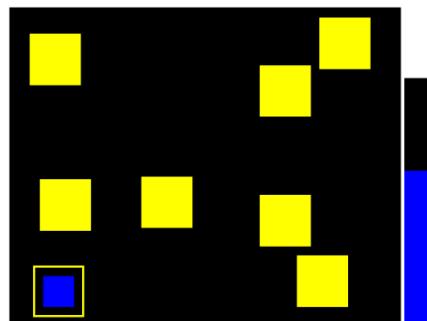


Figure 1. Image of the Spatial Working Memory Task. (Image taken from: <http://cambridgenurosciences.info/images/swm.png>)

Procedure

Participants were first mailed a number of self-administered questionnaires, including the UPDRS Part 2. Participants were then contacted to arrange a suitable day/time for assessment. The assessments occurred either in the participant's home or at ParkC. The assessments took place within one hour of the participant's last dose of anti-PD medication, to ensure that all participants were assessed in the 'on' period of the medication cycle. The testing occurred in three phases: two phases of cognitive tests followed by the UPDRS motor assessment. The HVLT-R was administered with six other tests during the first phase. After a short break the second phase began, comprised of the CANTAB SWM and seven other tasks. The UPDRS motor assessment was then completed. The sessions ran for 2 – 3 hours and participants were invited to return after two years.

Results

The subtyping questions of the UPDRS showed good internal consistency (PIGD $\alpha = .75$; TD $\alpha = .82$).

Inter-item correlations for all variables are presented in Table 2. Due to significant correlations with both criterion variables, age was retained as a control variable. Gender was only significantly correlated with HVLT-R Total, and so was retained as a control variable for VWM only.

SEM was used to test the hypotheses. Weighted least squares means and variance adjusted (WLSMV) estimation was used, as it allows for the use of categorical control

variables (gender) and is robust to violations of normality (Brown, 2006). WLSMV does not require a larger sample size when used in place of standard Maximum Likelihood Estimation (Beauducel & Herzberg, 2009). A Bonferroni-correction was applied to control the family wise error rate, adjusting the critical p -value to .0125 (.05/4).

Table 2

Means, Standard Deviations, and Correlations between Control Variables and Study Variables (N = 114)

Measure	1	2	3	4	5	6	7	M	SD
1. Gender	-							-	-
2. Age	-.165	-						66.89	9.22
3. HVLT-R	.397**	-.483**	-					23.41	6.64
4. SWM	-.041	.393**	-.285**	-				27.78	14.81
5. Mean Tremor	-.140	.153	-.128	-.012	-			.62	.51
6. Mean PIGD	.039	.128	-.118	.229*	-.201*	-		.68	.61
7. Subtype	.183	-.045	.105	.025	-.708**	.553**	-	-	-

Note: HVLT-R = Total number words recalled across three trials of Hopkins Verbal Learning Test – Revised (Time 2); SWM = Total number of errors on Spatial Working Memory task at eight squares (Time 2).

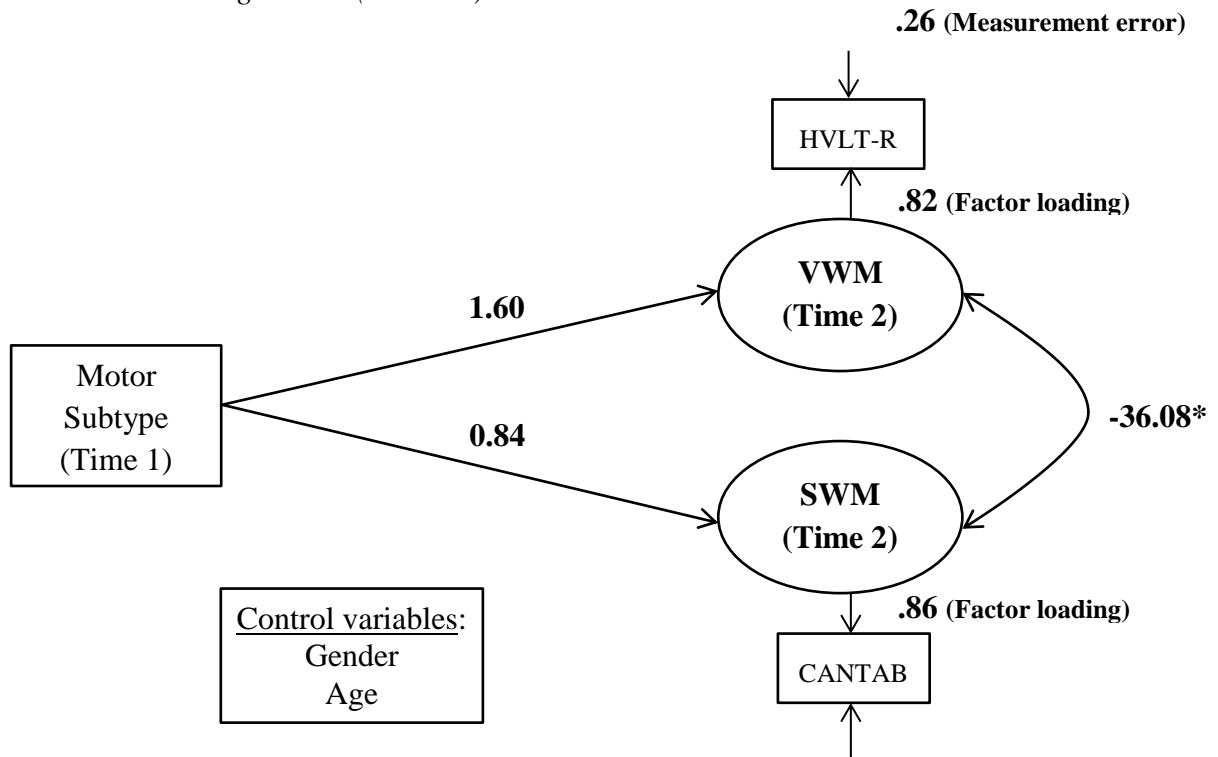
** $p < .001$, * $p < .05$

Motor subtype at Time 1 (PIGD/TD) was entered as an observed exogenous variable; VWM and SWM at Time 2 were entered as latent endogenous covariates (see Figure 1). Factor loadings and measurement error for VWM and SWM were set using the test-retest reliabilities from Conway Greig et al., (2004) and Lowe and Rabbitt (1998), respectively. Parameter estimates are shown in Figure 2 and Table 3.

The model demonstrated borderline fit $\chi^2(4) = 7.85$, $p = .09$; comparative-fit-index (CFI) = .93; non-normed fit index (NNFI) = .83; root mean square error of approximation (RMSEA) = .09. However, path coefficients between motor subtype and SWM/VWM were both non-significant (see Table 3). Indicating a potential relationship between subtype and WM, but the model needed to be re-specified. A second SEM was therefore conducted, whereby motor subtype was replaced with the mean tremor and PIGD scores for all participants (see Figure 3).

Figure 2

Model 1: Time 1 Motor Subtype Predicting Time 2 SWM and VWM – Unstandardised Estimates and Starting Values (N = 114)



* $p < .0125$ (Bonferroni-adjusted)

Table 3

Unstandardised and Standardised Parameter Estimates with Significance Levels for Model in Figure 2

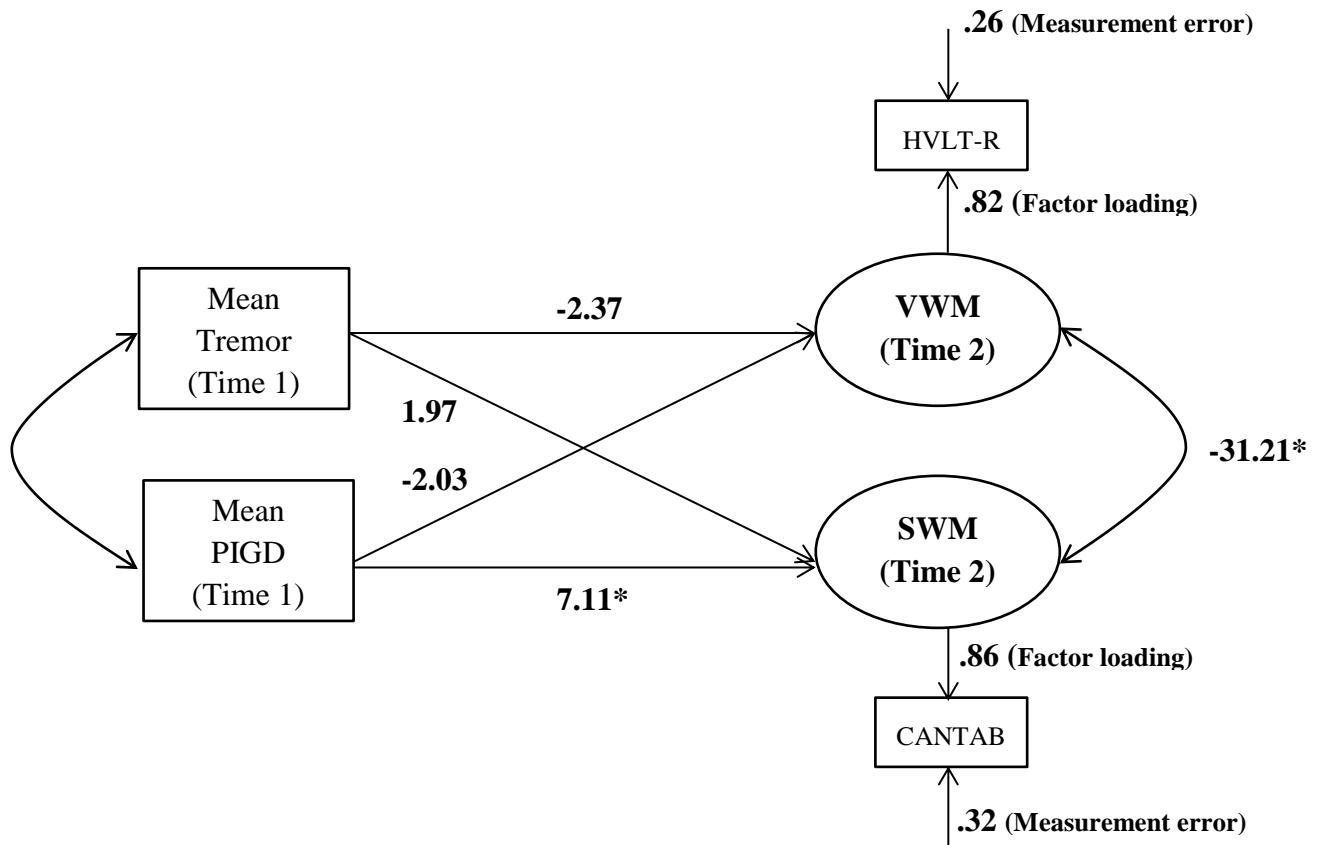
Parameter	Unstandardised Estimate (Standard Errors)	Standardised Estimate	p
Measurement Model			
VWM → HVLT-R	.86	.99	N/A
SWM → CANTAB	.82	.99	N/A
Error in HVLT-R	.26	.01	N/A
Error in CANTAB	.32	.002	N/A
Covariance VWM and SWM	-36.08 (11.75)	-.29	.002*
Structural Model			
Subtype → VWM	1.60 (1.47)	.10	.28
Subtype → SWM	.84 (3.14)	.03	.79
Residual for VWM	56.83 (9.47)	.99	< .001
Residual for SWM	271.83 (44.34)	.99	< .001

$\chi^2(4) = 7.85, p = .09$; CFI = .93; NNFI = .83; RMSEA = .09

* $p < .0125$ (Bonferroni-adjusted)

Figure 3

Model 2: Time 1 Mean Tremor and PIGD Score Predicting Time 2 SWM and VWM – Unstandardised Estimates and Starting Values (N = 114)



* $p < .0125$ (Bonferroni-adjusted)

The second SEM demonstrated poorer model fit than the first $\chi^2(6) = 10.71, p = .10$; CFI = .92; NNFI = .82; RMSEA = .08, but the path coefficient from the mean PIGD score to SWM was significant ($p = .01$; see Table 4). The relationship was positive; indicating that as PIGD scores increased so did the number of errors made on the SWM task. This suggested a relationship between physical symptoms and WM, but that subtype also needed to be considered. To this end, a multiple groups confirmatory factor analysis (CFA) was conducted, applying the model in Figure 2 to each subtype separately. In this way the associations between physical symptoms and WM can be examined for each subtype (TD/PIGD) independently.

Table 4

Unstandardised and Standardised Parameter Estimates with Significance Levels for Model in Figure 3

Parameter	Unstandardised Estimate (Standard Errors)	Standardised Estimate	p
Measurement Model			
VWM → HVLT-R	.86	.99	N/A
SWM → CANTAB	.82	.99	N/A
Error in HVLT-R	.26	.01	N/A
Error in CANTAB	.32	.002	N/A
Covariance VWM and SWM	-31.21 (11.13)	-.26	.005*
Structural Model			
PIGD → VWM	-2.03 (1.15)	-.15	.08
TD → VWM	-2.37 (1.50)	-.16	.11
PIGD → SWM	7.11 (2.76)	.24	.01*
TD → SWM	1.97 (2.88)	.06	.49
Residual for VWM	55.27 (8.99)	.96	< .001
Residual for SWM	256.73 (45.73)	.94	< .001

$\chi^2(6) = 10.71$, p = .10; CFI = .92; NNFI = .82; RMSEA = .08

*p < .0125 (Bonferroni-adjusted)

The CFA demonstrated good model fit $\chi^2(12) = 9.79$, p = .63; CFI = 1; NNFI = 1.11; RMSEA = 0. There was a significant path coefficient from PIGD to SWM (p = .001), and there was a trend towards significance in the path from PIGD to VWM (p = .02; see Table 5). As with the second model the relationship was positive, indicating increasing errors on the SWM task as mean PIGD score increased. The trend in the VWM path was negative, indicating that the participant recalled fewer words as mean PIGD score increased. These paths were only significant in the PIGD group.

The fit was also better than the first two models, suggesting that the improved model fit was due to the inclusion of both motor subtype and the scores for tremor/posture. Subtype membership alone was not sufficient to predict WM decline, nor was solely considering physical symptoms a good fit for the data. This indicates that physical symptoms needed to be assessed in the context of motor subtype; that the predictive ability of the symptoms differed between the subtypes.

Table 5

Unstandardised and Standardised Parameter Estimates with Significance Levels for Multiple Groups CFA 1

Parameter	Unstandardised Estimate (Standard Errors)	Standardised Estimate	p
PIGD (N = 51)			
Measurement Model			
VWM → HVLT-R	.86	.99	N/A
SWM → CANTAB	.82	.99	N/A
Error in HVLT-R	.26	.01	N/A
Error in CANTAB	.32	.002	N/A
Covariance VWM and SWM	-30.27 (13.28)	-.14	.02
Structural Model			
PIGD → VWM	-3.09 (1.36)	-.09	.02
TD → VWM	2.30 (3.83)	-.02	.55
PIGD → SWM	11.37 (3.55)	2.03	.001*
TD → SWM	-1.02 (9.20)	-.28	.91
Residual for VWM	44.31 (9.66)	.99	<.001
Residual for SWM	201.57 (55.21)	.83	<.001
TD (N = 63)			
Measurement Model			
VWM → HVLT-R	.86	.99	N/A
SWM → CANTAB	.82	.99	N/A
Error in HVLT-R	.26	.01	N/A
Error in CANTAB	.32	.002	N/A
Covariance VWM and SWM	-32.57 (18.48)	-.25	.08
Structural Model			
PIGD → VWM	-7.45 (5.15)	-.23	.15
TD → VWM	-.09 (2.68)	-.005	.97
PIGD → SWM	-3.47 (10.45)	-.05	.74
TD → SWM	.35 (6.98)	.01	.96
Residual for VWM	60.78 (14.65)	.95	<.001
Residual for SWM	284.28 (79.54)	.99	<.001

$\chi^2(12) = 9.79$, p = .63; CFI = 1; NNFI = 1.11; RMSR = .67; RMSEA = 0

*p<.0125 (Bonferroni-adjusted)

To confirm this, a second multiple groups CFA was conducted that assumed all parameters were equal between the two subtypes. The second CFA demonstrated very poor

model fit $\chi^2(24) = 51.65, p < .001$; CFI = .38; NNFI = .28; RMSEA = .14. This indicated that there was a difference in the ability of physical symptoms to predict WM within each subtype.

The significant path seen in Table 5 indicated that belonging to the PIGD subtype would be associated with future WM decline, yet the non-significant paths in the first model (see Table 3) contradict this. This suggests that the PIGD symptoms themselves are the best predictors of WM decline, regardless of subtype. This is supported by the significant path from mean PIGD score to SWM in the second model (See Table 4). Based on the results, the non-significant paths from mean PIGD score in the TD subtype are due to those symptoms not being as developed as they are in the PIGD subtype. This would be supported by the difference in the size of the parameter estimates in the TD subtype; with the PIGD score estimates markedly larger than their TD counterparts (see Table 5).

Discussion

The present study explored the relationship between motor subtype and working memory assessed at a two year follow up in a PD population. The study found no significant relationship between subtype and WM, supporting neither of the initial hypotheses. Post-hoc analyses found a significant relationship between PIGD symptoms and SWM, with a trend towards significance in VWM.

The non-significance of the motor subtypes was unexpected. It was expected that at belonging to a particular motor subtype would predict WM decline, but this was not seen. It was assumed that the motor subtypes would reflect distinct neuropathologies and would experience distinct cognitive outcomes. This was not seen; WM outcomes appeared dependent on the presence of PIGD symptoms, even in tremor dominant individuals. It would be reasonable to assume from these results that dichotomous subtyping could be inappropriate, as the non-dominant symptom could still hold clinical relevance. This may be due to an effect of disease duration on motor subtype, with many individuals transitioning from a TD to a PIGD subtype over time (Alves, 2006).

The associations of the PIGD symptoms in both subtypes were also unexpected. In the context of the neurotransmitter (dopamine and acetylcholine) imbalances it was assumed that a marked degeneration of either neurotransmitter system resulted in WM impairment (Calabresi et al., 2006; Mongillo, Barak, & Tsodyks, 2008). However, this study found that

degeneration of the dopaminergic system (represented by TD symptoms) did not impact WM. This was seen in the TD subtype, where the dopaminergic degeneration was greatest but WM was not impaired. These results would indicate that synaptic plasticity in PD is not affected by dopaminergic degeneration, but by cholinergic degeneration (represented by PIGD symptoms). This supports the proposal that synaptic plasticity is dependent on the initial activation of the cholinergic system (Calabresi, Picconi, Tozzi, & Di Filippo, 2007). This conceptualisation of plasticity in PD could account for the higher incidences of dementia generally found in PIGD individuals (Burn et al., 2006), with cognition becoming increasingly impaired as postural symptom severity increases.

This carries implications for risk factors of WM decline in PD. The current view is that an individual with predominantly postural difficulties is at a high risk of future decline (Burn et al., 2006). This study indicates that the presence of postural symptoms rather than their dominance should be viewed as a risk factor; individuals with primarily tremor symptoms should still monitor their postural symptoms. This would allow for early interventions for memory difficulties, using cognitive training or pharmacological treatments for the cholinergic system. Waiting until the individual is classified as PIGD would risk the associated WM impairments having progressed to a similar level of severity. For individuals with PD and their clinicians, monitoring postural difficulties would allow for screening for future memory impairment without repeated neuropsychological testing.

There are further implications for the pharmacological management of PD symptoms. Anticholinergic medications are generally given to counteract the overactivity of acetylcholine production that occurs in response to the dopaminergic degeneration (Calabresi et al., 2006). If cholinergic degeneration is associated with memory deficits, the use of anticholinergic medication could impact the individual's WM performance. The clinician would have to weigh the risk of future cognitive deficits against their use.

However, these implications need to be considered in the context of this study's limitations. Dopamine and acetylcholine levels were not directly assessed; they were inferred based on symptom severity. As such, conclusions made about cognition and acetylcholine should be taken with caution. Future studies should explore this association directly, using neuropsychological testing with neuroimaging. Similarly, this study did not control for the effects of medication which may have influenced motor symptoms. Future studies should explore the longitudinal cognitive effects of anticholinergic medication. Also to be

considered is the limitation of the measures used. The HVLT-R and CANTAB only assess the storage and retrieval of information from working memory, whereas past studies have shown its manipulation to be affected in PD (Lewis et al., 2003). Future research should explore the maintenance, manipulation, and integration of verbal and spatial information in WM and their association with postural symptoms. The UPDRS items used for subtype classification are not validated subscales; they are just common practice in the current literature. As their validity has not been established, it is unknown how accurately the subscales are assessing the subtypes, while discriminating against unrelated symptoms. Future research should explore the validation of these subscales.

Despite these limitations, this study has shown a clear, subtype-independent, predictive relationship between postural difficulties and future WM impairment. As this is the first study to find this, further confirmatory research is required. Should it be confirmed, it carries implications for the approach to reducing WM deterioration in PD. If postural symptoms are established as predictors of future memory decline, it would provide an understanding of the neurological systems involved with cognitive decline in PD. It would also allow for interventions for WM before impairments begin to present. Given the association between working memory impairment and poor quality of life in PD (Aarsland et al., 2010), early intervention could provide long term improvements in the daily life of people with Parkinson's disease.

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Extended Literature Review

Literature Review

Overview of Parkinson's Disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting older adults, with a mean age of onset of 52 (Dauer & Przedborski, 2003). PD presents clinically with four main motor symptoms; tremor at rest, bradykinesia/akinesia, rigidity and gait disturbance/postural instability (Dauer & Przedborski, 2003). Other motor symptoms include: bradykinesia (a slowness of movements), hypokinesia (a decrease in the amplitude of movements) and akinesia (a spontaneity of unconscious movements, such as gesturing while talking) (Dauer & Przedborski, 2003). Symptoms that fall under these categories are those such as masked faces (hypomimia), in which the individual shows little to no facial expression or micrographia, a decrease in the size of handwriting (Dauer & Przedborski, 2003). Rigidity is also a predominant motor symptom of PD, with many individuals finding their limbs becoming progressively stiffer over time and developing a 'stoop' to their posture (Dauer & Przedborski, 2003). Individuals may also experience dyskinesias (involuntary movements) due to the medication that is used to relieve other Parkinsonian symptoms (Dauer & Przedborski, 2003).

There are also many non-motor symptoms associated with PD; these include dementia, neuropsychiatric disorders, and memory impairments (Dauer & Przedborski, 2003). Both motor and non-motor symptoms may impair the quality of life of individuals with PD; due to the increased difficulties they may have with performing everyday tasks, as well as the psychological impacts of the non-motor symptoms (Martinez-Martin, Rodriguez-Blazquez, Kurtis, & Chaudhuri, 2011).

The cause of PD is a degeneration of the dopaminergic neurons within the substantia nigra (Dauer & Przedborski, 2003). This degeneration leads to dopamine denervation in the striatum which manifests as PD symptoms (Dauer & Przedborski, 2003). The exact pathogenesis of PD is not yet known. A number of gene mutations have been identified as a cause for the degeneration, but these mutations are only carried by approximately 5% of individuals with PD (Dauer & Przedborski, 2003). Recurrent head traumas, pesticides, and toxins are also speculated to influence the onset of PD (Chade, Kasten, & Tanner, 2006).

Motor Subtypes

The motor symptoms of PD often present in different ways; some individuals will have more severe symptoms than others, and some symptoms will worsen faster than others. Further exploration of the variable nature of motor symptoms gave rise to the concept that there are two distinct motor subtypes in PD (Zetusky et al., 1985). With the introduction of the Unified Parkinson's Disease Rating Scale (UPDRS), a scale for assessing and rating the severity of an individual's PD across multiple dimensions, these subtypes were able to be measured and quantified with greater ease and accuracy (Jankovic et al., 1990). Zetusky and colleagues (1985) were the first to explore potential motor subtypes of PD in a study involving 334 people with PD. They identified two subgroups in the population; those with tremor as the dominant feature and those with postural instability and gait difficulty as the dominant feature. It was also identified that those in the tremor dominant subgroup had a more favourable long-term prognosis (Zetusky et al., 1985). The tremor dominant subtype was more strongly associated with a preservation of mental status, while those of the postural and gait difficulty subtype were more likely to have a deterioration of mental status (Zetusky et al., 1985).

The Unified Parkinson's Disease Rating Scale (UPDRS) provides a method for clinicians and researchers to quantify individuals as belonging to one of the two motor subtypes (Burn et al., 2006). The UPDRS was introduced to provide a comprehensive measure of the effects of PD and as a means to monitor these effects over time (Movement Disorder Society Task Force on Rating Scales for Parkinson's disease, 2003). The UPDRS comprises four sections, each assessing a different dimension of the individual's life that is affected by PD; Part I assesses mentation, behaviour and mood, Part II assesses activities of daily living, Part III is a motor examination and Part IV assesses complications of therapy (Movement Disorder Society Task Force on Rating Scales for Parkinson's disease, 2003).

Jankovic and colleagues (1990) were the first to use the UPDRS as a means of classifying individuals into a specific subtype. This was achieved through assigning the individual a score for tremor dominance and a score for postural instability and gait difficulty. These scores were the average of the individual's scores on particular items in Parts II and III of the UPDRS, those that assessed motor functions (Jankovic et al., 1990). From a sample of 800 unmedicated individuals with PD 441 (55.13%) were classified as tremor dominant, 233 (29.13%) as postural instability dominant, and 126 (15.75%) as

undifferentiated (Jankovic et al., 1990). The postural subtype demonstrated higher levels of intellectual impairment, depression, and impairment on activities of daily living than the tremor subtype. Moreover, the postural subtype demonstrated faster progression of symptom severity (Jankovic et al., 1990).

Since the initial establishment of the two motor subtypes, further research has revealed that each subtype is associated with a different rate of disease progression and with differing co-morbidities, specifically dementia (Foltyne, Brayne, & Barker, 2002). It has been reported that an individual with a tremor-dominant classification is less likely to develop severe cognitive impairment than an individual with a postural instability and difficulty classification (Burn et al., 2006). Multiple studies have found that individuals who are classified as belonging to the postural instability and gait subtype have a much higher likelihood of developing dementia than those classified as tremor dominant (Foltyne et al., 2002). The postural instability and gait difficulty classification is also strongly associated with a faster rate of motor and cognitive decline, as well as individuals being more likely to experience mood disorders (e.g., depression; Foltyne et al., 2002).

While an individual classified as tremor dominant can eventually progress to postural instability and gait difficulty dominant, the reverse is far less common (Alves, Larsen, Emre, Wentzel-Larsen, & Aarsland, 2006).

Dopaminergic System

While the pathogenesis of Parkinson's disease is not yet fully understood, the pathophysiology has been well documented. The primary source of Parkinsonism is the degeneration of dopaminergic neurons in the pars compacta of the substantia nigra (Dauer & Przedborski, 2003). These dopaminergic neurons primarily project to the putamen and the caudate nucleus in the striatum with the pathway to the putamen showing the most degeneration (Dauer & Przedborski, 2003). When the motor symptoms first begin to present the substantia nigra has already lost 60% of its dopaminergic neurons and the level of putamenal dopamine has reduced by 80% (Dauer & Przedborski, 2003). The subsequent reduction of available dopamine impacts the neuronal activation in the pathways from the striatum to the globus pallidus pars interna and substantia nigra pars reticula, the outputs from the basal ganglia to the thalamus and then the cortex (Obeso et al., 2000). The impacted neuronal activation is thought to be the cause of the motor symptoms in PD (Dauer & Przedborski, 2003).

It has been suggested that this model of PD is responsible for the symptomatology present in tremor dominant PD (Bohnen & Albin, 2011). Given the efficacy of levodopa in the treatment of these symptoms, they have also been labelled as dopaminergic symptoms (Bohnen & Albin, 2011). Primate models of PD, where the condition is chemically induced using the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), have reported that lesions induced solely in the nigrostriatal pathway (with no damage to the cholinergic system) do not result in postural deficits (Müller & Bohnen, 2013).

Evidence suggests that the two PD motor subtypes have differing underlying neuropathologies, which may account for the differing rates of decline and incidence of dementia (Bohnen & Albin, 2011). The majority of this evidence comes from research investigating how the subtypes respond to particular medications, most commonly, how they respond to levodopa, a dopamine-replacement medication (Bohnen & Albin, 2011). Levodopa is a medication that, once processed by particular enzymes in the brain, is converted into dopamine and can be used by the various neural systems that depend on it and that were deprived due to the Parkinsonian degeneration (Cools, 2006). Levodopa has become a standard component of the pharmacological treatment of PD and leads to improvements in some of the motor and cognitive abilities affected by PD. In turn, this increases the quality of life for individuals with PD (Sethi, 2008).

Despite these improvements in functioning there are still multiple motor and cognitive skills that do not effectively respond to the use of levodopa-based medications (Bohnen & Albin, 2011). Indeed some cognitive abilities even deteriorate following levodopa medication (Bohnen & Albin, 2011; Sethi, 2008). Morrison et al. (2004) reported decreased performance on the Boston Naming Test and Stroop Interference Task when individuals were on levodopa ($N = 16$). Swainson et al. (2000) found significantly impaired performance on discrimination and reversal learning tasks in medicated PD individuals ($N = 22$), but not in unmedicated PD individuals ($N = 15$). This is likely due to the levodopa flooding areas with dopamine that were not damaged as part of PD, known as 'dopamine-overdose' (Bohnen & Albin, 2011). Previous studies have found that postural instability and gait difficulty symptoms respond little to the use of levodopa medications, while tremor and bradykinesia symptoms respond well (Sethi, 2008).

In light of this, it has been suggested that there are differing neurotransmitter systems underlying the two motor subtypes, which may account for the differing responses to dopamine-replacement medications (Bohnen & Albin, 2011).

Cholinergic System

While the loss of dopamine due to degeneration in PD has been well established, there is a second neurotransmitter system that degenerates over the course of PD, the cholinergic system (Bohnen et al., 2006). The cholinergic system is responsible for the production and transport of the neurotransmitter acetylcholine (ACh) and much like dopamine, ACh plays a large role in motor control (Müller & Bohnen, 2013). There are two main cholinergic projections, both located in the basal forebrain; the nucleus basalis of Meynert and the pedunculopontine nucleus-laterodorsal tegmental complex (PPN; Müller & Bohnen, 2013). Similar to the substantia nigra, both sources of cholinergic projections degenerate in PD, with the resulting loss of ACh denervation suggested to drive the symptomatology of the postural instability and gait difficulty subtype (Bohnen & Albin, 2011). The nucleus basalis and the PPN are also areas that degenerate in Alzheimer's Disease and Dementia with Lewy Bodies, a possible explanation for the higher incidence of dementia in the postural instability and gait difficulty subtype (Burn et al., 2006; Müller & Bohnen, 2013).

Experimental studies exploring the association between Ach and postural and gait difficulties support this. Bohnen and colleagues (2009) examined the association between incidences of falls and cholinergic levels. No significant difference was found in the levels of dopamine denervation between PD individuals with a history of falling and without, while it was found that thalamic levels of ACh were significantly lower in the PD fallers group (Bohnen et al., 2009). Similar associations are seen in healthy older adults. Nebes et al. (2007) reported a significant relationship between cholinergic levels and established predictors of falls; gait speed and simple manual response time.

A meta-analysis of anticholinergic medications in PD found that of the 9 available studies, 7 reported adverse cognitive effects such as memory difficulties and poor concentration (Katzenschlager, Sampaio, Costa, & Lees, 2002). Neuroimaging studies demonstrate a loss of acetylcholine receptors is associated with mild cognitive impairment in PD (Sabri, Kendziorra, Wolf, Gertz, & Brust, 2008). Bohnen et al. (2010) found impaired performance on the California Verbal Learning Test and the Stroop Interference test to be associated with cholinergic denervation. Bohnen et al. (2005) explored the relationship

between cognitive performance and an enzyme that breaks down ACh, acetylcholinesterase. Significant relationships were seen with the Judgement of Line Orientation, Stroop, Trail Making, and WAIS-III Digit span tasks (Bohnen et al., 2006). An eight year longitudinal study of a PD cohort ($N = 235$) found significant associations between the use of anticholinergic medications and cognitive decline (Ehrt, Broich, Larsen, Ballard, & Aarsland, 2010). Ehrt et al. (2010) also found that the severity of decline was significantly different to that of the individuals that were not taking anticholinergics. Given that the same level of effect is not seen in healthy individuals, it suggests that individuals with PD develop sensitivity to anti-cholinergic medications as a result of cholinergic denervation (Bohnen & Albin, 2011).

Based on the aforementioned evidence, it is apparent that there are two distinct motor subtypes in PD, each with different underlying neurological mechanisms.

Working Memory

Working memory is a type of memory used for storing a small amount of information for a short period of time so that it can be manipulated (Baddeley, 2000). Working memory supports cognitive processes such as reading comprehension, mental arithmetic and spatial planning (Baddeley, 2000). Baddeley's (2003) model of working memory comprises four main components: the visuospatial sketchpad, the phonological loop, the central executive and the episodic buffer (see Figure 1).

The visuospatial sketchpad is the component responsible for storing and manipulating visuospatial information and assessing the capacity of the visuospatial sketchpad reflects an individual's spatial working memory ability (Baddeley, 2003). The visuospatial sketchpad is further subdivided into two separate components of storage, one active and one passive (Repovš & Baddeley, 2006). The passive component is responsible for the storage and retrieval of information exactly as it was stored (e.g., for recalling a specific string of digits, this passive component was termed the 'visual cache'; Repovš & Baddeley, 2006). The active component of the visuospatial sketchpad is responsible for storing information to be manipulated or to be modified as part of recall (e.g. summing a number of digits, this component was termed the 'visual scribe'; Repovš & Baddeley, 2006).

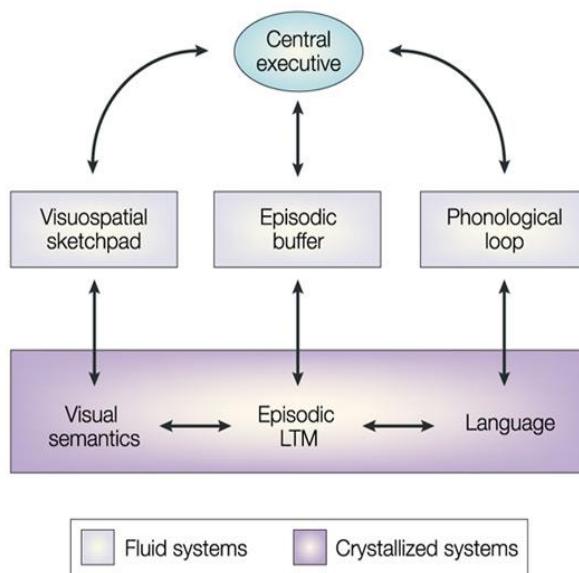


Figure 1. Representation of Baddeley's multi-component model of Working Memory. (Baddeley, 2003, p.835).

The phonological loop is responsible for the storage and manipulation of verbal information and similar to the visuospatial sketchpad is thought to be divided into two components; a short term store of information that quickly decays and a rehearsal process that allows information to held for a longer period of time (Repovš & Baddeley, 2006). The capacity of the phonological loop is measured by the amount of information that can be recalled and articulated before the stored information 'fades' (Baddeley, 2003). Past exploration of the phonological loop's short term store using an immediate serial recall task has shown that it has a capacity to store approximately five to eight items at a time (Repovš & Baddeley, 2006). This limit is further affected by the characteristics of the items being stored (Repovš & Baddeley, 2006). One such example of the influence of item characteristics is the phonological similarity effect, which is where sequences of similar sounding letters (E, V, B) are more difficult to recall than sequences of dissimilar-sounding letters (Q, H, G) (Repovš & Baddeley, 2006). The phonological loop's rehearsal process has been described as being analogous to a sub vocal rehearsal of the stored information (Repovš & Baddeley, 2006). The rehearsal process is similar to repeating the information without talking (Repovš & Baddeley, 2006).

The central executive is the regulatory component of working memory and is involved in the manipulation and integration of information stored in the visuospatial

sketchpad and phonological loop (Repovš & Baddeley, 2006). The central executive also influences complex cognitive tasks, playing a role in the regulation of attention, enabling the changing of the focus of attention as well as dividing attention between simultaneous tasks (Repovš & Baddeley, 2006). There has however, been some dispute as to whether the central executive is solely responsible for the regulation of attention (Repovš & Baddeley, 2006). Further exploration into the area has found that the other components of working memory also have some influence in the switching of attention with performance on tasks requiring dual attention being influenced by inhibiting the performance of the phonological loop (Repovš & Baddeley, 2006; Saeki & Saito, 2004). The central executive has also been found to use the phonological loop and visuospatial sketchpad as 'slave' components and will 'offload' specific tasks to these components as needed (Repovš & Baddeley, 2006). The phonological loop is used as storage space for execution of programs and the visuospatial sketchpad used in the guidance of visual attention (Repovš & Baddeley, 2006).

The episodic buffer is the fourth major component of working memory and can be visualised as an extended storage system for the other components (Repovš & Baddeley, 2006). The episodic buffer also acts a connecting structure to long-term memory (Repovš & Baddeley, 2006). Using this connection, as well as its connections to the other working memory components, the episodic buffer is able to be used for the integration of information from multiple sources to form a coherent structure, or 'episode' (Repovš & Baddeley, 2006). As such the episodic buffer is able to process both auditory and verbal information from their respective subdivisions.

Working Memory and Parkinson's Disease

Working memory is one of the many cognitive abilities that declines during the course of PD. The presentation of working memory deficits between individuals is not consistent, with individuals experiencing decline in different components (Lewis, Slabosz, Robbins, Barker, & Owen, 2005). Just as there are two specialised components of the working memory model, there are two specialised forms of working memory, dependent on those components; spatial working memory and verbal working memory (Repovš & Baddeley, 2006).

Differences in deficits have been found for each form of working memory (Lewis et al., 2003). Multiple studies report that it is the manipulation of stored information that is the most heavily impaired in PD, rather than maintenance or retrieval (Lewis et al., 2003). This

impairment was present for both verbal and spatial working memory (Lewis et al., 2005). Brain imaging studies have suggested a role of the striatum and dopamine in working memory (Dagher, Owen, Boecker, & Brooks, 2001). Activation of the caudate nucleus has been observed in healthy controls when completing a Tower of London executive functioning task but individuals with PD do not demonstrate such activation (Dagher, Owen, Boecker, & Brooks, 2001). Furthermore, levodopa based medication significantly increased spatial working memory performance in those with PD such that there was no significant difference between the performance of healthy controls and those with PD (Costa et al., 2003). It should be noted, however, that this study was conducted with a small sample and so should be treated with caution ($N = 19$; Costa et al., 2003).

Further research into the dopaminergic modulation of working memory has explored which processes of working memory (manipulation or retrieval of information) are influenced by the use of levodopa (Lewis et al., 2005). Lewis and colleagues (2005) investigated whether the simple retrieval, simple manipulation or complex manipulation of information was affected by levodopa dosage. It was found that both complex and simple manipulation scores were significantly improved with the use of levodopa, while simple retrieval scores were not significantly affected (Lewis et al., 2005). Lewis and colleagues (2005) did involve a slightly larger sample ($N = 39$) than that used by Costa et al. (2003).

As previously mentioned, there are two different neurotransmitter systems underlying the two motor subtypes (tremor dominant and postural instability and gait difficulty); the dopaminergic and cholinergic systems. Further research into motor subtype and working memory has produced inconsistent results. Domellöf, Elgh and Forsgren (2011) found that different motor functions were associated with different cognitive domains; bradykinesia was strongly associated with performance on the Wisconsin Card Sorting Test ($\beta = -0.246$). Postural instability and gait difficulty was significantly associated with performance on the Brief Visuospatial Memory Test-Revised ($r = -.36$; Domellöf et al., 2011). It was also found that tremor did not significantly correlate with any of the cognitive tests in the study (Domellöf et al., 2011). Conversely, Lyros et al. (2008) found that tremor dominant individuals demonstrated significantly impaired performance on the Rey Auditory Verbal Learning Test, but those with postural difficulty did not. In contrast, Sollinger et al. (2010) found that those with postural difficulty were more impaired on measures of memory and executive functioning than those with tremor. There is not yet a consistent association

between working memory difficulties and motor subtype. The relationship between motor subtype and working memory in PD remains unclear.

Justification for Study

It is evident that there are conflicting results as to how working memory is affected in PD and how this might be associated with motor subtype. Some studies have reported that both verbal and spatial working memory are affected (Lewis et al., 2003), while others have reported that only one component is impaired (Costa et al., 2003). Dopamine-replacement medications improve these deficits (Lewis et al., 2005), but the deficits are also significantly associated with non-dopaminergic motor features (Domellöf et al., 2011). However, many studies have used flawed methodologies. Sollinger et al.'s (2010) study did not report the level of impairment in memory or executive functioning, nor the criteria they used to define impairment. Lyros et al. (2008) used a small sample size ($N = 30$) and did not control for age and gender. This is a significant flaw, as both age and gender significantly impact working memory performance (Rypma & D'Esposito, 2000; Speck et al., 2000). Domellöf et al. (2011) used multiple linear regressions when the dependent variables were non-independent. These flaws could have influenced the results of these studies and call into question the validity of their conclusions.

The two motor subtypes are driven by different underlying neurotransmitter systems, tremor dominance by dopamine and postural difficulty by acetylcholine. Dopamine modulates working memory and would therefore be expected to influence working memory in the tremor subtype, but there is no clear association with either subtype. Several of the studies exploring the topic have methodological issues, such as low sample sizes or poor statistical analyses, limiting the validity of the results. Research into this area is also primarily cross-sectional and unable to examine how working memory changes across the course of PD. Given the inconsistent results of methodologically flawed studies, there is a need for methodologically sound exploration of this area. It is expected that a longitudinal study with an adequate sample size and appropriate analyses will show a clear relationship between one, or both, motor subtypes and WM. There are two primary hypotheses of the present study. Firstly, that after controlling for age and gender, motor subtype (TD/PIGD) at Time 1 will account for a significant amount of variance in verbal working memory assessed at a two-year follow-up. Secondly, that after controlling for age and gender, motor subtype

(TD/PIGD) at Time 1 will account for a significant amount of variance in spatial working memory assessed at a two-year follow-up.

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Extended Results

Data Screening

The data were visually inspected and a descriptive analysis was conducted to identify data entry errors. Any mistakes were cross-referenced with the original file at ParkC and corrected. Data screening identified two extreme univariate outliers ($SD \geq 3.29$; Tabachnick & Fidell, 2013). One outlier was identified for the spatial working memory scores ($z = 4.03$) and one for the postural instability and gait difficulty (PIGD) scores ($z = 4.10$; see Supplementary Materials I). A second PIGD case was also identified as an outlier ($z = 3.45$), but inspection of the Cook's distance and trimmed mean (see Supplementary Materials I) indicated that the case was not influential and so was retained. Little's MCAR was non-significant ($p = .57$) and only .67% of data were missing. As recommended by Tabachnick and Fidell (2013), expectation-maximisation was used to replace missing values. A repeat descriptive analysis was conducted following value replacements and no errors were identified. The Mahalanobis Distance was used to assess multivariate outliers and no cases exceeded the critical chi-square for four degrees of freedom ($\chi^2 = 18.467$, $\alpha = .001$). The subtyping questions of the UPDRS demonstrated good internal consistency (PIGD $\alpha = .75$; TD $\alpha = .82$; see Supplementary Material J). Inter-item correlations for all variables are presented in Table 2. Due to significant correlations with both criterion variables, age was retained as a control variable in the analysis. Gender was only significantly correlated with HVLT-R Total, and so was retained as a control variable for VWM only.

Assumption Testing

The data were assessed against the assumptions for SEM, including: (i) an adequate number of cases per free parameter, (ii) multicollinearity, (iii) multivariate normality, and (iv) linearity. Kline (2010) recommends a minimum of 10 participants per free parameter; given six free parameters in the model a minimum sample of 60 participants is required. The present sample of 114 is therefore acceptable. Multicollinearity was assessed by calculating Tolerance and VIF values. All Tolerance values were $>.1$ and all VIF statistics were >10 , indicating that multicollinearity was not an issue (Allen & Bennet, 2012). Visual inspection of boxplots and histograms indicated that the PIGD and tremor dominance (TD) variables were not normally distributed. This was supported by the skewness and kurtosis statistics which exceeded 1.96 (see Supplementary Materials I). As the mean tremor and postural items were univariate non-normal, the assumption of multivariate normality was violated and so an estimator robust to this was used in the analysis (Weighted least squares means and variance

adjusted; WLSMV). Linearity was assessed with scatterplots of the bivariate relationship between study variables. No curvilinear trend was present, indicating that the assumption of linearity was met (see Supplementary Materials I).

Table 2

Means, Standard Deviations, and Correlations between Control Variables and Study Variables (N = 114)

Measure	1	2	3	4	5	6	7	M	SD
1. Gender	-							-	-
2. Age	-.165	-						66.89	9.22
3. HVLT-R	.397**	-.483**	-					23.41	6.64
4. SWM	-.041	.393**	-.285**	-				27.78	14.81
5. Mean Tremor	-.140	.153	-.128	-.012	-			.62	.51
6. Mean PIGD	.039	.128	-.118	.229*	-.201*	-		.68	.61
7. Subtype	.183	-.045	.105	.025	-.708**	.553**	-	-	-

Note: HVLT-R = Total number words recalled across three trials of Hopkins Verbal Learning Test – Revised (Time 2); SWM = Total number of errors on Spatial Working Memory task at eight squares (Time 2).

** $p < .001$, * $p < .05$

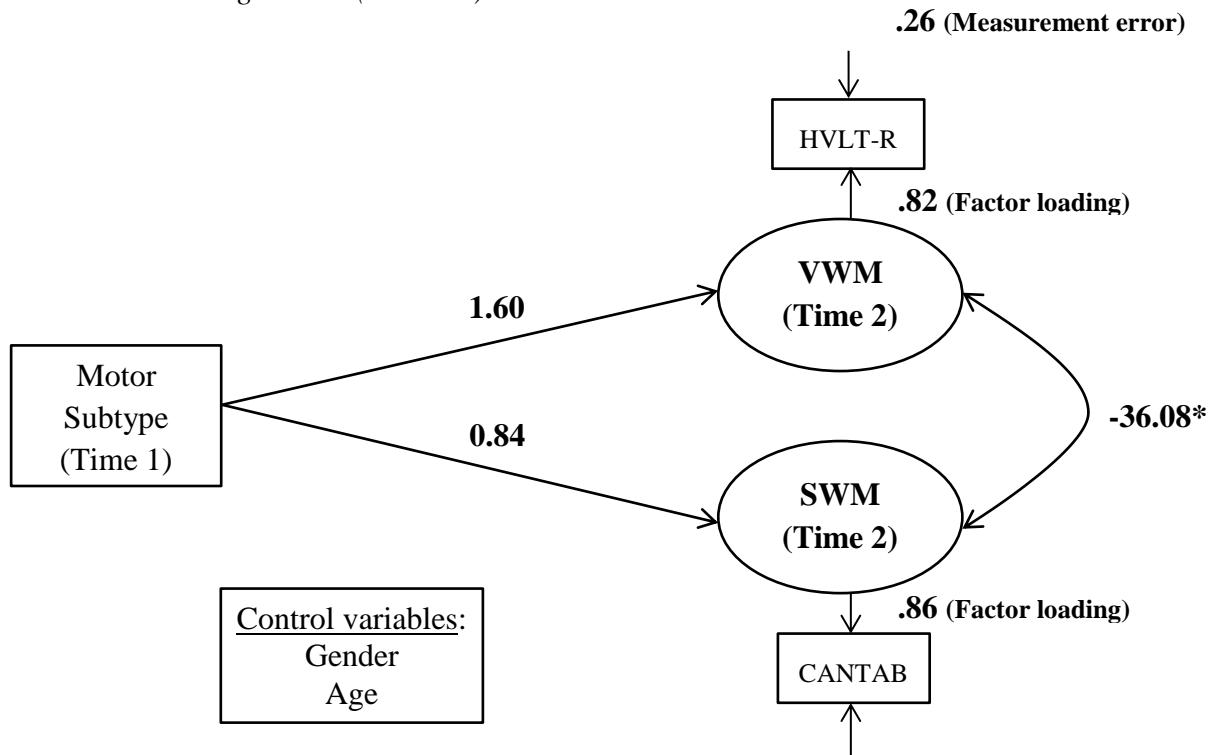
Analysis

SEM was used to test the hypotheses. Weighted least squares means and variance adjusted (WLSMV) estimation was used, as it allows for the use of categorical control variables (gender) and is robust to violations of normality (Brown, 2006). WLSMV does not require a larger sample size when used in place of standard Maximum Likelihood Estimation (Beauducel & Herzberg, 2009). A Bonferroni-correction was applied to control the family wise error rate, adjusting the critical p -value to .0125 (.05/4).

Motor subtype at Time 1 (PIGD/TD) was entered as an observed exogenous variable; VWM and SWM at Time 2 were entered as latent endogenous covariates (see Figure 1). Factor loadings and measurement error for VWM and SWM were set using the test-retest reliabilities from Conway Greig et al., (2004) and Lowe and Rabbitt (1998), respectively. Parameter estimates are shown in Figure 1 and Table 3.

Figure 1

Model 1: Time 1 Motor Subtype Predicting Time 2 SWM and VWM – Unstandardised Estimates and Starting Values (N = 114)



* $p < .0125$ (Bonferroni-adjusted)

Table 3

Unstandardised and Standardised Parameter Estimates with Significance Levels for Model in Figure 1

Parameter	Unstandardised Estimate (Standard Errors)	Standardised Estimate	p
Measurement Model			
VWM → HVLT-R	.86	.99	N/A
SWM → CANTAB	.82	.99	N/A
Error in HVLT-R	.26	.01	N/A
Error in CANTAB	.32	.002	N/A
Covariance VWM and SWM	-36.08 (11.75)	-.29	.002*
Structural Model			
Subtype → VWM	1.60 (1.47)	.10	.28
Subtype → SWM	.84 (3.14)	.03	.79
Residual for VWM	56.83 (9.47)	.99	< .001
Residual for SWM	271.83 (44.34)	.99	< .001

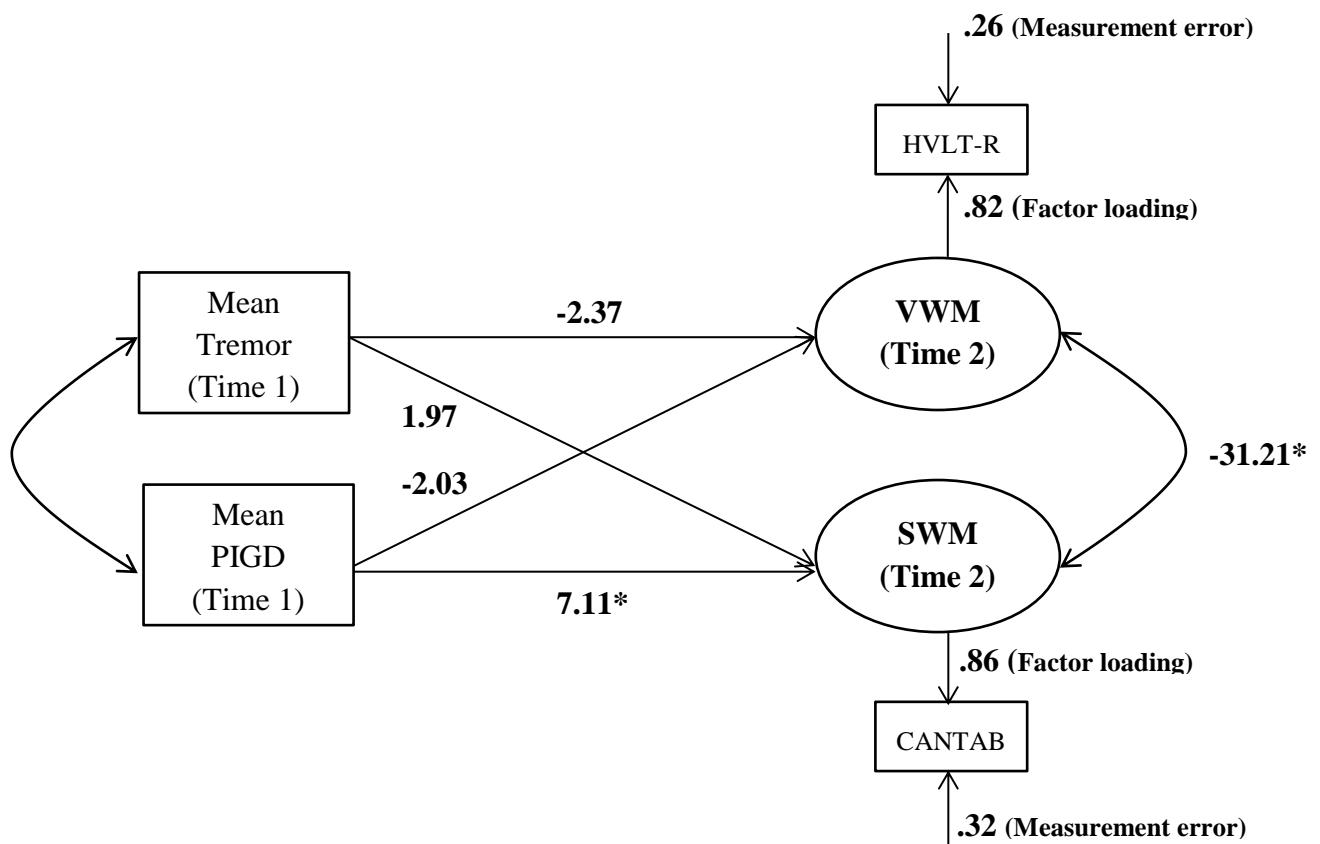
$\chi^2(4) = 7.85, p = .09$; CFI = .93; NNFI = .83; RMSEA = .09

* $p < .0125$ (Bonferroni-adjusted)

The model demonstrated borderline fit $\chi^2(4) = 7.85, p = .09$; comparative-fit-index (CFI) = .93; non-normed fit index (NNFI) = .83; root mean square error of approximation (RMSEA) = .09 (see Supplementary Material K). However, path coefficients between motor subtype and SWM/VWM were both non-significant (see Table 3). This indicates a potential relationship between subtype and WM, but the model needed to be re-specified. A second SEM was therefore conducted, whereby motor subtype was replaced with the mean tremor and PIGD scores for all participants (see Figure 2).

Figure 2

Model 2: Time 1 Mean Tremor and PIGD Score Predicting Time 2 SWM and VWM – Unstandardised Estimates and Starting Values (N = 114)



* $p < .0125$ (Bonferroni-adjusted)

The second SEM demonstrated poorer model fit than the first $\chi^2(6) = 10.71, p = .10$; CFI = .92; NNFI = .82; RMSEA = .08 (see Supplementary Material K), but the path coefficient from the mean PIGD score to SWM was significant ($p = .01$; see Table 4). The relationship was positive; indicating that as mean PIGD score increased so did the number of errors made on the SWM task. This suggested a relationship between physical symptoms and

WM, but that subtype also needed to be considered. To this end, a multiple groups confirmatory factor analysis (CFA) was conducted, applying the model in Figure 2 to each subtype separately. In this way the associations between physical symptoms and WM can be examined for each subtype (TD/PIGD) independently.

Table 4

Unstandardised and Standardised Parameter Estimates with Significance Levels for Model in Figure 2

Parameter	Unstandardised Estimate (Standard Errors)	Standardised Estimate	p
Measurement Model			
VWM → HVLT-R	.86	.99	N/A
SWM → CANTAB	.82	.99	N/A
Error in HVLT-R	.26	.01	N/A
Error in CANTAB	.32	.002	N/A
Covariance VWM and SWM	-31.21 (11.13)	-.26	.005*
Structural Model			
PIGD → VWM	-2.03 (1.15)	-.15	.08
TD → VWM	-2.37 (1.50)	-.16	.11
PIGD → SWM	7.11 (2.76)	.24	.01*
TD → SWM	1.97 (2.88)	.06	.49
Residual for VWM	55.27 (8.99)	.96	< .001
Residual for SWM	256.73 (45.73)	.94	< .001

$\chi^2(6) = 10.71$, p = .10; CFI = .92; NNFI = .82; RMSEA = .08

*p < .0125 (Bonferroni-adjusted)

The CFA demonstrated good model fit $\chi^2(12) = 9.79$, p = .63; CFI = 1; NNFI = 1.11; RMSEA = 0 (see Supplementary Material K). There was a significant path coefficient from PIGD to SWM (p = .001), and there was a trend towards significance in the path from PIGD to VWM (p = .02; see Table 5). As with the second model the relationship was positive, indicating increasing errors on the SWM task as mean PIGD score increased. The trend in the VWM path was negative, indicating that the participant recalled fewer words as mean PIGD score increased. These paths were only significant for the PIGD group.

The fit was also better than the first two models, suggesting that the improved model fit was due to the inclusion of both motor subtype *and* the scores for tremor/posture. Subtype membership alone was not sufficient to predict WM decline, nor was solely considering physical symptoms a good fit for the data. This indicates that physical symptoms needed to

be assessed in the context of motor subtype and that the predictive ability of the symptoms differed between the subtypes.

Table 5

Unstandardised and Standardised Parameter Estimates with Significance Levels for Multiple Groups CFA 1

Parameter	Unstandardised Estimate (Standard Errors)	Standardised Estimate	p
PIGD (N = 51)			
Measurement Model			
VWM → HVLT-R	.86	.99	N/A
SWM → CANTAB	.82	.99	N/A
Error in HVLT-R	.26	.01	N/A
Error in CANTAB	.32	.002	N/A
Covariance VWM and SWM	-30.27 (13.28)	-.14	.02
Structural Model			
PIGD → VWM	-3.09 (1.36)	-.09	.02
TD → VWM	2.30 (3.83)	-.02	.55
PIGD → SWM	11.37 (3.55)	2.03	.001*
TD → SWM	-1.02 (9.20)	-.28	.91
Residual for VWM	44.31 (9.66)	.99	<.001
Residual for SWM	201.57 (55.21)	.83	<.001
TD (N = 63)			
Measurement Model			
VWM → HVLT-R	.86	.99	N/A
SWM → CANTAB	.82	.99	N/A
Error in HVLT-R	.26	.01	N/A
Error in CANTAB	.32	.002	N/A
Covariance VWM and SWM	-32.57 (18.48)	-.25	.08
Structural Model			
PIGD → VWM	-7.45 (5.15)	-.23	.15
TD → VWM	-.09 (2.68)	-.005	.97
PIGD → SWM	-3.47 (10.45)	-.05	.74
TD → SWM	.35 (6.98)	.01	.96
Residual for VWM	60.78 (14.65)	.95	<.001
Residual for SWM	284.28 (79.54)	.99	<.001

$\chi^2(12) = 9.79$, p = .63; CFI = 1; NNFI = 1.11; RMSR = .67; RMSEA = 0

* $p < .0125$ (Bonferroni-adjusted)

To confirm this, a second multiple groups CFA was conducted that assumed all parameters were equal between the two subtypes. The second CFA demonstrated very poor model fit $\chi^2(24) = 51.65, p < .001$; CFI = .38; NNFI = .28; RMSEA = .14 (see Supplementary Material K). This indicated that there was a difference in the ability of physical symptoms to predict WM within each subtype.

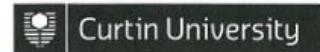
The significant path seen in Table 5 indicated that belonging to the PIGD subtype would be associated with future WM decline, yet the non-significant paths in the first model (see Table 3) seemingly contradict this. This suggests that the PIGD symptoms themselves are the best predictors of WM decline, regardless of motor subtype. This is supported by the significant path from mean PIGD score to SWM in the second model (See Table 4). It is likely that the non-significant paths from mean PIGD score in the TD subtype are due to those symptoms not being as developed as they are in the PIGD subtype. This would be supported by the difference in the size of the parameter estimates in the TD subtype; with the PIGD score estimates markedly larger than their TD counterparts (see Table 5).

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Supplementary Material A

Ethics Approval Number


Memorandum

To	Dr Andrea Loftus, Psychology and Speech Pathology
From	Professor Stephan Millett, Chair, Human Research Ethics Committee
Subject	Protocol Approval HR 158/2013
Date	17 October 2013
Copy	Dr Natalie Gasson, Psychology and Speech Pathology, Professor Romola Bucks, University of Western Australia, Dr Meghan Thomas, Edith Cowan University and University of Western Australia (adjunct).

Office of Research and Development
Human Research Ethics Committee

TELEPHONE 9266 2784
FACSIMILE 9266 3793
EMAIL hrec@curtin.edu.au

Thank you for your application submitted to the Human Research Ethics Committee (HREC) for the project titled "*Cognitive and motor heterogeneity in Idiopathic Parkinson's Disease*". The Committee notes the prior approval by Edith Cowan University HREC (2736) and has reviewed your application consistent with Chapter 5.3 of the *National Statement on Ethical Conduct in Human Research*.

- You have ethics clearance to undertake the research as stated in your proposal.
- The approval number for your project is **HR 158/2013**. Please quote this number in any future correspondence.
- Approval of this project is for a period of four years **17-10-2013 to 17-10-2017**.
- Annual progress reports on the project must be submitted to the Ethics Office.
- If you are a Higher Degree by Research student, data collection must not begin before your Application for Candidacy is approved by your Faculty Graduate Studies Committee.
- The following standard statement **must be** included in the information sheet to participants:
This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number HR 158/2013). The Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning 9266 2784 or by emailing hrec@curtin.edu.au.

Applicants should note the following:

It is the policy of the HREC to conduct random audits on a percentage of approved projects. These audits may be conducted at any time after the project starts. In cases where the HREC considers that there may be a risk of adverse events, or where participants may be especially vulnerable, the HREC may request the chief investigator to provide an outcomes report, including information on follow-up of participants.

The attached **Progress Report** should be completed and returned to the Secretary, HREC, C/- Office of Research & Development annually.

Our website https://research.curtin.edu.au/guides/ethics/non_low_risk_hrec_forms.cfm contains all other relevant forms including:

- Completion Report (to be completed when a project has ceased)
- Amendment Request (to be completed at any time changes/amendments occur)
- Adverse Event Notification Form (If a serious or unexpected adverse event occurs)

Yours sincerely

Professor Stephan Millett
Chair Human Research Ethics Committee

Supplementary Material B

Participant Information Sheet



Curtin University

School of Psychology and
Speech Pathology

Parkinson's Centre
Attn: Dr Andrea Loftus
GPO Box U1987
Perth Western Australia 6845

Telephone +61 8 9266 3441
Facsimile +61 8 9266 2464
Email caitlin.timms@curtin.edu.au

INFORMATION SHEET

Project titled: COGNITIVE AND MOTOR HETEROGENEITY
IN IDIOPATHIC PARKINSON'S DISEASE.

Chief Investigator(s): Dr Andrea Loftus, PhD (*Senior Lecturer, School of Psychology and Speech Pathology, Faculty of Health Sciences, Curtin University*), Associate Professor Natalie Gasson, PhD (*Program Director for Undergraduate Psychology, School of Psychology and Speech Pathology, Faculty of Health Sciences, Curtin University*), Miss Caitlin Timms (*Research Assistant, ParkC, School of Psychology and Speech Pathology, Faculty of Health Sciences, Curtin University*). **Co-Investigator(s):** Dr Meghan Thomas, PhD (*Founder of ParkC and Postdoctoral Research Fellow, School of Medical Sciences, Faculty of Health, Engineering and Science, Edith Cowan University*), Professor Romola Bucks, PhD (*UK Trained Clinical Neuropsychologist and Lecturer, School of Psychology, University of Western Australia*),

We would like to invite you to participate in the following research which will investigate the relationship between motor (i.e. balance, walking, tremor, rigidity), and non-motor (i.e., problems with memory, thinking, and mood) symptoms of Parkinson's disease (PD). Information regarding the relationship between the motor and non-motor symptoms will be used to identify subtypes of PD.

Currently, the cause of PD is unknown. It is possible that some (but not all) individuals may have a genetic predisposition to developing PD and the current research aims to explore this further.

Please take time to read the following information carefully and discuss it with others if you wish.

What are the possible benefits of taking part?

The information we gain from your participation will help us better to understand the motor (balance, walking, tremor, rigidity) cognitive (thinking and memory) and affective (mood) problems that can occur as a result of PD. The information we gain from your participation will help us to identify subtypes of PD and the identification of subtypes will have implications for the clinical management of future patients with PD.

Why have I been invited to participate in this research?

You have been invited to participate in this research because you have been diagnosed with PD or Parkinsonism.

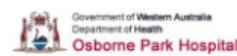
What will I be asked to do?

There are three parts to this study: Part 1) involves the completion of questionnaires or surveys; Part 2) involves some computer and paper-based assessments; and Part 3) involves an assessment of motor (i.e. balance, walking, tremor, rigidity) symptoms.

Part 1: We will provide you with a questionnaire package via post and ask that you complete some surveys regarding your mood, memory, and personality, how sleepy you are during the day and possible sleep



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Government of Western Australia
Department of Health
Osborne Park Hospital

CRICOS Provider Code 00301J (WA), 02637B (NSW)

difficulties, how your Parkinson's symptoms influence your everyday life, and how you cope with things in general. All of these surveys are designed to be self-completed; therefore, you may complete the surveys at home and bring them with you to your appointment at ParkC, if you decide to participate in Part 2 of the study. You are also free to complete all or part of the questionnaires at the end of your appointment at ParkC if you wish. A research staff member from ParkC will sit with you and discuss any questions you may have regarding the questionnaires. If you do not wish to take part in Part 2 of this research, you may still complete the questionnaires and we will provide you with a reply paid envelope to return your questionnaires.

A questionnaire will be included which is to be completed by a relative/ friend. Completion of this questionnaire will be taken to indicate that you consent for the information that is provided by the relative/ friend to be used in the study.

Part 2: If you are happy to participate in Part 2 of this research, we will go over the information sheet with you when you arrive at ParkC, explain what is going to happen during the appointment, and answer any questions you might have. You will then be asked to participate in some tasks that are designed to look at your memory and thinking skills. These will be both paper-based and computer-based tasks. The session will be made as enjoyable as possible for you; however some of these tasks can be challenging. If you feel at any point during the assessment that you would like to stop, please tell the research staff and they will end the session immediately. You do not have to give a reason why and you will not be asked any further questions.

Part 3: Lastly, you will be asked to perform some simple motor (i.e. balance, walking, tremor, rigidity) tasks as part of the Unified Parkinson's Disease Rating Scale (UPDRS), a standardised assessment for the motor symptoms of PD. These motor tasks will include: finger tapping, hand rotations, fist clenching/opening, finger to nose movements, leg and toe tapping, rising from a chair, and a 10 metre walk. The investigator will also give you a slight pull on the shoulders to assess your balance and will stand behind you to provide support should you become unbalanced. Assessments of speech, facial expression, rigidity (stiffness of neck, arms and legs), and tremor will be made via observation during this assessment period. You will also be asked some questions regarding dyskinesias (involuntary movements), fluctuations in functioning due to medications cycles and dystonia (painful cramps and/or muscle spasms) which you may or may not experience. **All of these assessments will be videotaped to allow for independent review and rating by experts in the field of Parkinson's, although you can decline to have the session videotaped.** We will also take a measurement of your height, weight and waist circumference.

The motor assessment requires manipulation of the hips and legs. Please wear comfortable clothing; trousers are preferred.

Throughout the appointment you will be encouraged to ask questions and while the testing is anticipated to take no more than 2 hours, you will be given regular breaks.

Blood sample for Genetic Analysis

There is a fourth optional part of this project. As part of the appointment at ParkC, we ask participants if they would be happy to donate a small sample of blood so that we can look at genetic make-up (i.e. your DNA). **Please note that the decision to have a blood sample taken is completely optional and forms a different part of the study. You can decide not to have a blood sample without affecting any other data we collect about you for the study. Your participation will be of equal value, with or without the blood sample.**

Blood and DNA samples will be stored for the length of this research project and will be analysed for a range of DNA markers.

Initially we will screen for the known genetic mutations that cause familial PD. These mutations occur in the SNCA, LRRK2, Parkin, PINK1, DJ-1 and Parkin 9 genes. Familial PD occurs in only 10% of PD cases so is uncommon. If we find a known genetic cause of PD we will (with your consent) inform your treating

physician who will be able to arrange appropriate Genetic Screening to confirm our research findings.

We also intend to screen for a range of genetic measures that may be associated with the various aspects of PD. The technology for genotyping DNA is changing rapidly and is producing more and more complex data. Further the known genetic influences that may affect different aspects of PD are still unclear. Therefore we would like to screen for a range of as yet unspecified markers, with your consent. In the short term this research is more about trying to find associations between your DNA and your PD symptoms. It is very experimental and at this stage not able to influence any treatment approaches although we hope that in the future it will have clear treatment implications.

If you provide written consent, indicating that you are happy to provide a blood sample, a qualified phlebotomist will take your blood sample. We are grateful to everyone who agrees to give a sample.

What about my medication?

We would ask you to take your medication as normal. No changes will be made to your medication and you will not be asked to stop taking your current medication at any point during this study.

What will happen when the research study stops?

This is a longitudinal study and so it does not have a specific end date. At the end of your appointment, we will ask whether you might like to participate in a further follow-up appointment scheduled for approximately two years later.

What are the possible disadvantages and risks of taking part in this research?

There are no foreseeable risks or disadvantages associated with taking part in this study, aside from the possibility of becoming a little tired as a result of undertaking these assessments. However, you will be provided with regular breaks to help avoid becoming fatigued.

There are no foreseeable risks or disadvantages associated with Part 3 (motor assessment), aside from the minimal risk of a fall during the balance assessment. The investigator conducting the balance assessment will stand behind you to support you in the case that you become unbalanced. The balance assessment conducted as part of the UPDRS is standard in clinical practice for PD.

The discomforts associated with taking a blood sample are minimal. There is a risk that sometimes bruising and minor infection may occur and the arm might become sore. Risk of bruising or infection will be minimised because all blood samples will be performed by an experienced phlebotomist (lab technician). The total amount of blood we need is small (10-40ml).

Confidentiality – who will have access to the data?

ParkC complies with the requirements of the National Health and Medical Research Council (NHMRC) guidelines with regard to collection, storage, processing, and disclosure of personal information and is committed to upholding the Act's core data protection principles. All information that is collected about you during the course of the research will be kept strictly confidential. Some of your data may include personal information such as your name, date of birth and/or a reference number. This information will be held in secure, locked filing cabinets at ParkC, or on a password protected computer database held on a secure system, which allows access to authorized individuals only. On completion of the study, all data will be stored for a period of 5 years before being destroyed by secure shredding facilities and permanent deletion of video files.

The video files and data collected during Part 3 of the research may be used in future research projects conducted at ParkC which are in the same general area of research interest, if you agree. These data will only be accessed by research staff and individuals affiliated with ParkC, Curtin University.

Although the researchers at ParkC are not qualified to comment on the clinical implications of individual test performance, we are able to forward the results of your assessment to your treating specialist, with your

consent.

Do I have to take part?

Participation in this study is completely voluntary. We will describe the study and go through this information sheet with you. If you do decide to take part you will be given this information sheet to keep and will be asked to sign a consent form, of which you will get a copy. If you decide to take part you are still free to withdraw at any time and you do not need to give a reason. A decision to withdraw from this research will not affect the standard of care you receive and there will be no effect on your legal rights, medical care, or your relationship with the hospital or your doctors. You are also welcome to participate in other research projects conducted by ParkC if you decide to withdraw from this particular study.

If you do decide to withdraw, we will ask you whether you are happy for us to use the data that we might have already collected from you. If you are not happy for us to use any of the data collected from you, any data relating to your participation in this study will be destroyed.

Who is organising and funding the research?

ParkC was established by Edith Cowan University (ECU), donations from the McCusker Foundation, the Rotary Club of Morley, and donations from members of the public and Parkinson's community. ParkC is now being funded by Curtin University.

Who has approved the study?

This research has been approved by Curtin University's Human Research Ethics Committee, Edith Cowan University's Human Research Ethics Committee, Parkinson's Western Australia (PWA) Inc., Joondalup Health Campus Human Research Ethics Committee and the Sir Charles Gairdner Group Human Research Ethics Committee.

Who can I contact about this study?

If you have any questions about this study or would like more information, please contact either Miss Caitlin Timms or Dr Andrea Loftus on (08) 9266 3441 or email caitlin.timms@curtin.edu.au

What if there is a problem and I want to make a complaint?

This study has been approved by several institutions. If you have any concerns about the ethics or code of practice of the study, please contact:

- Curtin University Human Research Ethics Committee by telephoning (08) 9266 2784 or emailing hrec@curtin.edu.au. Alternatively you may write to the Office of Research and Development, Curtin University, GPO Box U1987, Perth WA 6845. OR
- Joondalup Health Campus Human Research Ethics Committee through the Executive Office on (08) 9400 9404. OR
- Executive Officer of the Sir Charles Gairdner Group Human Research Ethics Committee on (08) 9346 2999

Any complaint you make will be treated in confidence and investigated, and you will be informed of the outcome.

What will happen to the study results?

We will let you know the results of the study in our annual newsletter which will be posted via mail and on the ParkC website (www.ParkC.org.au). However, if you would like to know anything further please feel free to contact the research team at ParkC before then and we will be happy to share the findings with you.

The results of this study will also be communicated via presentations at National and International conferences as well as being written into manuscripts which will be submitted to peer-reviewed journals. All of your identifying features will be removed in such cases.

Do I get to keep a copy of the Information Sheet and Consent form?

You will be given a copy of this Information Sheet to keep. If you decide to take part in this research and sign the consent form, you will be given a copy of this signed consent form for your records also.



Signature

Dr Andrea Loftus
Director, Parkinson's Centre (ParkC)
Curtin University
Phone: (08) 9266 2308
Fax: (08) 9266 2464
Email: andrea.loftus@curtin.edu.au



Caitlin Timms
Research Assistant, Parkinson's Centre (ParkC)
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Supplementary Material C

Participant Consent Form



Curtin University

**School of Psychology and
Speech Pathology**

Parkinson's Centre
Attn: Dr Andrea Loftus
GPO Box U1987
Perth Western Australia 6845

Telephone +61 8 9288 3441
Facsimile +61 8 9288 2464
Email caitlin.timms@curtin.edu.au

CONSENT FORM

**Project titled: COGNITIVE AND MOTOR HETEROGENEITY
IN IDIOPATHIC PARKINSON'S DISEASE.**

Please tick box

- 1. I have read and understood the 'Information Sheet' for this study.
- 2. The nature and the possible effects of this study have been explained to me.
- 3. Any questions that I have asked have been answered to my satisfaction
- 4. I understand that this research involves a number of computer and paper-based tasks.
- 5. I understand that the UPDRS, a standardised assessment of the motor symptoms of Parkinson's will be administered and that this assessment involves a number of simple motor tasks, an assessment of balance, and various observations of speech, tremor, rigidity, and posture.
- 6. I understand that I will be videotaped undertaking the assessment of motor (i.e. balance, walking, tremor, rigidity) symptoms. I consent for:
 - a. The video files of my UPDRS assessment to only be used in this study for the purposes of confirming my diagnosis of Parkinson's and that the recording will be deleted upon completion of the study.
 - b. The video file of my UPDRS assessment to be used in future approved research projects conducted at ParkC which are in the same general area of Parkinson's research.
- 7. I consent to my results being released to my treating physician/neurologist if requested.
- 8. I understand that all research data will be securely stored at ParkC, Curtin University, for a minimum period of five years following the study end date. I also understand that the data will be securely stored on password protected computers and locked cabinets at ParkC until no longer required, at which time it will be destroyed.
- 9. I understand that there are no foreseeable risks associated with this research, aside from the possibility of fatigue and minimal risk of falls associated with the balance assessment conducted in Part 3 of the research.

Parkinson's Centre (ParkC), Curtin University. (2008, Amended, 2010, 2011, 2012, 2013)



- 10. I agree that research data for the study may be published and that I will not be identified as a participant.
- 11. I understand that my identity will be kept confidential and that any information I supply to the researchers will be used only for the purposes of this research and/or research in the same general area.
- 12. I agree to participate in this investigation and understand that I may withdraw at anytime without giving a reason, and without my medical care or legal rights being affected. I also understand that if I so wish, I may request that any personal data gathered be withdrawn from the research.
- 13. I agree to donate a sample of blood for research purposes. I understand that this sample will be used for the purpose of genetic tests. I consent for:
 - a. My blood samples to only be used in this study and that they will be destroyed at the completion of the study
 - b. My blood sample to be used as explained so far and for any other analysis that may arise during the course of the study.
 - c. My blood samples to be held for future studies that may or may not be related to Parkinson's but that have received ethics approval from a recognised institution.
 - d. ParkC to inform my treating physician if a mutation in a known familial PD gene is found
- 14. I consent for a friend/relative to provide information about me in the Cambridge Behavioural Inventory.

Name of Participant _____

Signature of Participant _____ Date _____

For the Investigator

I have explained this project and the implications of participation to this volunteer and believe that the consent is informed and that he/she understands the implications of participation.

Name of Investigator _____

Signature of Investigator _____ Date _____

Parkinson's Centre (ParkC), Curtin University. (2008, Amended, 2010, 2011, 2012, 2013)





Curtin University

School of Psychology and
Speech Pathology

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CONSENT FORM

Project titled: COGNITIVE AND MOTOR HETEROGENEITY
IN IDIOPATHIC PARKINSON'S DISEASE.

ParkC is happy to share clinically appropriate test results with the doctor who treats your Parkinson's, should this be helpful for your care. This also streamlines assessment of your Parkinson's. If your treating doctor contacts us, do you consent to your assessment results being forwarded to them?

Please circle:

I DO / DO NOT consent to the release of my results to my treating doctor.

A very small percentage of people with Parkinson's go on to develop cognitive problems (i.e. thinking and memory), including dementia. Our Human Research Ethics Committee prefers that we ask you, in advance, for permission to approach you regarding follow-up assessment in the event of cognitive decline at some stage in the future. This does not affect your right to change your mind.

Please circle:

I WOULD/ WOULD NOT like to be assessed as part of the follow-up of this study.

I WOULD/ WOULD NOT like to be contacted about other research projects.

Name of Participant_____

Signature of Participant_____ Date_____

For the Investigator

I have explained this project and the implications of participation to this volunteer and believe that the consent is informed and that he/she understands the implications of participation.

Name of Investigator_____

Signature of Investigator_____ Date_____

Parkinson's Centre (ParkC), Curtin University. (2008, Amended, 2010, 2011, 2012, 2013)



Supplementary Material D

United Kingdom Brain Bank Criteria

UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria

(Hughes AJ et al. J Neurol Neurosurg Psychiatry 1992;55:181-4)

Inclusion criteria	Exclusion criteria	Supportive criteria
Bradykinesia (slowness of initiation of voluntary movement with progressive reduction in speed and amplitude of repetitive actions)	History of repeated strokes with stepwise progression of parkinsonian features	(Three or more required for diagnosis of definite PD)
And at least one of the following:		
Muscular rigidity	Neuroleptic treatment at onset of symptoms	Persistent asymmetry affecting side of onset most
4-6 Hz rest tremor	More than one affected relative	Excellent response (70-100%) to levodopa
Postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction	Sustained remission	Severe levodopa-induced chorea
	Strictly unilateral features after 3 yr	Levodopa response for 5 yr or more
	Supranuclear gaze palsy	Clinical course of 10 yr or more
	Cerebellar signs	
	Early severe autonomic involvement	
	Early severe dementia with disturbances of memory, language, and praxis	
	Babinski sign	
	Presence of cerebral tumour or communicating hydrocephalus on CT scan	
	Negative response to large doses of L-dopa (if malabsorption excluded)	
	MPTP exposure	

Supplementary Material E

Mini-Mental State Examination

FOLSTEIN MINI-MENTAL STATE

I. ORIENTATION (ask the following questions)		Response	Score
What is today's date?	Date (e.g. 21 st)		/3
What is the year?	Year		
What is the month?	Month		
What day of the week is it?	Day (e.g. Monday)		/1
What season is it?	Season		/1
What is the name of this Department/Institution?	2 points= ECU AND ParkC, 1 point= ECU/ ParkC/ Parkinson's/ School of Medical Sciences	Total	/5
What City/Suburb are we in?	City or suburb		/1
What State are we in?	State		/1
What Country are we in?	Country	Total	/5
II. IMMEDIATE RECALL		Response	Score
I am going to say some words to you (pause), listen carefully (pause), and then repeat them back to me. So, I say the words (pause) and then you say them.	"Ball" "Flag" "Tree" Number of trials _____	Total	/3
BALL (pause) FLAG (pause) TREE (pause).			
III. ATTENTION / CALCULATION		Response ✓	Response ✓
I've got some mental arithmetic for you. Starting with 100 take away 7(pause). Take away 7 from that number (pause), now take away 7 from that number (pause) and again (pause) and again (pause). Continue for 5 subtractions. Spell the word "WORLD" backwards (pause), as in the world that we live in.	93 86 79 72 65	D L R O W Total /5	Total /5
IV. RECALL		Response	Score
I asked you to repeat some words earlier. What were they? Score 0 - 3.	"Ball" "Flag" "Tree"	Total	/3
V. LANGUAGE		Response	Score
What is this called? Show analogue wrist watch. And this? Show a pencil.	Watch Pencil		/1 /1
I'm going to say a short sentence to you. It's an unusual one. Listen carefully and then repeat it after me (pause). So I say the sentence and then you say it (pause). "No ifs (pause) ands (pause) or buts".	Repetition		/1
"Take this piece of paper in your right hand (pause), Fold it in half (pause), and place it on your knee".	Right hand Folds in half Paper on knee		/1 /1 /1
Please write a sentence (pause). Write anything you like as long as it makes sense. It doesn't have to be long.	Writes sentence		/1
Copy this picture (pause). It doesn't have to be a work of art, just get all the corners in.	Draws pentagons		/1
Read this and do as it says.. If necessary add: <i>do as it says.</i>	Reading command		/1
TOTAL SCORE (maximum score is 30)	Serial 7s	WORLD bk	/9

Supplementary Material F

Unified Parkinson's Disease Rating Scale – Parts II & III

Rate what you see. In situations where it is impossible to test use the notation "UR" for unable to rate.

- Rate performance by taking co morbid conditions into account.
- No half or missing ratings.
- If one limb is slightly poorer than the other, but not enough to warrant a higher score, mark with a + & - to signify a difference. Score the same in the database.

1.1 SPEECH		SCORE
Instructions:		
<ul style="list-style-type: none"> • On greeting the participant, listen to their free flowing speech while you engage in conversation (e.g., ask how the participant got to the testing venue, their work, hobbies, the weather etc). • Evaluate volume, rhythm, clarity/slurring including rapid speech. 		
0: Normal	No speech problems.	
1: Slight:	Loss of rhythm and/or volume, all words are easy to understand.	
2: Mild:	Loss of rhythm, and/or volume, few words are unclear, but the overall sentences are easy to follow.	<input type="checkbox"/>
3: Moderate:	Speech is difficult to understand; some but not all sentences are poorly understood.	
4: Severe:	Most speech is difficult to understand or unintelligible.	

1.2 FACIAL EXPRESSION		SCORE
Script: "I would like you to look into the camera for about 10 seconds. Just sit as you would normally without talking."		
Instructions:		
<ul style="list-style-type: none"> • Also observe the participant when talking after this 10 second period. • Evaluate: eye-blink frequency, masked or loss of facial expression (particularly evident around mouth and cheeks), and amount of spontaneous smiling and parting of the lips. 		
0: Normal	Normal facial expression.	
1: Slight:	Minimal loss of facial expression, decreased eye-blink frequency only.	
2: Mild:	Decreased eye-blink frequency PLUS loss of facial expression in the lower face e.g., fewer mouth movements, less spontaneous smiling, lips NOT parted.	<input type="checkbox"/>
3: Moderate:	Loss of facial expression PLUS lips parted SOME of the time at rest.	
4: Severe:	Loss of facial expression PLUS lips parted MOST of the time at rest.	

1.3 RIGIDITY		SCORE															
Script: You may ask the participant if they experience rigidity as part of your assessment. Some participants find it difficult to relax and not to assist the movement. Distract the participant by talking to them during the assessment and be quite vigorous during your assessment.		<input type="checkbox"/> Neck															
Make sure participant is in a sitting position. "I'm going to look for rigidity in your neck, arms, and legs. I need you to relax as much as possible."		<input type="checkbox"/> Right Upper Extremity															
Make sure the person has no injury/arthritis affecting the neck and upper/lower extremities.		<input type="checkbox"/> Left Upper Extremity															
"Firstly, I would like you to relax your neck and I am going to gently move your head from side to side."		<input type="checkbox"/> Right Lower Extremity															
"Now I am going to move your arms, one at a time, like this (demonstrate). Please remain as relaxed as you try not to assist the movement". Move arm towards participant, side to side and in a circular motion also. Assess both limbs and perform Action Manuver if no rigidity is detected. Action manuver may include asking the participant to wave their arm in the air. If testing the right arm/leg perform action maneuver in the left arm/leg and vice versa.		<input type="checkbox"/> Left Lower Extremity															
ACTION MANUVER: "I didn't feel any rigidity there, so I would like you to tap your fingers (opposite hand) like this (demonstrate)". Tap your index finger and thumb together as fast and as big as possible. OR "wave your arm in the air".																	
Rate other arm.																	
"Now I am going to look for rigidity in your legs. I need you to relax as much as possible, and again, try not to assist the movement". Test the hip and knee joints simultaneously (while the participant is sitting, gently lift leg and pull leg inward at the knee joint).																	
ACTION MANUVER: "I didn't feel any rigidity there, so I would like you to tap your toes (opposite limb) on the ground like this (demonstrate)". Keep your heel on the ground and tap your toes as fast and high as you can.																	
Rate other leg.																	
<table> <tr> <td>0: Normal</td> <td>No rigidity.</td> <td></td> </tr> <tr> <td>1: Slight:</td> <td>Rigidity only detected with action maneuver.</td> <td></td> </tr> <tr> <td>2: Mild:</td> <td>Rigidity detected without action maneuver, full range of motion is easily achieved.</td> <td></td> </tr> <tr> <td>3: Moderate:</td> <td>Rigidity detected without action maneuver, full range of motion achieved with effort.</td> <td></td> </tr> <tr> <td>4: Severe:</td> <td>Rigidity detected without action maneuver, full range of motion not achieved.</td> <td></td> </tr> </table>			0: Normal	No rigidity.		1: Slight:	Rigidity only detected with action maneuver.		2: Mild:	Rigidity detected without action maneuver, full range of motion is easily achieved .		3: Moderate:	Rigidity detected without action maneuver, full range of motion achieved with effort .		4: Severe:	Rigidity detected without action maneuver, full range of motion not achieved.	
0: Normal	No rigidity.																
1: Slight:	Rigidity only detected with action maneuver.																
2: Mild:	Rigidity detected without action maneuver, full range of motion is easily achieved .																
3: Moderate:	Rigidity detected without action maneuver, full range of motion achieved with effort .																
4: Severe:	Rigidity detected without action maneuver, full range of motion not achieved.																

1.4 FINGER TAPPING		SCORE
<p>Script: "I'll demonstrate what I would like you to do first, then I'll ask you to do it. I would like you to move your index finger and thumb together like this (demonstrate) about 10 or so times (pause) as big and as fast as you can. I'll tell you when to stop".</p> <p>"Ok"</p> <p>If the participant is making very small movements to begin with, ask them to start again and to make the movement bigger. "Big movements....nice and quickly". If the participant still fails to make a large movement, demonstrate by physically separating their fingers yourself.</p> <p>Repeat with other hand.</p> <ul style="list-style-type: none"> • Evaluate: SPEED, AMPLITUDE, AMPLITUDE DECREMENTS HESITATIONS/HALTS 		
0: Normal No problems.		
1: Slight: Any of the following: <ul style="list-style-type: none"> • Regular rhythm is broken with 1 or 2 interruptions. • Slight slowing. • Amplitude decrements near End of 10 taps. 		<input type="checkbox"/> Right Hand
2: Mild: Any of the following: <ul style="list-style-type: none"> • 3-5 interruptions. • Mild slowing. • Amplitude decrements Midway in the 10-taps. 		<input type="checkbox"/> Left Hand
3: Moderate: Any of the following: <ul style="list-style-type: none"> • More than 5 interruptions OR at least 1 long freeze in taps. • Moderate slowing. • Amplitude decrements After 1st tap. 		
4: Severe: Cannot or can only barely perform the tap because of any of the following throughout the 10 taps: <ul style="list-style-type: none"> • Slowing • Interruptions • Amplitude decrements. 		

1.5 HAND MOVEMENTS		SCORE
<p>Script: "Now I would like you to clench your fist like this (demonstrate, make a tight fist with your arm bent at the elbow, palm outward facing, open and close hand) and open and close your hand about 10 or so times, as big and as fast as you can. I'll tell you when to stop".</p>		
<p>"Ok"</p>		
<p>Repeat with other hand.</p> <ul style="list-style-type: none"> • If the participant fails to make a tight fist or open the hand fully, remind them. • Evaluate: SPEED, AMPLITUDE, AMPLITUDE DECREMENTS HESITATIONS/HALTS 		
0: Normal	No problems.	
1: Slight:	<p>Any of the following:</p> <ul style="list-style-type: none"> • Regular rhythm is broken with 1 or 2 interruptions. • Slight slowing. • Amplitude decrements near End of the sequence. 	<input type="checkbox"/> Right Hand
2: Mild:	<p>Any of the following:</p> <ul style="list-style-type: none"> • 3-5 interruptions. • Mild slowing. • Amplitude decrements Midway in the sequence. 	<input type="checkbox"/> Left Hand
3: Moderate:	<p>Any of the following:</p> <ul style="list-style-type: none"> • More than 5 interruptions OR at least 1 long freeze in taps. • Moderate slowing. • Amplitude decrements After 1st open-close sequence. 	
4: Severe:	<p>Cannot or can only barely perform the tap because of any of the following throughout the sequence:</p> <ul style="list-style-type: none"> • Slowing • Interruptions • Amplitude decrements. 	

		SCORE
1.6 PRONATION-SUPINATION		
Script: "Now I would like you to hold your arm out like this (demonstrate: extend arm out in front of body, palm down) and turn you palm over and back about 10 or so times as fast and as fully as you can. I'll tell you when to stop".		
"Ok".		
Prompt the participant if they are not performing the movement 'fully'. Assess what is a full range of movement as assess accordingly (e.g., full range of movement may not be achieved due to previous injury, arthritis etc).		
Repeat with other arm.		
Instructions:		
<ul style="list-style-type: none"> • Rate each hand separately, demonstrate task but not while participant is being tested. • Instruct participant to extend the arm out in front of their body with palms down. • Instruct participant to turn the palm up and down alternately 10 times as Fast and as Fully and as possible. • Evaluate: SPEED, AMPLITUDE, AMPLITUDE DECREMENTS HESITATIONS/HALTS 		
0: Normal	No problems.	
1: Slight:	Any of the following: <ul style="list-style-type: none"> • Regular rhythm is broken with 1 or 2 interruptions. • Slight slowing. • Amplitude decrements near End of the sequence. 	<input type="checkbox"/> Right Hand
2: Mild:	Any of the following: <ul style="list-style-type: none"> • 3-5 interruptions. • Mild slowing. • Amplitude decrements Midway in the sequence. 	<input type="checkbox"/> Left Hand
3: Moderate:	Any of the following: <ul style="list-style-type: none"> • More than 5 interruptions OR at least 1 long freeze in taps. • Moderate slowing. • Amplitude decrements After 1st pronation-supination sequence. 	
4: Severe:	Cannot or can only barely perform the action because of any of the following throughout the sequence: <ul style="list-style-type: none"> • Slowing • Interruptions • Amplitude decrements. 	

1.7 TOE TAPPING (Observe lower extremity tremor for 1.17. Ask participant to remove their socks and shoes if they have a splint. Use your own discretion).		SCORE
<p>Script: "If it is ok with you, I would like you to remove your shoes and socks". If the participant has difficulty or it is not appropriate to do so, rate resting tremor 1.17 UR.</p> <p>"Please sit with your feet flat on the floor". Participant may need to sit forward in the chair to do so. "With your heel on the floor, tap your toes 10 or so times, as big and as fast as you can. I'll tell you when to stop"</p> <p>(Demonstrate)</p> <p>"Ok".</p> <p>Repeat with other foot.</p> <ul style="list-style-type: none"> • Evaluate: SPEED, AMPLITUDE, AMPLITUDE DECREMENTS HESITATIONS/HALTS 		
0: Normal	No problems.	
1: Slight:	Any of the following: <ul style="list-style-type: none"> • Regular rhythm is broken with 1 or 2 interruptions. • Slight slowing. • Amplitude decrements near End of 10 taps. 	<input type="checkbox"/> Right Foot
2: Mild:	Any of the following: <ul style="list-style-type: none"> • 3-5 interruptions. • Mild slowing. • Amplitude decrements Midway in the 10 taps. 	<input type="checkbox"/> Left Foot
3: Moderate:	Any of the following: <ul style="list-style-type: none"> • More than 5 interruptions OR at least 1 long freeze in taps. • Moderate slowing. • Amplitude decrements After 1st toe tap. 	
4: Severe:	Cannot or can only barely perform the tap because of any of the following throughout the task:	
	<ul style="list-style-type: none"> • Slowing • Interruptions • Amplitude decrements. 	

1.8 LEG AGILITY		SCORE
Script: "This task is looking at movement at the hip and thigh and requires a big movement".		
"Please sit with your feet flat on the floor". Participant may need to sit forward in the chair to do so.		
"I would like you to raise and stomp your foot on the ground 10 times, as high and as fast as you can".		
Demonstrate		
"Ok"		
Repeat with other foot		
<hr/> <ul style="list-style-type: none"> • Evaluate: SPEED, AMPLITUDE, AMPLITUDE DECREMENTS HESITATIONS/HALTS <hr/>		
0: Normal	No problems.	
1: Slight:	Any of the following: <ul style="list-style-type: none"> • Regular rhythm is broken with 1 or 2 interruptions. • Slight slowing. • Amplitude decrements near End of 10 stomps. 	<input type="checkbox"/> Right Leg
2: Mild:	Any of the following: <ul style="list-style-type: none"> • 3-5 interruptions. • Mild slowing. • Amplitude decrements Midway in the 10 stomps 	<input type="checkbox"/> Left Leg
3: Moderate:	Any of the following: <ul style="list-style-type: none"> • More than 5 interruptions OR at least 1 long freeze in stomps • Moderate slowing. • Amplitude decrements After 1st stomp. 	
4: Severe:	Cannot or can only barely perform the tap because of any of the following throughout the task: <ul style="list-style-type: none"> • Slowing • Interruptions • Amplitude decrements. 	

1.9 CHAIR RISE (Observe posture for section 1.13) Script: "For this task I would like you to cross your hands over your chest like this (demonstrate) and then get up out of your chair."		SCORE														
<p>Make sure the participant is sitting in a straight-back chair, with both feet on the floor and sitting back in the chair. You may need a different size chair for some participants.</p> <p>"Ok".</p> <p>"And sit back down".</p> <ul style="list-style-type: none"> • If participant is not successful, repeat this attempt max 2 more times. • If still unsuccessful, allow participant to move forward in the chair and arise with arms across chest. Only 1 attempt. • If unsuccessful, allow participant to rise by pushing off the chairs arms, max 3 times. • If still not successful EITHER assist patient to arise, or evaluate accordingly. <table> <tr> <td>0: Normal</td> <td>No problems.</td> <td></td> </tr> <tr> <td>1: Slight:</td> <td>Chair rise is slower than normal (could be normal for an older adult) OR: <ul style="list-style-type: none"> • Need more than one attempt. • Need to move forward on the chair to arise but Does Not use the arms of the chair. </td> <td><input type="checkbox"/></td> </tr> <tr> <td>2: Mild:</td> <td>Pushes self up from the arms of the chair without difficulty.</td> <td><input type="checkbox"/></td> </tr> <tr> <td>3: Moderate:</td> <td>Needs to push off, but tends to fall back OR <ul style="list-style-type: none"> • Needs more than one attempt arise using arms of the chair. • Can arise from the chair without assistance. </td> <td><input type="checkbox"/></td> </tr> <tr> <td>4: Severe:</td> <td>Unable to arise without help.</td> <td><input type="checkbox"/></td> </tr> </table>	0: Normal	No problems.		1: Slight:	Chair rise is slower than normal (could be normal for an older adult) OR: <ul style="list-style-type: none"> • Need more than one attempt. • Need to move forward on the chair to arise but Does Not use the arms of the chair. 	<input type="checkbox"/>	2: Mild:	Pushes self up from the arms of the chair without difficulty.	<input type="checkbox"/>	3: Moderate:	Needs to push off, but tends to fall back OR <ul style="list-style-type: none"> • Needs more than one attempt arise using arms of the chair. • Can arise from the chair without assistance. 	<input type="checkbox"/>	4: Severe:	Unable to arise without help.	<input type="checkbox"/>	
0: Normal	No problems.															
1: Slight:	Chair rise is slower than normal (could be normal for an older adult) OR: <ul style="list-style-type: none"> • Need more than one attempt. • Need to move forward on the chair to arise but Does Not use the arms of the chair. 	<input type="checkbox"/>														
2: Mild:	Pushes self up from the arms of the chair without difficulty.	<input type="checkbox"/>														
3: Moderate:	Needs to push off, but tends to fall back OR <ul style="list-style-type: none"> • Needs more than one attempt arise using arms of the chair. • Can arise from the chair without assistance. 	<input type="checkbox"/>														
4: Severe:	Unable to arise without help.	<input type="checkbox"/>														

<p>1.10 GAIT (Observe 'freezing' for section 1.10 AND posture for section 1.13) Script: "Now I would like you to go for a short walk. I want you to walk to the end of the corridor (at least 10 meters away), turn, and walk back.</p> <ul style="list-style-type: none"> Evaluate: STRIDE AMPLITUDE, STRIDE SPEED, HEIGHT OF FOOT LIFT, HEEL STRIKE, TURNING, AND ARM SWING. Typically, look for short shuffling steps, walking speed, and difficulty turning. Assess both sides. If the participant cannot walk unassisted, take the participants word for this and assess accordingly. DO NOT assist participant to walk. 	SCORE
<p>0: Normal No problems.</p> <p>1: Slight: Independent walking with minor gait impairment.</p> <p>2: Mild: Independent walking with substantial gait impairment.</p> <p>3: Moderate: Requires an assistance device for safe walking (walking stick, walker) but not a person.</p> <p>4: Severe: Cannot walk at all or only with a person's assistance. <small>(take participants word and rate accordingly. DO NOT assist participant to walk.)</small></p>	<input type="text"/>
<p>1.11 FREEZING OF GAIT (Ratings made from section 1.10)</p> <p>Instructions:</p> <ul style="list-style-type: none"> While assessing gait, also assess for the presence of freezing. Observe for START HESITATIONS, STUTTERING MOVEMENTS especially when turning and reaching the end of the task. Instruct participant not to use any sensory cues during the assessment if safe to do so. 	SCORE
<p>0: Normal No Freezing</p> <p>1: Slight: Freezes on starting, turning or walking through doorway with a single halt, then continues smoothly without freezing during straight walking.</p> <p>2: Mild: Freezes on starting, turning or walking through doorway with more than one halt, then continues smoothly without freezing during straight walking.</p> <p>3: Moderate: Freezes Once during straight walking.</p> <p>4: Severe: Freezes Multiple times during straight walking.</p>	<input type="text"/>

1.12 POSTURAL STABILITY DO NOT attempt this section if participant uses a walker or is not mobile.	SCORE
<p>Make sure that there is a solid wall at least 1-2 meters behind the examiner.</p> <p>Script: "I want you to stand facing the wall and I am going to stand behind you and pull on your shoulders to get you a little off balance. You may need to take a couple of steps backwards to avoid falling and that's ok. I will be right behind you to catch you if you fall".</p> <p>"You will feel my hands on your shoulders and I'm going to give you a little pull first as a practice run". The first pull is milder and not rated.</p> <p>"I'm going to pull on your shoulders a bit harder this time. Don't worry, I will be right behind you to make sure you don't fall."</p> <p>Place your hands on the participants shoulders THEN pull the shoulders briskly and forcefully towards the examiner with enough force to displace the center of gravity so the participant must take a step backwards.</p> <p>Be prepared to catch the participant, but stand back to allow room for the participant to take a number of recovery steps if needed.</p> <p>Observe the number of steps.</p> <p>Repeat if the participant misunderstands the task or was not prepared.</p> <hr/> <p>0: Normal No problems: recovers with 1 or 2 steps.</p> <p>1: Slight: 3-5 steps, but recovers unaided.</p> <p>2: Mild: More than 5 steps, but recovers unaided.</p> <p>3: Moderate: Stands safely, no postural response, will fall if not caught by examiner.</p> <p>4: Severe: Very unstable, tends to lose balance spontaneously or with just a gentle pull on the shoulders.</p>	<input type="checkbox"/>

1.13 POSTURE		SCORE
Script: "Please stand facing me" "now stand facing to the right" "and facing to the left".		
If you notice poor posture, ask the participant to stand up straight and see if posture improves.		
	<ul style="list-style-type: none"> • Rate the worst posture seen during the three observation points • Evaluate: STOOPING and SIDE TO SIDE LEANING. 	
0: Normal	No problems.	
1: Slight:	Not quite erect, posture could be normal for an older person.	
2: Mild:	Definite stooping or leaning to one side, but patient can correct posture when asked to do so.	<input type="checkbox"/>
3: Moderate:	Stooped posture, leaning to one side that cannot be corrected.	
4: Severe:	Stooping, leaning with extreme abnormality of posture	

1.14 GLOBAL SPONTANEITY OF MOVEMENT (BRADYKINESIA)		SCORE
(Based on overall observations of all sections)		
Instructions:		
<ul style="list-style-type: none">• This global rating includes all observations of slowness, hesitancy, small amplitude and poverty of movement in general.• Also includes reduction of gesturing and crossing of arms and legs.• Observe spontaneous gestures while sitting, chair rise, and walking.		
0: Normal	No problems.	
1: Slight:	Slight global slowness and poverty of movement.	
2: Mild:	Mild global slowness and poverty of movement.	<input type="checkbox"/>
3: Moderate:	Moderate global slowness and poverty of movement.	
4: Severe:	Severe global slowness and poverty of movement.	

TREMOR SUBSECTIONS

1.15 RESTING TREMOR OF THE HANDS		SCORE
Script: "Now I would like you to stretch your arms out in front of your body like this" (demonstrate: palms down). "your wrists should be straight and fingers comfortably separated." (demonstrate).		
Observe tremor for 10 seconds. Tremor must be rhythmical- do not rate dyskinesia.		
0: Normal	No tremor	
1: Slight:	Tremor is present but less than 1cm in amplitude. (slight and infrequently present)	<input type="checkbox"/> Right Hand
2: Mild:	Tremor is 1cm but <3cm in amplitude. (Mild amplitude and persistent OR moderate in amplitude and intermittently present)	<input type="checkbox"/> Left Hand
3: Moderate:	Tremor is 3cm but <10cm in amplitude. (Moderate in amplitude, present most of the time)	
4: Severe:	Tremor is at least 10cm in amplitude. (Marked in amplitude, present most of the time)	

1.16 KINETIC TREMOR OF THE HANDS Script: "I am going to put my finger out and I want you to touch the end of my finger and then touch your nose".		SCORE
Repeat with both hands.	Perform at least 3 finger-to nose maneuvers for each hand. Move your finger to different locations.	
Movements should be performed slowly as not to hide tremor occurring with fast movements.	Tremor can be present throughout the movement or when reaching the target (finger or nose).	<input type="checkbox"/> Right Hand <input type="checkbox"/> Left Hand

0: Normal No tremor

1: Slight: Tremor is present but **less than 1cm** in amplitude.
(slight and infrequently present)

2: Mild: Tremor is **1cm but <3cm** in amplitude.
(Mild amplitude and persistent OR moderate in amplitude and intermittently present)

3: Moderate: Tremor is **3cm but <10cm** in amplitude.
(Moderate in amplitude, present most of the time)

4: Severe: Tremor is at least 10cm in amplitude.
(Marked in amplitude, present most of the time)

1.17 REST TREMOR AMPLITUDE (Ratings based on section 1.15 for the hands, 1.7 and 1.8 for lower extremities, and 1.2 for tremor of the lip and jaw)		SCORE	
<p>Instructions:</p> <ul style="list-style-type: none"> Rest tremor may appear at any time during this assessment and you should base your ratings on your overall observations. Score the maximal amplitude that is seen at any time as the final score. Only rate the amplitude not persistence. If you need more information than that observed in the sections outlined above, ask the participant to sit quietly in a chair, both hands on the arms of the chair and feet comfortably on the floor. Observe for 10 seconds. 		<input type="checkbox"/> Right Upper Extremity	
Extremity Ratings			
0: Normal	No tremor	<input type="checkbox"/> Left Upper Extremity	
1: Slight:	< 1cm in maximum amplitude.		
2: Mild:	> 1cm but < 3cm in maximum amplitude.		
3: Moderate:	3-10 cm in maximum amplitude.		<input type="checkbox"/> Right Lower Extremity
4: Severe:	>10cm in maximum amplitude.		
Lip/Jaw Ratings			
0: Normal	No tremor		
1: Slight:	<1cm in maximum amplitude.	<input type="checkbox"/> Left Lower Extremity	
2: Mild:	> 1cm but <2cm in maximum amplitude.		
3: Moderate:	>2cm but <3cm in maximum amplitude.		
4: Severe:	> 3cm in maximum amplitude		

ADMINISTER PATIENT QUESTIONNAIRE WHILE YOU RATE REST TREMOR, CONSTANCY OF TREMOR, DYSKINESIA, AND HOEHN AND YAHR STAGE.

OFFER A BREAK BEFORE QUESTIONNAIRE.

Participant Questionnaire can be completed before motor complications (IV) if you need time to complete your ratings. Explain questionnaire to the participant and be available to answer questions.

1.18 CONSTANCY OF TREMOR		SCORE
Instructions:		
<ul style="list-style-type: none"> Evaluate the constancy of Resting tremor observed throughout the examination period when different body parts are at rest (i.e., sections 1.2, 1.7, 1.8, 1.15, 1.16). 		
0: Normal	No tremor	
1: Slight:	Tremor at rest is present <25% of the examination period.	
2: Mild:	Tremor at rest is present 26-50% of the examination period.	
3: Moderate:	Tremor at rest is present 51-75% of the examination period.	
4: Severe:	Tremor at rest is present > 75% of the examination period.	

DYSKINESIA IMPACT ON MOTOR RATINGS		
Dyskinesia= involuntary, random movements.		
A. Were dyskinesias present during the examination? NO <input type="checkbox"/> YES <input type="checkbox"/>		
B. If yes, did these movements interfere with your ratings? NO <input type="checkbox"/> YES <input type="checkbox"/>		

HOEHN AND Yahr Stage		
<p>These ratings are based on the overall scores for the UPDRS. Assess unilateral involvement by assessing severity of symptoms of the left and right upper and lower extremities.</p>		
0: Asymptomatic		
1: Unilateral involvement only		
2: Bilateral involvement without impaired balance.		
3: Mild to moderate involvement; some postural instability but physically independent. Needs assistance to recover from the pull test.		
4: Severe disability; still able to walk or stand unassisted.		
5: Wheelchair bound or bedridden unless aided.		

Supplementary Material G

Hopkins Verbal Learning Test - Revised**(HVLT-R) Score Sheet**

Participant ID _____ Date _____

FREE RECALL

	TRIAL 1	TRIAL 2	TRIAL 3
LION			
EMERALD			
HORSE			
TENT			
SAPPHIRE			
HOTEL			
CAVE			
OPAL			
TIGER			
PEARL			
COW			
HUT			
Number Correct			

DELAYED RECALL

Time interval: _____

	Trial 4
LION	
EMERALD	
HORSE	
TENT	
SAPPHIRE	
HOTEL	
CAVE	
OPAL	
TIGER	
PEARL	
COW	
HUT	
Number Correct	

Learning & Recall Scores	
Total Trials 1-3	____ (/36)
Learning Index	_____
Total Trial 4	____ (/12)
% Retained	_____

Recognition Scores	
Correct	____ (/12)
*False Positives Related	____ (/6)
False Positives Unrel'd	____ (/6)
Total False Positives	____ (/12)
Discrimination Index	_____
Bias Index	_____

DELAYED RECOGNITION

HORSE	ruby*	CAVE	balloon	coffee	LION
house*	OPAL	TIGER	boat	scarf	PEARL
HUT	EMERALD	SAPPHIRE	dog*	apartment*	penny
TENT	mountain	cat*	HOTEL	COW	diamond*

Supplementary Material H

ParkC Clinical Test Battery

Completed Prior to Session:

- Medical History and Demographic: Cognitive and Motor Heterogeneity and Idiopathic Parkinson's
- Meta-Memory Questionnaire (MMQ)
- Big Five Aspects Scale (BFAS)
- Cambridge Behavioural Inventory (CBI)
- Depression, Anxiety and Stress Scale (DASS)
- Ways of Coping Questionnaire (WAYS)
- The Geriatric Depression Scale (GDS)
- Parkinson's Disease Questionnaire (PDQ-39)
- Epworth Sleepiness Scale (ESS)
- Parkinson's Disease Sleep Scale- Revised (PDSS-R)
- UPDRS Part 2 - Activities of Daily Living Scale

Completed during session:

- Mini Mental State Examination (MMSE)
- Australian National Adult Reading Test (AUSNART)
- HVLT-R
- Line Bisection
- Star Cancellation
- Cube Analysis
- Number Location
- Verbal Fluency – Phonemic (FAS)
- Verbal Fluency – Semantic
- CANTAB
 - Spatial Working Memory
 - Spatial Recognition Memory
 - Pattern Recognition Memory
 - Stockings of Cambridge
- HVLT Awareness Question
- State-Trait Anxiety Inventory (STAI)
- Body Mass Index and Waist Circumference
- UPDRS Part 1 - Non-Motor and Motor Symptoms Patient Questionnaire
- UPDRS Part 3 - Motor Assessment
- UPDRS Part 4 – Motor Complications

Supplementary Material I

SPSS Statistical Output

Descriptive and Skewness and Kurtosis Statistics

Descriptive Statistics

Zscore Extreme Values

Extreme Values

		Case Number	Value
Zscore: Age.2: Age at participation in Cognitive Study	Highest 1	62	2.18006
	2	83	2.07167
	3	37	1.96327
	4	60	1.85487
	5	13	1.74648
	Lowest 1	2	-2.80614
	2	87	-2.58935
	3	66	-2.15577
	4	55	-1.93897
	5	23	-1.83058
Zscore: HVLTTot.2: HVLT total of 3 trials	Highest 1	34	1.89650
	2	58	1.74592
	3	87	1.74592
	4	91	1.74592
	5	8	1.44477 ^a
	Lowest 1	110	-2.16910
	2	21	-2.16910
	3	95	-2.01852
	4	63	-2.01852
	5	40	-2.01852
Zscore: SWMT8.2: CANTAB- SWM Total errors (8 boxes)	Highest 1	10	4.03160
	2	21	2.31013
	3	40	1.50003
	4	62	1.50003
	5	69	1.43252
	Lowest 1	112	-1.87540
	2	106	-1.87540
	3	67	-1.87540
	4	48	-1.87540
	5	37	-1.87540 ^b
Zscore: UPDRS Visit 1 Mean tremor score	Highest 1	114	2.53672
	2	84	2.17961
	3	105	2.17961
	4	70	2.00106
	5	85	2.00106 ^c
	Lowest 1	52	-1.21295
	2	48	-1.21295
	3	46	-1.21295
	4	45	-1.21295
	5	38	-1.21295 ^d
Zscore: UPDRS Visit 1 Mean PIGD score	Highest 1	25	4.10068
	2	21	3.45085
	3	26	3.12593
	4	29	2.47610
	5	22	2.15118 ^e
	Lowest 1	109	-1.09800
	2	108	-1.09800
	3	106	-1.09800
	4	98	-1.09800
	5	90	-1.09800 ^f

a. Only a partial list of cases with the value 1.44477 are shown in the table of upper extremes.

b. Only a partial list of cases with the value -1.87540 are shown in the table of lower extremes.

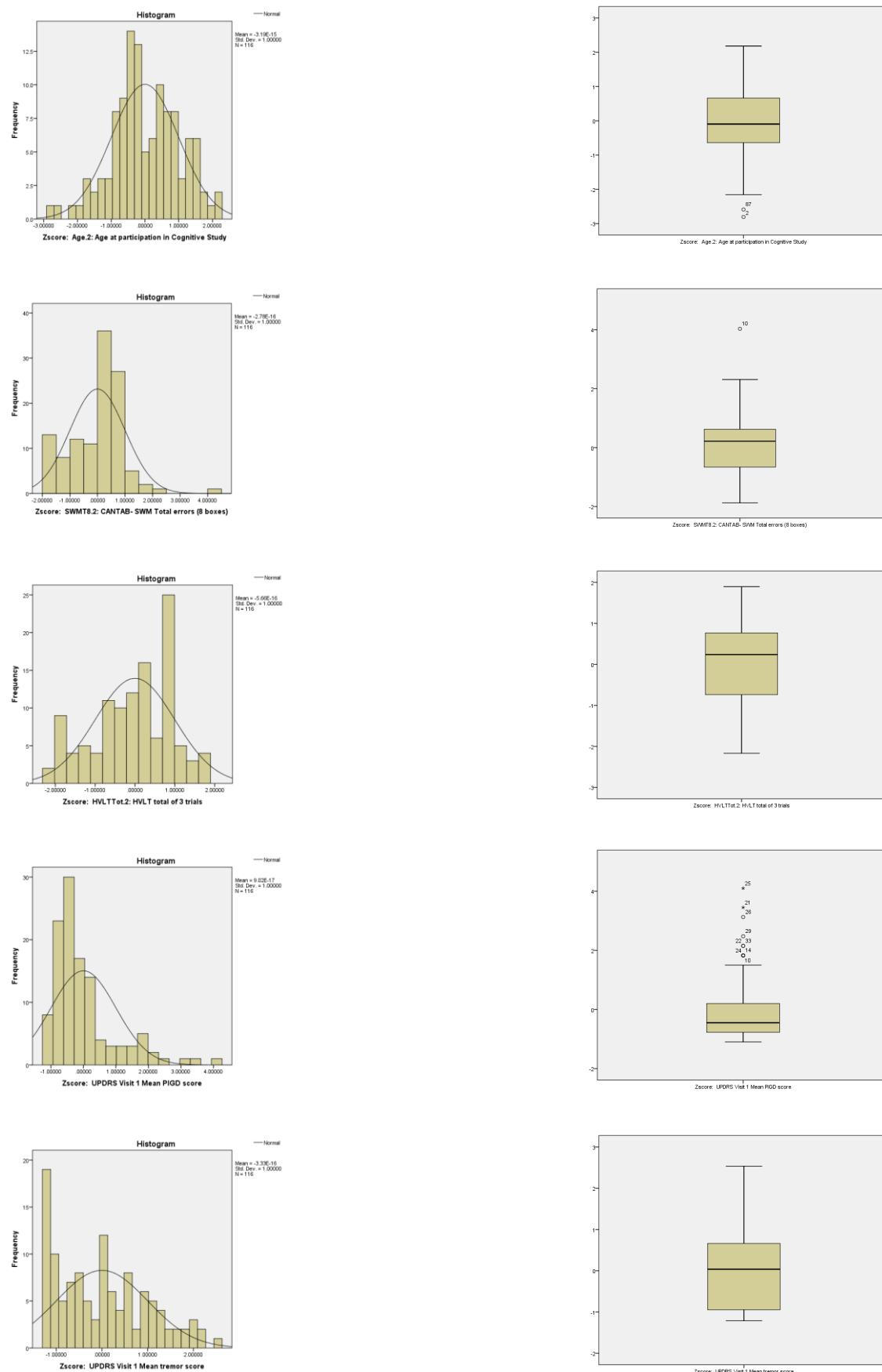
c. Only a partial list of cases with the value 2.00106 are shown in the table of upper extremes.

d. Only a partial list of cases with the value -1.21295 are shown in the table of lower extremes.

e. Only a partial list of cases with the value 2.15118 are shown in the table of upper extremes.

f. Only a partial list of cases with the value -1.09800 are shown in the table of lower extremes.

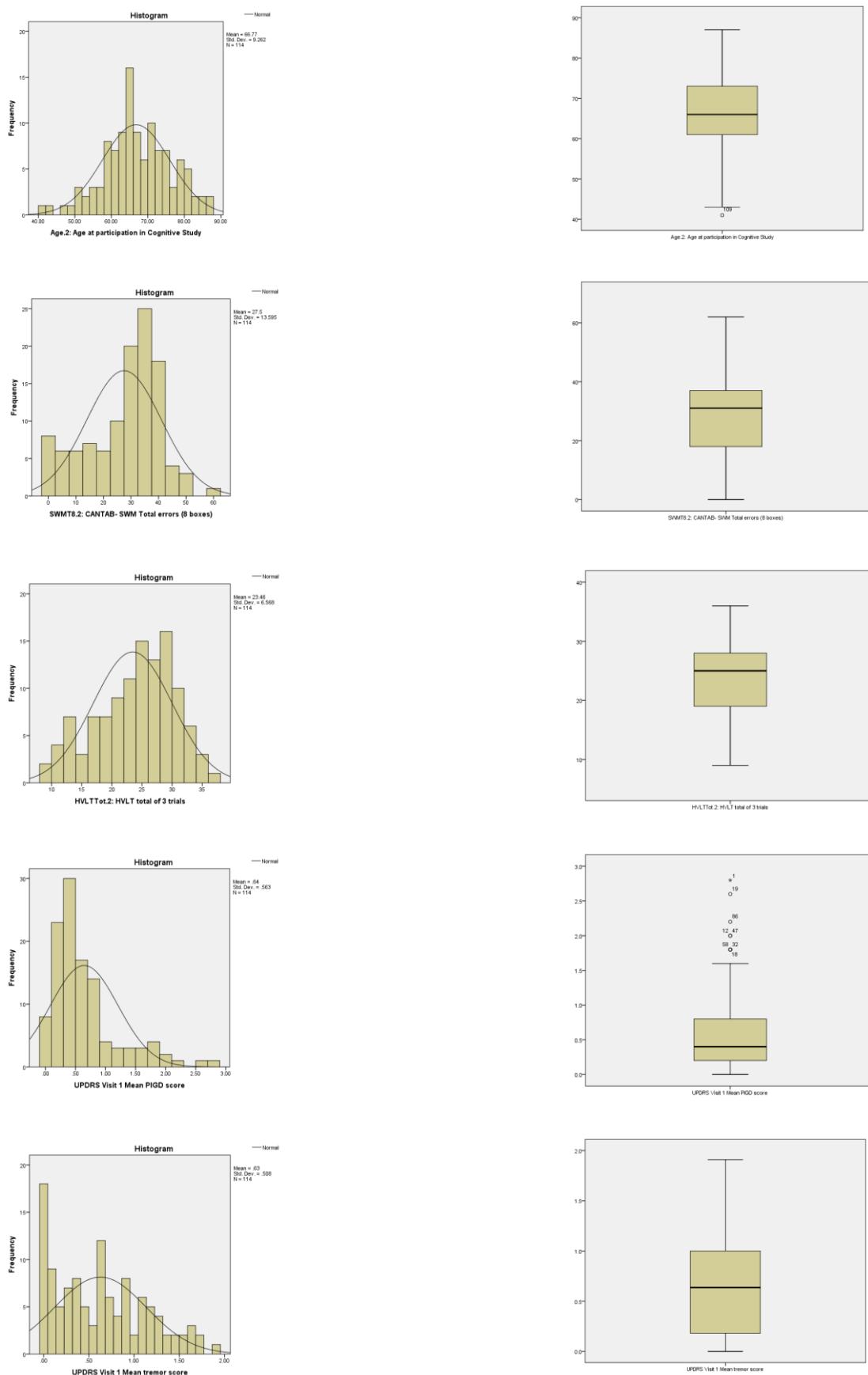
Zscore Frequency Histograms and Boxplots



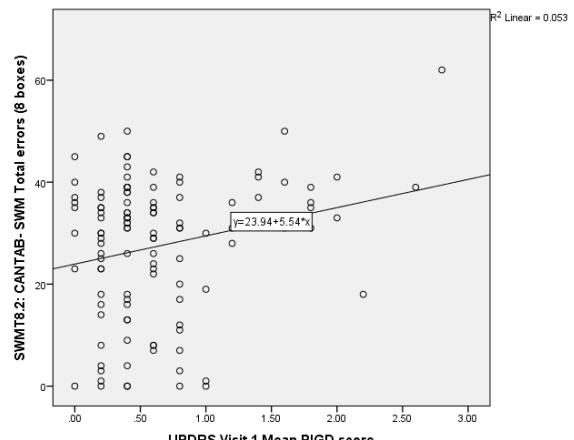
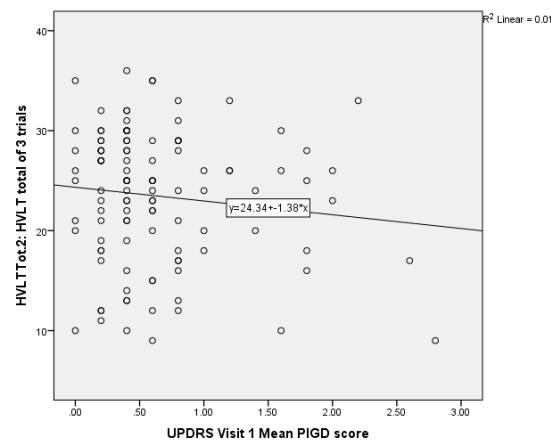
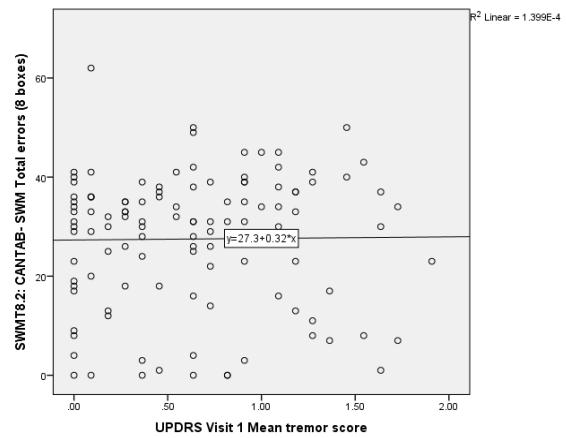
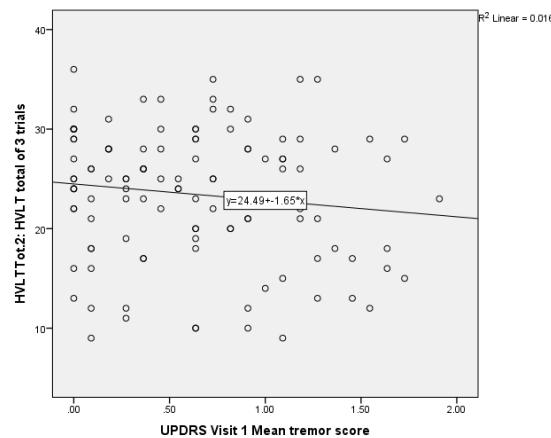
Descriptive Statistics Following Outlier Removal

Descriptives		
Sex	Mean	.1.27 .041
	95% Confidence Interval for Mean	Lower Bound 1.19 Upper Bound 1.35
	5% Trimmed Mean	1.24
	Median	1.00
	Variance	.198
	Std. Deviation	.444
	Minimum	1
	Maximum	2
	Range	1
	Interquartile Range	1
	Skewness	1.066 .225
	Kurtosis	-.880 .446
Age:2: Age at participation in Cognitive Study	Mean	66.8879 .85656
	95% Confidence Interval for Mean	Lower Bound 65.1912 Upper Bound 68.5846
	5% Trimmed Mean	67.0268
	Median	66.0000
	Variance	85.109
	Std. Deviation	9.22546
	Minimum	41.00
	Maximum	87.00
	Range	46.00
	Interquartile Range	12.00
	Skewness	-.183 .225
	Kurtosis	.000 .446
HVLTTot.2: HVLT total of 3 trials	Mean	23.41 .617
	95% Confidence Interval for Mean	Lower Bound 22.18 Upper Bound 24.63
	5% Trimmed Mean	23.54
	Median	25.00
	Variance	44.104
	Std. Deviation	6.641
	Minimum	9
	Maximum	36
	Range	27
	Interquartile Range	11
	Skewness	-.439 .225
	Kurtosis	-.583 .446
SWMT8 2: CANTAB- SWM Total errors (8 boxes)	Mean	27.78 1.375
	95% Confidence Interval for Mean	Lower Bound 25.06 Upper Bound 30.50
	5% Trimmed Mean	27.66
	Median	31.00
	Variance	219.423
	Std. Deviation	14.813
	Minimum	0
	Maximum	88
	Range	88
	Interquartile Range	19
	Skewness	.066 .225
	Kurtosis	1.393 .446
UPDRS Visit 1 Mean tremor score	Mean	.6176 .04727
	95% Confidence Interval for Mean	Lower Bound .5239 Upper Bound .7112
	5% Trimmed Mean	.5909
	Median	.6364
	Variance	.259
	Std. Deviation	.50914
	Minimum	.00
	Maximum	1.91
	Range	1.91
	Interquartile Range	.86
	Skewness	.528 .225
	Kurtosis	-.676 .446
UPDRS Visit 1 Mean PIGD score	Mean	.6759 .05715
	95% Confidence Interval for Mean	Lower Bound .5627 Upper Bound .7891
	5% Trimmed Mean	.6130
	Median	.4000
	Variance	.379
	Std. Deviation	.61554
	Minimum	.00
	Maximum	3.20
	Range	3.20
	Interquartile Range	.60
	Skewness	1.768 .225
	Kurtosis	3.334 .446
UPDRS Visit 1 - Tremor dominant ratio (Mean tremor/Mean PIGD)	Mean	1.4569 .04645
	95% Confidence Interval for Mean	Lower Bound 1.3649 Upper Bound 1.5489
	5% Trimmed Mean	1.4521
	Median	1.0000
	Variance	.250
	Std. Deviation	.50030
	Minimum	1.00
	Maximum	2.00
	Range	1.00
	Interquartile Range	1.00
	Skewness	.175 .225
	Kurtosis	-.2004 .446

Histograms and Boxplots Following Outlier Removal



Scatterplots of the Bivariate Relationship



Supplementary Material J

UPDRS Internal Consistency

PIGD Subscale

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.753	.759	5

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
UPDR2.12.1: UPDRS ADL- Q2.12 - Walking and Balance	2.35	4.885	.608	.395	.674
UPDR2.13.1: UPDRS ADL- Q2.13 - Freezing	2.74	4.780	.611	.426	.673
UPDR3.10.1: UPDRS Motor Assessment- Q3. 10 - Gait	2.21	5.230	.611	.395	.677
UPDR3.11.1: UPDRS Motor Assessment- Q3. 11 - Freezing of Gait	2.98	6.584	.421	.179	.747
UPDR3.12.1: UPDRS Motor Assessment- Q3. 12 - Postural Stability	2.60	5.446	.400	.166	.759

Inter-Item Correlation Matrix

	UPDR2.12.1: UPDRS ADL- Q2.12 - Walking and Balance	UPDR2.13.1: UPDRS ADL- Q2.13 - Freezing	UPDR3.10.1: UPDRS Motor Assessment- Q3.10 - Gait	UPDR3.11.1: UPDRS Motor Assessment- Q3.11 - Freezing of Gait	UPDR3.12.1: UPDRS Motor Assessment- Q3.12 - Postural Stability
UPDR2.12.1: UPDRS ADL- Q2.12 - Walking and Balance	1.000	.563	.505	.340	.326
UPDR2.13.1: UPDRS ADL- Q2.13 - Freezing	.563	1.000	.561	.318	.298
UPDR3.10.1: UPDRS Motor Assessment- Q3. 10 - Gait	.505	.561	1.000	.342	.330
UPDR3.11.1: UPDRS Motor Assessment- Q3. 11 - Freezing of Gait	.340	.318	.342	1.000	.278
UPDR3.12.1: UPDRS Motor Assessment- Q3. 12 - Postural Stability	.326	.298	.330	.278	1.000

TD Subscale

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.808	.811	11

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
UPDR2.10.1: UPDRS ADL- Q2.10 - Tremor	5.82	26.187	.408	.216	.800
UPD3.15a.1: UPDRS Motor Assessment- Q3. 15a - Resting Tremor of the Hands (Postural Tremor) - Right Hand	6.38	26.556	.546	.631	.787
UPD3.15b.1: UPDRS Motor Assessment- Q3. 15b - Resting Tremor of the Hands (Postural Tremor) - Left Hand	6.36	26.162	.558	.528	.785
UPD3.16a.1: UPDRS Motor Assessment- Q3. 16a - Kinetic Tremor of the Hands - Right Hand	6.37	27.474	.494	.515	.793
UPD3.16b.1: UPDRS Motor Assessment- Q3. 16b - Kinetic Tremor of the Hands - Left Hand	6.16	27.497	.375	.430	.801
UPD3.17a.1: UPDRS Motor Assessment- Q3. 17a - Rest Tremor Amplitude - Right Upper Extremity	6.12	24.445	.587	.695	.779
UPD3.17b.1: UPDRS Motor Assessment- Q3. 17b - Rest Tremor Amplitude - Left Upper Extremity	6.26	25.328	.533	.694	.786
UPD3.17c.1: UPDRS Motor Assessment- Q3. 17c - Rest Tremor Amplitude - Right Lower Extremity	6.75	29.023	.385	.304	.802
UPD3.17d.1: UPDRS Motor Assessment- Q3. 17d - Rest Tremor Amplitude - Left Lower Extremity	6.67	28.242	.384	.341	.801
UPD3.17e.1: UPDRS Motor Assessment- Q3. 17e - Lip/Jaw resting tremor amplitude	6.82	29.939	.282	.247	.808
UPD3.18.1: UPDRS Motor Assessment- Q3. 18 - Constancy of Rest	5.34	18.262	.758	.734	.763

Inter-Item Correlation Matrix														
	UPDRS 1.15a:1; UPDRS Motor Assessment-Q3.15a - Resting Tremor of the Hands (Postural Tremor) - Right Hand	UPDRS 1.15b:1; UPDRS Motor Assessment-Q3.15b - Resting Tremor of the Hands (Postural Tremor) - Left Hand	UPDRS 1.16a:1; UPDRS Motor Assessment-Q3.16a - Kinetic Tremor of the Hands - Right Hand	UPDRS 1.16b:1; UPDRS Motor Assessment-Q3.16b - Kinetic Tremor of the Hands - Left Hand	UPDRS 1.17a:1; UPDRS Motor Assessment-Q3.17a - Rest Tremor Amplitude - Right Upper Extremity	UPDRS 1.17b:1; UPDRS Motor Assessment-Q3.17b - Rest Tremor Amplitude - Left Upper Extremity	UPDRS 1.17c:1; UPDRS Motor Assessment-Q3.17c - Rest Tremor Amplitude - Right Lower Extremity	UPDRS 1.17d:1; UPDRS Motor Assessment-Q3.17d - Rest Tremor Amplitude - Left Lower Extremity	UPDRS 1.17e:1; UPDRS Motor Assessment-Q3.17e - Lip/Jaw resting tremor amplitude	UPDRS 1.18:1; UPDRS Motor Assessment-Q3.18 - Constancy of Rest	ADL-Q2.10 - Tremor	UPDRS 1.5a:1; UPDRS Motor Assessment-Q3.15a - Resting Tremor of the Hands (Postural Tremor) - Right Hand	UPDRS 1.5b:1; UPDRS Motor Assessment-Q3.15b - Resting Tremor of the Hands (Postural Tremor) - Left Hand	
UPDRS 2.10.1; UPDRS ADL-Q2.10 - Tremor	1.000	.307	.194	.194	.192	.331	.191	.239	.168	.227	.394			
	.307	1.000	.239	.565	.174	.721	.046	.321	.015	.190	.524			
	.194	.239	1.000	.317	.475	.179	.626	.198	.441	.111	.463			
	.194	.565	.317	1.000	.467	.506	.132	.245	.034	.025	.377			
	.192	.174	.475	.467	1.000	.087	.382	.-034	.213	.-045	.276			
	.331	.721	.179	.506	.087	.000	.143	.452	.098	.321	.623			
	.191	.046	.626	.132	.382	.-143	.1000	.110	.494	.223	.628			
	.239	.321	.198	.245	.-034	.452	.1000	.261	.278		.315			
	.168	.015	.441	.034	.213	.098	.494	.261	.1000	.217	.359			
	.227	.190	.111	.025	.-045	.321	.223	.278	.247	.1000	.202			
	.394	.524	.463	.377	.276	.623	.628	.315	.359	.202	.1000			

Supplementary Material K

MPlus Statistical Outputs

MPlus Output: Model 1

```
C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours\Thesis\Supps\MPlu...\\Model 1.out
_____
Mplus VERSION 7.2 DEMO
MUTHEN & MUTHEN

INPUT INSTRUCTIONS

TITLE: Stats

DATA:
FILE = "C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours
\Analysis\Database\Re-Mplus\SWM8_03.csv";

VARIABLE:
NAMES = Sex Age_2 HVTot_2 SWT8_2 TD_1 PIGD_1 SubG_1;
USEVARIABLES = SubG_1 HVTot_2 SWT8_2 Sex Age_2;
CATEGORICAL ARE Sex;

MODEL:
SWM BY SWT8_2@0.82;
SWT8_2@0.32;
VWM BY HVTot_2@0.86;
HVTot_2@0.26;
VWM SWM ON SubG_1;
VWM WITH SWM Sex Age_2;
SWM WITH Age_2;

OUTPUT: SAMPSTAT STDYX;

INPUT READING TERMINATED NORMALLY

Stats

SUMMARY OF ANALYSIS

Number of groups                               1
Number of observations                         114
Number of dependent variables                 4
Number of independent variables                1
Number of continuous latent variables          2

Observed dependent variables

Continuous
  HVTOT_2      SWT8_2      AGE_2
Binary and ordered categorical (ordinal)
  SEX

Observed independent variables

  SUBG_1

Continuous latent variables

  SWM          VWM

Estimator                                     WLSMV
Maximum number of iterations                  1000
Convergence criterion                         0.500D-04
Maximum number of steepest descent iterations 20
Parameterization                             DELTA
```

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Input data file(s)
 C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours\Analysis\Database\Re-Mplus\S
 Input data format FREE

UNIVARIATE PROPORTIONS AND COUNTS FOR CATEGORICAL VARIABLES

SEX			
Category 1	0.737	84.000	
Category 2	0.263	30.000	

SAMPLE STATISTICS

ESTIMATED SAMPLE STATISTICS

MEANS/INTERCEPTS/THRESHOLDS			
	HVTOT_2	SWT8_2	SEX\$1
1	21.467	26.499	1.375
			67.972

SLOPES	
	SUBG_1

HVTOT_2	1.374
SWT8_2	0.692
SEX	0.499
AGE_2	-0.829

CORRELATION MATRIX (WITH VARIANCES ON THE DIAGONAL)			
	HVTOT_2	SWT8_2	SEX
HVTOT_2	42.290		
SWT8_2	-0.289	183.096	
SEX	0.601	-0.063	
AGE_2	-0.482	0.395	-0.222
			84.865

THE MODEL ESTIMATION TERMINATED NORMALLY

MODEL FIT INFORMATION

Number of Free Parameters 13

Chi-Square Test of Model Fit

Value	7.853*
Degrees of Freedom	4
P-Value	0.0971

* The chi-square value for MLM, MLMV, MLR, ULSMV, WLSM and WLSMV cannot be used for chi-square difference testing in the regular way. MLM, MLR and WLSM chi-square difference testing is described on the Mplus website. MLMV, WLSMV, and ULSMV difference testing is done using the DIFFTEST option.

RMSEA (Root Mean Square Error Of Approximation)

Estimate	0.092
----------	-------

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90 Percent C.I.	0.000	0.187
Probability RMSEA <= .05	0.190	

CFI/TLI

CFI	0.931
TLI	0.827

Chi-Square Test of Model Fit for the Baseline Model

Value	65.573
Degrees of Freedom	10
P-Value	0.0000

WRMR (Weighted Root Mean Square Residual)

Value	0.684
-------	-------

MODEL RESULTS

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
SWM BY SWT8_2	0.820	0.000	999.000	999.000
VWM BY HVTOT_2	0.860	0.000	999.000	999.000
VWM ON SUBG_1	1.598	1.468	1.089	0.276
SWM ON SUBG_1	0.844	3.141	0.269	0.788
VWM WITH SWM	-36.082	11.752	-3.070	0.002
SEX	4.542	1.017	4.467	0.000
AGE_2	-33.568	7.114	-4.718	0.000
SWM WITH AGE_2	60.025	14.988	4.005	0.000
Means AGE_2	67.972	2.607	26.075	0.000
Intercepts HVTOT_2	21.467	1.835	11.698	0.000
SWT8_2	26.499	3.944	6.719	0.000
Thresholds SEXS1	1.375	0.406	3.385	0.001
Variances AGE_2	84.865	11.474	7.397	0.000
Residual Variances HVTOT_2	0.260	0.000	999.000	999.000
SWT8_2	0.320	0.000	999.000	999.000
SWM	271.826	44.343	6.130	0.000
VWM	56.827	9.469	6.002	0.000

STANDARDIZED MODEL RESULTS

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STDYX Standardization

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
SWM BY SWT8_2	0.999	0.000	7035.002	0.000
VWM BY HVTOT_2	0.997	0.001	1959.408	0.000
VWM ON SUBG_1	0.105	0.095	1.103	0.270
SWM ON SUBG_1	0.026	0.095	0.268	0.788
VWM WITH SWM	-0.290	0.073	-3.980	0.000
SEX	0.602	0.106	5.710	0.000
AGE_2	-0.483	0.063	-7.623	0.000
SWM WITH AGE_2	0.395	0.067	5.882	0.000
Means AGE_2	7.378	0.558	13.224	0.000
Intercepts HVTOT_2	3.283	0.409	8.034	0.000
SWT8_2	1.958	0.306	6.406	0.000
Thresholds SEX\$1	1.375	0.406	3.385	0.001
Variances AGE_2	1.000	0.000	999.000	999.000
Residual Variances HVTOT_2	0.006	0.001	5.993	0.000
SWT8_2	0.002	0.000	6.154	0.000
SWM	0.999	0.005	205.355	0.000
VWM	0.989	0.020	49.181	0.000

STDY Standardization

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
SWM BY SWT8_2	0.999	0.000	7035.002	0.000
VWM BY HVTOT_2	0.997	0.001	1959.408	0.000
VWM ON SUBG_1	0.211	0.191	1.106	0.269
SWM ON SUBG_1	0.051	0.191	0.268	0.788
VWM WITH SWM	-0.290	0.073	-3.980	0.000

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SEX	0.602	0.106	5.710	0.000
AGE_2	-0.483	0.063	-7.623	0.000
SWM WITH AGE_2	0.395	0.067	5.882	0.000
Means AGE_2	7.378	0.558	13.224	0.000
Intercepts HVTOT_2	3.283	0.409	8.034	0.000
SWT8_2	1.958	0.306	6.406	0.000
Thresholds SEXS1	1.375	0.406	3.385	0.001
Variances AGE_2	1.000	0.000	999.000	999.000
Residual Variances HVTOT_2	0.006	0.001	5.993	0.000
SWT8_2	0.002	0.000	6.154	0.000
SWM	0.999	0.005	205.355	0.000
VWM	0.989	0.020	49.181	0.000

R-SQUARE

Observed Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	Residual Variance
HVTOT_2	0.994	0.001	979.704	0.000	
SWT8_2	0.998	0.000	3517.501	0.000	
Latent Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	
SWM	0.001	0.005	0.134	0.893	
VWM	0.011	0.020	0.551	0.581	

QUALITY OF NUMERICAL RESULTS

Condition Number for the Information Matrix (ratio of smallest to largest eigenvalue) 0.596E-03

DIAGRAM INFORMATION

Use View Diagram under the Diagram menu in the Mplus Editor to view the diagram. If running Mplus from the Mplus Diagrammer, the diagram opens automatically.

Diagram output
c:\users\andrew johnson\dropbox\uni\y4s2\honours\analysis\results - initial\m1w2\subg.dgm

Beginning Time: 23:00:55
Ending Time: 23:00:55
Elapsed Time: 00:00:00

Mplus VERSION 7.2 DEMO has the following limitations:
Maximum number of dependent variables: 6
Maximum number of independent variables: 2
Maximum number of between variables: 2

MPlus Output: Model 2

```
C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours\Thesis\Supps\MPlu...\\Model 2.out
Mplus VERSION 7.2 DEMO
MUTHEN & MUTHEN

INPUT INSTRUCTIONS

TITLE: Model 2

DATA:
FILE = "C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours
\Analysis\DATABASES\Re-Mplus\SWM8_O3.csv";

VARIABLE:
NAMES = Sex Age_2 HVTot_2 SWT8_2 TD_1 PIGD_1 SubG_1;
USEVARIABLES = Age_2 Sex HVTot_2 SWT8_2 TD_1 PIGD_1;
CATEGORICAL ARE Sex;

ANALYSIS:
ESTIMATOR = WLSMV;
MODEL:
SWM BY SWT8_2@0.82;
SWT8_2@0.32;
VWM BY HVTot_2@0.86;
HVTot_2@0.26;
VWM SWM ON TD_1 PIGD_1;
VWM WITH SWM Sex Age_2;
SWM WITH Age_2;

OUTPUT: SAMPSTAT STANDARDIZED;

INPUT READING TERMINATED NORMALLY

Model 2

SUMMARY OF ANALYSIS

Number of groups 1
Number of observations 114

Number of dependent variables 4
Number of independent variables 2
Number of continuous latent variables 2

Observed dependent variables

Continuous
AGE_2      HVTOT_2      SWT8_2
Binary and ordered categorical (ordinal)
SEX

Observed independent variables
TD_1      PIGD_1

Continuous latent variables
SWM      VWM

Estimator          WLSMV
Maximum number of iterations 1000
```

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Convergence criterion 0.500D-04
 Maximum number of steepest descent iterations 20
 Parameterization DELTA

Input data file(s) C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours\Analysis\Database\Re-Mplus\S

Input data format FREE

UNIVARIATE PROPORTIONS AND COUNTS FOR CATEGORICAL VARIABLES

SEX
Category 1 0.737 84.000
Category 2 0.263 30.000

SAMPLE STATISTICS

ESTIMATED SAMPLE STATISTICS

MEANS/INTERCEPTS/THRESHOLDS			
	AGE_2	SEX\$1	HVTOT_2
1	62.893	0.415	25.861
			22.732

SLOPES	
	TD_1 PIGD_1
AGE_2	3.396 2.714
SEX	-0.398 0.026
HVTOT_2	-2.040 -1.746
SWT8_2	1.617 5.829

CORRELATION MATRIX (WITH VARIANCES ON THE DIAGONAL)			
	AGE_2	SEX	HVTOT_2
AGE_2	80.824		
SEX	-0.207		
HVTOT_2	-0.460 0.598	41.141	
SWT8_2	0.373 -0.060	-0.261	172.943

THE MODEL ESTIMATION TERMINATED NORMALLY

MODEL FIT INFORMATION

Number of Free Parameters	15
Chi-Square Test of Model Fit	
Value	10.708*
Degrees of Freedom	6
P-Value	0.0978

* The chi-square value for MLM, MLMV, MLR, ULSMV, WLSM and WLSMV cannot be used for chi-square difference testing in the regular way. MLM, MLR and WLSM chi-square difference testing is described on the Mplus website. MLMV, WLSMV, and ULSMV difference testing is done using the DIFFTEST option.

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RMSEA (Root Mean Square Error Of Approximation)

Estimate	0.083
90 Percent C.I.	0.000 0.162
Probability RMSEA <= .05	0.213

CFI/TLI

CFI	0.921
TLI	0.817

Chi-Square Test of Model Fit for the Baseline Model

Value	73.872
Degrees of Freedom	14
P-Value	0.0000

WRMR (Weighted Root Mean Square Residual)

Value	0.724
-------	-------

MODEL RESULTS

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
SWM BY SWT8_2	0.820	0.000	999.000	999.000
VWM BY HVTOT_2	0.860	0.000	999.000	999.000
VWM ON TD_1	-2.372	1.499	-1.582	0.114
	-2.030	1.148	-1.769	0.077
SWM ON TD_1	1.972	2.880	0.685	0.494
	7.109	2.758	2.577	0.010
VWM WITH SWM	-31.208	11.128	-2.804	0.005
SEX	4.462	0.973	4.585	0.000
AGE_2	-30.865	6.641	-4.648	0.000
SWM WITH AGE_2	53.759	13.996	3.841	0.000
Means AGE_2	62.893	2.141	29.380	0.000
Intercepts HVTOT_2	25.861	1.413	18.301	0.000
SWT8_2	22.732	2.726	8.337	0.000
Thresholds SEX\$1	0.415	0.286	1.451	0.147
Variances AGE_2	80.824	10.472	7.718	0.000
Residual Variances HVTOT_2	0.260	0.000	999.000	999.000
SWT8_2	0.320	0.000	999.000	999.000

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SWM	256.726	45.729	5.614	0.000
VWM	55.275	8.996	6.144	0.000

STANDARDIZED MODEL RESULTS

STDYX Standardization

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	
SWM BY SWT8_2	0.999	0.000	6634.781	0.000	
VWM BY HVTOT_2	0.997	0.001	1950.401	0.000	
VWM ON TD_1	-0.159	0.097	-1.640	0.101	
	PIGD_1	0.151	0.083	-1.821	0.069
SWM ON TD_1	0.061	0.089	0.684	0.494	
	PIGD_1	0.243	0.093	2.612	0.009
VWM WITH SWM	-0.262	0.076	-3.428	0.001	
SEX	0.600	0.103	5.815	0.000	
AGE_2	-0.462	0.066	-7.012	0.000	
SWM WITH AGE_2	0.373	0.067	5.588	0.000	
Means AGE_2	6.996	0.530	13.202	0.000	
Intercepts HVTOT_2	3.954	0.291	13.602	0.000	
SWT8_2	1.679	0.233	7.205	0.000	
Thresholds SEX\$1	0.415	0.286	1.451	0.147	
Variances AGE_2	1.000	0.000	999.000	999.000	
Residual Variances HVTOT_2	0.006	0.001	5.964	0.000	
SWT8_2	0.002	0.000	5.801	0.000	
SWM	0.943	0.043	21.862	0.000	
VWM	0.962	0.035	27.517	0.000	

STDY Standardization

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
SWM BY SWT8_2	0.999	0.000	6634.781	0.000
VWM BY HVTOT_2	0.997	0.001	1950.401	0.000
VWM ON				

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TD_1	-0.313	0.190	-1.650	0.099
PIGD_1	-0.268	0.146	-1.834	0.067
SWM ON				
TD_1	0.120	0.175	0.684	0.494
PIGD_1	0.431	0.163	2.647	0.008
VWM WITH				
SWM	-0.262	0.076	-3.428	0.001
SEX	0.600	0.103	5.815	0.000
AGE_2	-0.462	0.066	-7.012	0.000
SWM WITH				
AGE_2	0.373	0.067	5.588	0.000
Means				
AGE_2	6.996	0.530	13.202	0.000
Intercepts				
HVTOT_2	3.954	0.291	13.602	0.000
SWT8_2	1.679	0.233	7.205	0.000
Thresholds				
SEX\$1	0.415	0.286	1.451	0.147
Variances				
AGE_2	1.000	0.000	999.000	999.000
Residual Variances				
HVTOT_2	0.006	0.001	5.964	0.000
SWT8_2	0.002	0.000	5.801	0.000
SWM	0.943	0.043	21.862	0.000
VWM	0.962	0.035	27.517	0.000
STD Standardization				
	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
SWM BY				
SWT8_2	13.527	1.168	11.583	0.000
VWM BY				
HVTOT_2	6.520	0.550	11.856	0.000
VWM ON				
TD_1	-0.313	0.190	-1.650	0.099
PIGD_1	-0.268	0.146	-1.834	0.067
SWM ON				
TD_1	0.120	0.175	0.684	0.494
PIGD_1	0.431	0.163	2.647	0.008
VWM WITH				
SWM	-0.262	0.076	-3.428	0.001
SEX	0.600	0.103	5.815	0.000
AGE_2	-4.152	0.731	-5.683	0.000
SWM WITH				
AGE_2	3.355	0.717	4.682	0.000
Means				
AGE_2	62.893	2.141	29.380	0.000
Intercepts				

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HVTOT_2	25.861	1.413	18.301	0.000
SWT8_2	22.732	2.726	8.337	0.000
Thresholds				
SEX\$1	0.415	0.286	1.451	0.147
Variances				
AGE_2	80.824	10.472	7.718	0.000
Residual Variances				
HVTOT_2	0.260	0.000	999.000	999.000
SWT8_2	0.320	0.000	999.000	999.000
SWM	0.943	0.043	21.862	0.000
VWM	0.962	0.035	27.517	0.000

R-SQUARE

Observed Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	Residual Variance
HVTOT_2	0.994	0.001	975.200	0.000	
SWT8_2	0.998	0.000	3317.390	0.000	
Latent Variable					
SWM	0.057	0.043	1.312	0.189	
VWM	0.038	0.035	1.097	0.273	

QUALITY OF NUMERICAL RESULTS

Condition Number for the Information Matrix (ratio of smallest to largest eigenvalue) 0.559E-03

DIAGRAM INFORMATION

Use View Diagram under the Diagram menu in the Mplus Editor to view the diagram. If running Mplus from the Mplus Diagrammer, the diagram opens automatically.

Diagram output
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Beginning Time: 23:12:27
Ending Time: 23:12:27
Elapsed Time: 00:00:00

Mplus VERSION 7.2 DEMO has the following limitations:
Maximum number of dependent variables: 6
Maximum number of independent variables: 2
Maximum number of between variables: 2

MUTHEN & MUTHEN
3463 Stoner Ave.
Los Angeles, CA 90066

Tel: (310) 391-9971
Fax: (310) 391-8971
Web: www.StatModel.com
Support: Support@StatModel.com

MPlus Outputs: Confirmatory Factor Analysis 1

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_____
Mplus VERSION 7.2 DEMO
MUTHEN & MUTHEN

INPUT INSTRUCTIONS

TITLE: CFA 1

DATA:
FILE = "C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours
\Analysis\DATABASES\Re-Mplus\SWM8_O3.csv";

VARIABLE:
NAMES = Sex Age_2 HVTot_2 SWT8_2 TD_1 PIGD_1 SubG_1 SubR_1;
USEVARIABLES = HVTot_2 SWT8_2 Sex Age_2 SubG_1 SubR_1;
CATEGORICAL ARE Sex;
GROUPING = SubG_1 (1=TD 2=PIGD);

ANALYSIS:
TYPE = mgroup;

MODEL:
SWM BY SWT8_2@0.82;
SWT8_2@0.32;
VWM BY HVTot_2@0.86;
HVTot_2@0.26;
VWM SWM ON SubR_1;
VWM WITH SWM Sex Age_2;
SWM WITH Age_2;

OUTPUT: SAMPSTAT STANDARDIZED;

INPUT READING TERMINATED NORMALLY

CFA 1

SUMMARY OF ANALYSIS

Number of groups                                2
Number of observations
  Group ID                                         28
  Group PIGD                                       29
  Total sample size                                 57

Number of dependent variables                   4
Number of independent variables                 1
Number of continuous latent variables          2

Observed dependent variables
  Continuous
    HVTOT_2      SWT8_2      AGE_2
  Binary and ordered categorical (ordinal)
    SEX

Observed independent variables
  SUBR_1

Continuous latent variables
```

Page: 1

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SWM	VWM
-----	-----

Variables with special functions

Grouping variable	SUBG_1
-------------------	--------

Estimator WLSMV
 Maximum number of iterations 1000
 Convergence criterion 0.500D-04
 Maximum number of steepest descent iterations 20
 Parameterization DELTA

Input data file(s)
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Input data format FREE

UNIVARIATE PROPORTIONS AND COUNTS FOR CATEGORICAL VARIABLES

Group TD		
SEX		
Category 1	0.714	20.000
Category 2	0.286	8.000

Group PIGD		
SEX		
Category 1	0.621	18.000
Category 2	0.379	11.000

SAMPLE STATISTICS

ESTIMATED SAMPLE STATISTICS FOR TD

MEANS/INTERCEPTS/THRESHOLDS			
	HVTOT_2	SWT8_2	SEX\$1
1	29.333	31.417	0.423
			61.333

SLOPES	
	SUBR_1
HVTOT_2	-5.792
SWT8_2	-2.583
SEX	-0.126
AGE_2	4.083

CORRELATION MATRIX (WITH VARIANCES ON THE DIAGONAL)			
	HVTOT_2	SWT8_2	SEX
HVTOT_2	42.025		
SWT8_2	-0.176	165.931	
SEX	0.713	0.041	
AGE_2	-0.525	0.526	-0.383
			125.529

ESTIMATED SAMPLE STATISTICS FOR PIGD

MEANS/INTERCEPTS/THRESHOLDS			
	HVTOT_2	SWT8_2	SEX\$1
			AGE_2

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1	19.182	32.506	0.517	64.909
---	--------	--------	-------	--------

SLOPES
SUBR_1

HVTOT_2	4.909
SWT8_2	-4.325
SEX	0.169
AGE_2	0.545

CORRELATION MATRIX (WITH VARIANCES ON THE DIAGONAL)

	HVTOT_2	SWT8_2	SEX	AGE_2
HVTOT_2	27.166			
SWT8_2	-0.509	206.555		
SEX	0.376	-0.001		
AGE_2	-0.362	0.536	-0.076	80.119

THE MODEL ESTIMATION TERMINATED NORMALLY

MODEL FIT INFORMATION

Number of Free Parameters 26

Chi-Square Test of Model Fit

Value	5.093*
Degrees of Freedom	8
P-Value	0.7476

Chi-Square Contribution From Each Group

TD	4.843
PIGD	0.251

* The chi-square value for MLM, MLMV, MLR, ULSMV, WLSM and WLSMV cannot be used for chi-square difference testing in the regular way. MLM, MLR and WLSM chi-square difference testing is described on the Mplus website. MLMV, WLSMV, and ULSMV difference testing is done using the DIFFTEST option.

RMSEA (Root Mean Square Error Of Approximation)

Estimate	0.000
90 Percent C.I.	0.000 0.157
Probability RMSEA <= .05	0.784

CFI/TLI

CFI	1.000
TLI	1.308

Chi-Square Test of Model Fit for the Baseline Model

Value	43.621
Degrees of Freedom	20
P-Value	0.0017

WRMR (Weighted Root Mean Square Residual)

Value	0.525
-------	-------

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MODEL RESULTS

	Estimate	S.E.	Two-Tailed Est./S.E.	P-Value
Group TD				
SWM BY SWT8_2	0.820	0.000	999.000	999.000
VWM BY HVTOT_2	0.860	0.000	999.000	999.000
VWM ON SUBR_1	-6.734	3.626	-1.857	0.063
SWM ON SUBR_1	-3.150	11.733	-0.269	0.788
VWM WITH SWM	-20.670	19.591	-1.055	0.291
	5.377	1.819	2.956	0.003
	-43.780	21.973	-1.992	0.046
SWM WITH AGE_2	92.263	41.791	2.208	0.027
Means AGE_2	61.333	8.497	7.219	0.000
Intercepts				
HVTOT_2	29.333	3.920	7.483	0.000
SWT8_2	31.411	11.085	2.834	0.005
SWM	0.000	0.000	999.000	999.000
VWM	0.000	0.000	999.000	999.000
Thresholds				
SEX\$1	0.423	0.870	0.486	0.627
Variances				
AGE_2	126.411	43.195	2.926	0.003
Residual Variances				
HVTOT_2	0.260	0.000	999.000	999.000
SWT8_2	0.320	0.000	999.000	999.000
SWM	248.736	85.283	2.917	0.004
VWM	56.833	20.658	2.751	0.006
Group PIGD				
SWM BY SWT8_2	0.820	0.000	999.000	999.000
VWM BY HVTOT_2	0.860	0.000	999.000	999.000
VWM ON SUBR_1	5.708	2.483	2.299	0.022
SWM ON SUBR_1	-5.274	8.218	-0.642	0.521
VWM WITH				

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SWM	-53.932	20.892	-2.581	0.010
SEX	2.279	1.562	1.459	0.145
AGE_2	-19.643	7.926	-2.478	0.013
SWM WITH AGE_2	83.908	36.544	2.296	0.022
Means AGE_2	64.909	6.156	10.545	0.000
Intercepts				
HVTOT_2	29.333	3.920	7.483	0.000
SWT8_2	31.411	11.085	2.834	0.005
SWM	1.339	17.023	0.079	0.937
VWM	-11.804	5.729	-2.061	0.039
Thresholds				
SEX\$1	0.517	0.725	0.714	0.475
Variances				
AGE_2	81.167	23.379	3.472	0.001
Residual Variances				
HVTOT_2	0.260	0.000	999.000	999.000
SWT8_2	0.320	0.000	999.000	999.000
SWM	304.466	86.827	3.507	0.000
VWM	36.379	9.656	3.768	0.000

STANDARDIZED MODEL RESULTS

STDYX Standardization

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
Group TD				
SWM BY SWT8_2	0.999	0.000	2993.113	0.000
VWM BY HVTOT_2	0.997	0.001	1004.310	0.000
VWM ON SUBR_1	-0.303	0.155	-1.955	0.051
SWM ON SUBR_1	-0.071	0.261	-0.272	0.785
VWM WITH				
SWM	-0.174	0.148	-1.172	0.241
SEX	0.713	0.139	5.142	0.000
AGE_2	-0.517	0.141	-3.652	0.000
SWM WITH AGE_2	0.520	0.132	3.933	0.000
Means AGE_2	5.455	1.263	4.318	0.000
Intercepts				
HVTOT_2	4.299	0.767	5.603	0.000
SWT8_2	2.420	0.762	3.175	0.001
SWM	0.000	0.000	999.000	999.000

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VWM	0.000	0.000	999.000	999.000
Thresholds				
SEX\$1	0.423	0.870	0.486	0.627
Variances				
AGE_2	1.000	0.000	999.000	999.000
Residual Variances				
HVTOT_2	0.006	0.002	2.820	0.005
SWT8_2	0.002	0.001	2.849	0.004
SWM	0.995	0.037	26.869	0.000
VWM	0.908	0.094	9.646	0.000
Group PIGD				
SWM BY				
SWT8_2	0.999	0.000	4601.026	0.000
VWM BY				
HVTOT_2	0.996	0.001	918.353	0.000
VWM ON				
SUBR_1	0.381	0.153	2.492	0.013
SWM ON				
SUBR_1	-0.131	0.202	-0.646	0.519
VWM WITH				
SWM	-0.512	0.111	-4.604	0.000
SEX	0.378	0.237	1.596	0.111
AGE_2	-0.361	0.096	-3.763	0.000
SWM WITH				
AGE_2	0.534	0.137	3.890	0.000
Means				
AGE_2	7.205	0.906	7.949	0.000
Intercepts				
HVTOT_2	5.207	0.977	5.327	0.000
SWT8_2	2.175	0.827	2.630	0.009
SWM	0.076	0.966	0.079	0.937
VWM	-1.809	0.874	-2.071	0.038
Thresholds				
SEX\$1	0.517	0.725	0.714	0.475
Variances				
AGE_2	1.000	0.000	999.000	999.000
Residual Variances				
HVTOT_2	0.008	0.002	3.793	0.000
SWT8_2	0.002	0.000	3.535	0.000
SWM	0.983	0.053	18.632	0.000
VWM	0.855	0.117	7.334	0.000
STDY Standardization				
	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
Group TD				
SWM BY				

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SWT8_2	0.999	0.000	2993.113	0.000
VWM BY HVTOT_2	0.997	0.001	1004.310	0.000
VWM ON SUBR_1	-0.851	0.423	-2.012	0.044
SWM ON SUBR_1	-0.199	0.731	-0.272	0.785
VWM WITH SWM	-0.174	0.148	-1.172	0.241
SEX	0.713	0.139	5.142	0.000
AGE_2	-0.517	0.141	-3.652	0.000
SWM WITH AGE_2	0.520	0.132	3.933	0.000
Means AGE_2	5.455	1.263	4.318	0.000
Intercepts				
HVTOT_2	4.299	0.767	5.603	0.000
SWT8_2	2.420	0.762	3.175	0.001
SWM	0.000	0.000	999.000	999.000
VWM	0.000	0.000	999.000	999.000
Thresholds				
SEX\$1	0.423	0.870	0.486	0.627
Variances				
AGE_2	1.000	0.000	999.000	999.000
Residual Variances				
HVTOT_2	0.006	0.002	2.820	0.005
SWT8_2	0.002	0.001	2.849	0.004
SWM	0.995	0.037	26.869	0.000
VWM	0.908	0.094	9.646	0.000
Group PIGD				
SWM BY SWT8_2	0.999	0.000	4601.026	0.000
VWM BY HVTOT_2	0.996	0.001	918.353	0.000
VWM ON SUBR_1	0.875	0.338	2.592	0.010
SWM ON SUBR_1	-0.300	0.463	-0.648	0.517
VWM WITH SWM	-0.512	0.111	-4.604	0.000
SEX	0.378	0.237	1.596	0.111
AGE_2	-0.361	0.096	-3.763	0.000
SWM WITH AGE_2	0.534	0.137	3.890	0.000
Means AGE_2	7.205	0.906	7.949	0.000
Intercepts				

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HVTOT_2	5.207	0.977	5.327	0.000
SWT8_2	2.175	0.827	2.630	0.009
SWM	0.076	0.966	0.079	0.937
VWM	-1.809	0.874	-2.071	0.038
Thresholds				
SEX\$1	0.517	0.725	0.714	0.475
Variances				
AGE_2	1.000	0.000	999.000	999.000
Residual Variances				
HVTOT_2	0.008	0.002	3.793	0.000
SWT8_2	0.002	0.000	3.535	0.000
SWM	0.983	0.053	18.632	0.000
VWM	0.855	0.117	7.334	0.000
STD Standardization				
	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
Group TD				
SWM BY SWT8_2	12.965	2.280	5.687	0.000
VWM BY HVTOT_2	6.804	1.213	5.609	0.000
VWM ON SUBR_1	-0.851	0.423	-2.012	0.044
SWM ON SUBR_1	-0.199	0.731	-0.272	0.785
VWM WITH SWM	-0.174	0.148	-1.172	0.241
	SEX	0.713	0.139	5.142
	AGE_2	-5.807	2.301	-2.524
SWM WITH AGE_2	5.850	2.038	2.871	0.004
Means				
AGE_2	61.333	8.497	7.219	0.000
Intercepts				
HVTOT_2	29.333	3.920	7.483	0.000
SWT8_2	31.411	11.085	2.834	0.005
SWM	0.000	0.000	999.000	999.000
VWM	0.000	0.000	999.000	999.000
Thresholds				
SEX\$1	0.423	0.870	0.486	0.627
Variances				
AGE_2	126.411	43.195	2.926	0.003
Residual Variances				
HVTOT_2	0.260	0.000	999.000	999.000
SWT8_2	0.320	0.000	999.000	999.000
SWM	0.995	0.037	26.869	0.000
VWM	0.908	0.094	9.646	0.000

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Group PIGD

SWM	BY			
SWT8_2		14.432	2.045	7.058
VWM	BY			
HVTOT_2		5.610	0.746	7.524
VWM	ON			
SUBR_1		0.875	0.338	2.592
SWM	ON			
SUBR_1		-0.300	0.463	-0.648
VWM	WITH			
SWM		-0.512	0.111	-4.604
SEX		0.378	0.237	1.596
AGE_2		-3.257	1.170	-2.784
SWM	WITH			
AGE_2		4.809	1.738	2.767
Means				
AGE_2		64.909	6.156	10.545
Intercepts				
HVTOT_2		29.333	3.920	7.483
SWT8_2		31.411	11.085	2.834
SWM		0.076	0.966	0.079
VWM		-1.809	0.874	-2.071
Thresholds				
SEX\$1		0.517	0.725	0.714
Variances				
AGE_2		81.167	23.379	3.472
Residual Variances				
HVTOT_2		0.260	0.000	999.000
SWT8_2		0.320	0.000	999.000
SWM		0.983	0.053	18.632
VWM		0.855	0.117	7.334

R-SQUARE

Group TD

Observed Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	Residual Variance
HVTOT_2	0.994	0.002	502.155	0.000	
SWT8_2	0.998	0.001	1496.557	0.000	
Latent Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	
SWM	0.005	0.037	0.136	0.892	
VWM	0.092	0.094	0.977	0.328	

Group PIGD

Observed Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	Residual Variance
HVTOT_2	0.992	0.002	459.176	0.000	

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SWT8_2	0.998	0.000	2300.513	0.000
Latent Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
SWM	0.017	0.053	0.323	0.747
VWM	0.145	0.117	1.246	0.213

QUALITY OF NUMERICAL RESULTS

Condition Number for the Information Matrix
(ratio of smallest to largest eigenvalue) 0.861E-04

DIAGRAM INFORMATION

Use View Diagram under the Diagram menu in the Mplus Editor to view the diagram.
If running Mplus from the Mplus Diagrammer, the diagram opens automatically.

Diagram output
c:\users\andrew johnson\dropbox\uni\y4s2\honours\analysis\results - initial\m1w2\mgroup diff.dgm

Beginning Time: 23:18:05
Ending Time: 23:18:05
Elapsed Time: 00:00:00

Mplus VERSION 7.2 DEMO has the following limitations:
Maximum number of dependent variables: 6
Maximum number of independent variables: 2
Maximum number of between variables: 2

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Web: www.StatModel.com
Support: Support@StatModel.com

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MPlus Output: Confirmatory Factor Analysis 2

```
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_____
Mplus VERSION 7.2 DEMO
MUTHEN & MUTHEN

INPUT INSTRUCTIONS

TITLE: CFA 2

DATA:
FILE = "C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours
\Analysis\DATABASES\Re-Mplus\SWM8_O3.csv";

VARIABLE:
NAMES = Sex Age_2 HVTot_2 SWT8_2 TD_1 PIGD_1 SubG_1;
USEVARIABLES = PIGD_1 TD_1 HVTot_2 SWT8_2 Sex Age_2 SubG_1;
CATEGORICAL ARE Sex;
GROUPING = SubG_1 (1=TD 2=PIGD);

ANALYSIS:
TYPE = mgroup

MODEL:
SWM BY SWT8_2@0.82;
SWT8_2@0.32;
VWM BY HVTot_2@0.86;
HVTot_2@0.26;
  VWM SWM ON PIGD_1 (1);
  VWM SWM ON TD_1(2);
  VWM WITH SWM Sex Age_2 (3);
  SWM WITH Age_2 (4);
  VWM (5);
  SWM (6);

OUTPUT: SAMPSTAT STANDARDIZED;

INPUT READING TERMINATED NORMALLY

CFA 2

SUMMARY OF ANALYSIS

Number of groups                                2
Number of observations
  Group TD                                         63
  Group PIGD                                       51
  Total sample size                                 114

Number of dependent variables                   4
Number of independent variables                 2
Number of continuous latent variables          2

Observed dependent variables

  Continuous
    HVTOT_2      SWT8_2      AGE_2
```

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Binary and ordered categorical (ordinal)
SEX

Observed independent variables
PIGD_1 TD_1

Continuous latent variables
SWM VWM

Variables with special functions

Grouping variable SUBG_1

Estimator WLSMV
Maximum number of iterations 1000
Convergence criterion 0.500D-04
Maximum number of steepest descent iterations 20
Parameterization DELTA

Input data file(s)
C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours\Analysis\Database\Re-Mplus\S

Input data format FREE

UNIVARIATE PROPORTIONS AND COUNTS FOR CATEGORICAL VARIABLES

Group TD
SEX
Category 1 0.810 51.000
Category 2 0.190 12.000
Group PIGD
SEX
Category 1 0.647 33.000
Category 2 0.353 18.000

SAMPLE STATISTICS

ESTIMATED SAMPLE STATISTICS FOR TD

	MEANS/INTERCEPTS/THRESHOLDS		
	HVTOT_2	SWT8_2	SEX\$1
1	25.253	27.922	0.755
			62.475

	SLOPES	
	PIGD_1	TD_1
HVTOT_2	-6.404	-0.077
SWT8_2	-2.739	0.283
SEX	0.155	-0.189
AGE_2	1.824	4.215

CORRELATION MATRIX (WITH VARIANCES ON THE DIAGONAL)				
	HVTOT_2	SWT8_2	SEX	AGE_2
HVTOT_2	45.303			
SWT8_2	-0.236	192.632		
SEX	0.633	0.010		
AGE_2	-0.598	0.466	-0.309	90.871

Page: 2

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ESTIMATED SAMPLE STATISTICS FOR PIGD

	MEANS/INTERCEPTS/THRESHOLDS			
	HVTOT_2	SWT8_2	SEX\$1	AGE_2
1	26.387	18.852	0.162	62.935
SLOPES				
	PIGD_1	TD_1		
HVTOT_2	-2.659	1.981		
SWT8_2	9.325	-0.803		
SEX	-0.318	0.390		
AGE_2	3.217	0.868		
CORRELATION MATRIX (WITH VARIANCES ON THE DIAGONAL)				
	HVTOT_2	SWT8_2	SEX	AGE_2
HVTOT_2	33.033			
SWT8_2	-0.325	135.573		
SEX	0.554	-0.085		
AGE_2	-0.243	0.228	-0.086	67.879

THE MODEL ESTIMATION TERMINATED NORMALLY

MODEL FIT INFORMATION

Number of Free Parameters 16

Chi-Square Test of Model Fit

Value	52.362*
Degrees of Freedom	26
P-Value	0.0016

Chi-Square Contribution From Each Group

TD	24.538
PIGD	27.823

* The chi-square value for MLM, MLMV, MLR, ULSMV, WLSM and WLSMV cannot be used for chi-square difference testing in the regular way. MLM, MLR and WLSM chi-square difference testing is described on the Mplus website. MLMV, WLSMV, and ULSMV difference testing is done using the DIFFTEST option.

RMSEA (Root Mean Square Error Of Approximation)

Estimate	0.133
90 Percent C.I.	0.080 0.185
Probability RMSEA <= .05	0.009

CFI/TLI

CFI	0.411
TLI	0.365

Chi-Square Test of Model Fit for the Baseline Model

<hr/> C:\Users\Andrew Johnson\Dropbox\Uni\Y4S2\Honours\Thesis\Supps\MPlus ...\\CFA 2.out <hr/>				
Value	72.720			
Degrees of Freedom	28			
P-Value	0.0000			
WRMR (Weighted Root Mean Square Residual)				
Value	1.735			
MODEL RESULTS				
	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
Group TD				
SWM BY SWT8_2	0.820	0.000	999.000	999.000
VWM BY HVTOT_2	0.860	0.000	999.000	999.000
VWM ON PIGD_1 TD_1	-1.622 0.588	0.920 1.969	-1.764 0.298	0.078 0.765
SWM ON PIGD_1 TD_1	-1.622 0.588	0.920 1.969	-1.764 0.298	0.078 0.765
VWM WITH SWM SEX AGE_2	3.339 3.339 3.339	0.810 0.810 0.810	4.124 4.124 4.124	0.000 0.000 0.000
SWM WITH AGE_2	34.003	10.608	3.205	0.001
Means AGE_2	62.489	3.558	17.563	0.000
Intercepts HVTOT_2 SWT8_2 SWM VWM	25.258 27.910 0.000 0.000	2.536 5.144 0.000 0.000	9.959 5.426 999.000 999.000	0.000 0.000 999.000 999.000
Thresholds SEX\$1	0.755	0.681	1.108	0.268
Variances AGE_2	90.910	17.830	5.099	0.000
Residual Variances HVTOT_2 SWT8_2 SWM VWM	0.260 0.320 228.855 49.355	0.000 0.000 45.356 8.063	999.000 999.000 5.046 6.121	999.000 999.000 0.000 0.000
Group PIGD				
SWM BY SWT8_2	0.820	0.000	999.000	999.000
VWM BY				

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HVTOT_2	0.860	0.000	999.000	999.000
VWM ON				
PIGD_1	-1.622	0.920	-1.764	0.078
TD_1	0.588	1.969	0.298	0.765
SWM ON				
PIGD_1	-1.622	0.920	-1.764	0.078
TD_1	0.588	1.969	0.298	0.765
VWM WITH				
SWM	3.339	0.810	4.124	0.000
SEX	3.339	0.810	4.124	0.000
AGE_2	3.339	0.810	4.124	0.000
SWM WITH				
AGE_2	34.003	10.608	3.205	0.001
Means				
AGE_2	62.927	2.479	25.386	0.000
Intercepts				
HVTOT_2	25.258	2.536	9.959	0.000
SWT8_2	27.910	5.144	5.426	0.000
SWM	-11.053	7.345	-1.505	0.132
VWM	1.320	3.419	0.386	0.699
Thresholds				
SEX\$1	0.163	0.349	0.466	0.641
Variances				
AGE_2	67.871	13.728	4.944	0.000
Residual Variances				
HVTOT_2	0.260	0.000	999.000	999.000
SWT8_2	0.320	0.000	999.000	999.000
SWM	228.855	45.356	5.046	0.000
VWM	49.355	8.063	6.121	0.000

STANDARDIZED MODEL RESULTS

STDYX Standardization

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
Group TD				
SWM BY				
SWT8_2	0.999	0.000	4870.255	0.000
VWM BY				
HVTOT_2	0.996	0.001	1737.182	0.000
VWM ON				
PIGD_1	-0.056	0.032	-1.758	0.079
TD_1	0.035	0.117	0.298	0.766
SWM ON				
PIGD_1	-0.026	0.015	-1.711	0.087
TD_1	0.016	0.054	0.297	0.766
VWM WITH				
SWM	0.031	0.007	4.498	0.000

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SEX	0.475	0.095	4.978	0.000
AGE_2	0.050	0.011	4.519	0.000
SWM WITH AGE_2	0.236	0.063	3.728	0.000
Means AGE_2	6.554	0.741	8.842	0.000
Intercepts				
HVTOT_2	4.160	0.475	8.767	0.000
SWT8_2	2.247	0.418	5.377	0.000
SWM	0.000	0.000	999.000	999.000
VWM	0.000	0.000	999.000	999.000
Thresholds				
SEX\$1	0.755	0.681	1.108	0.268
Variances				
AGE_2	1.000	0.000	999.000	999.000
Residual Variances				
HVTOT_2	0.007	0.001	6.171	0.000
SWT8_2	0.002	0.000	5.061	0.000
SWM	0.999	0.001	1147.560	0.000
VWM	0.997	0.004	253.020	0.000
Group PIGD				
SWM BY SWT8_2	0.999	0.000	4904.020	0.000
VWM BY HVTOT_2	0.997	0.001	1753.590	0.000
VWM ON PIGD_1	-0.149	0.084	-1.782	0.075
	0.023	0.076	0.298	0.766
SWM ON PIGD_1	-0.070	0.041	-1.713	0.087
	0.011	0.036	0.297	0.766
VWM WITH SWM	0.031	0.007	4.498	0.000
SEX	0.475	0.095	4.978	0.000
AGE_2	0.058	0.014	4.075	0.000
SWM WITH AGE_2	0.273	0.065	4.200	0.000
Means AGE_2	7.638	0.877	8.707	0.000
Intercepts				
HVTOT_2	4.124	0.462	8.924	0.000
SWT8_2	2.243	0.417	5.380	0.000
SWM	-0.729	0.487	-1.498	0.134
VWM	0.186	0.483	0.385	0.700
Thresholds				
SEX\$1	0.163	0.349	0.466	0.641
Variances				
AGE_2	1.000	0.000	999.000	999.000

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Residual Variances				
	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
HVTOT_2	0.007	0.001	6.119	0.000
SWT8_2	0.002	0.000	5.076	0.000
SWM	0.996	0.005	196.153	0.000
VWM	0.980	0.022	43.947	0.000
 STDY Standardization				
 Group TD				
SWM BY SWT8_2				
	0.999	0.000	4870.255	0.000
VWM BY HVTOT_2				
	0.996	0.001	1737.182	0.000
VWM ON PIGD_1				
	-0.231	0.130	-1.780	0.075
	0.084	0.280	0.298	0.765
SWM ON PIGD_1				
	-0.107	0.062	-1.731	0.083
	0.039	0.131	0.297	0.766
VWM WITH SWM				
	0.031	0.007	4.498	0.000
VWM WITH SEX				
	0.475	0.095	4.978	0.000
VWM WITH AGE_2				
	0.050	0.011	4.519	0.000
SWM WITH AGE_2				
	0.236	0.063	3.728	0.000
Means AGE_2				
	6.554	0.741	8.842	0.000
Intercepts HVTOT_2				
	4.160	0.475	8.767	0.000
Intercepts SWT8_2				
	2.247	0.418	5.377	0.000
Intercepts SWM				
	0.000	0.000	999.000	999.000
Intercepts VWM				
	0.000	0.000	999.000	999.000
Thresholds SEX\$1				
	0.755	0.681	1.108	0.268
Variances AGE_2				
	1.000	0.000	999.000	999.000
Residual Variances HVTOT_2				
	0.007	0.001	6.171	0.000
Residual Variances SWT8_2				
	0.002	0.000	5.061	0.000
Residual Variances SWM				
	0.999	0.001	1147.560	0.000
Residual Variances VWM				
	0.997	0.004	253.020	0.000
 Group PIGD				
SWM BY SWT8_2				
	0.999	0.000	4904.020	0.000
VWM BY HVTOT_2				
	0.997	0.001	1753.590	0.000
VWM ON				

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PIGD_1	-0.228	0.126	-1.810	0.070
TD_1	0.083	0.278	0.298	0.766
SWM ON				
PIGD_1	-0.107	0.062	-1.738	0.082
TD_1	0.039	0.130	0.297	0.766
VWM WITH				
SWM	0.031	0.007	4.498	0.000
SEX	0.475	0.095	4.978	0.000
AGE_2	0.058	0.014	4.075	0.000
SWM WITH				
AGE_2	0.273	0.065	4.200	0.000
Means				
AGE_2	7.638	0.877	8.707	0.000
Intercepts				
HVTOT_2	4.124	0.462	8.924	0.000
SWT8_2	2.243	0.417	5.380	0.000
SWM	-0.729	0.487	-1.498	0.134
VWM	0.186	0.483	0.385	0.700
Thresholds				
SEX\$1	0.163	0.349	0.466	0.641
Variances				
AGE_2	1.000	0.000	999.000	999.000
Residual Variances				
HVTOT_2	0.007	0.001	6.119	0.000
SWT8_2	0.002	0.000	5.076	0.000
SWM	0.996	0.005	196.153	0.000
VWM	0.980	0.022	43.947	0.000
STD Standardization				
	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
Group TD				
SWM BY				
SWT8_2	12.408	1.228	10.101	0.000
VWM BY				
HVTOT_2	6.050	0.494	12.254	0.000
VWM ON				
PIGD_1	-0.231	0.130	-1.780	0.075
TD_1	0.084	0.280	0.298	0.765
SWM ON				
PIGD_1	-0.107	0.062	-1.731	0.083
TD_1	0.039	0.131	0.297	0.766
VWM WITH				
SWM	0.031	0.007	4.498	0.000
SEX	0.475	0.095	4.978	0.000
AGE_2	0.475	0.095	4.978	0.000
SWM WITH				
AGE_2	2.248	0.608	3.694	0.000

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Means				
AGE_2	62.489	3.558	17.563	0.000
Intercepts				
HVTOT_2	25.258	2.536	9.959	0.000
SWT8_2	27.910	5.144	5.426	0.000
SWM	0.000	0.000	999.000	999.000
VWM	0.000	0.000	999.000	999.000
Thresholds				
SEX\$1	0.755	0.681	1.108	0.268
Variances				
AGE_2	90.910	17.830	5.099	0.000
Residual Variances				
HVTOT_2	0.260	0.000	999.000	999.000
SWT8_2	0.320	0.000	999.000	999.000
SWM	0.999	0.001	1147.560	0.000
VWM	0.997	0.004	253.020	0.000
Group PIGD				
SWM BY				
SWT8_2	12.432	1.227	10.132	0.000
VWM BY				
HVTOT_2	6.104	0.502	12.154	0.000
VWM ON				
PIGD_1	-0.228	0.126	-1.810	0.070
TD_1	0.083	0.278	0.298	0.766
SWM ON				
PIGD_1	-0.107	0.062	-1.738	0.082
TD_1	0.039	0.130	0.297	0.766
VWM WITH				
SWM	0.031	0.007	4.498	0.000
SEX	0.475	0.095	4.978	0.000
AGE_2	0.475	0.095	4.978	0.000
SWM WITH				
AGE_2	2.248	0.608	3.694	0.000
Means				
AGE_2	62.927	2.479	25.386	0.000
Intercepts				
HVTOT_2	25.258	2.536	9.959	0.000
SWT8_2	27.910	5.144	5.426	0.000
SWM	-0.729	0.487	-1.498	0.134
VWM	0.186	0.483	0.385	0.700
Thresholds				
SEX\$1	0.163	0.349	0.466	0.641
Variances				
AGE_2	67.871	13.728	4.944	0.000
Residual Variances				
HVTOT_2	0.260	0.000	999.000	999.000
SWT8_2	0.320	0.000	999.000	999.000
SWM	0.996	0.005	196.153	0.000
VWM	0.980	0.022	43.947	0.000

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R-SQUARE

Group TD

Observed Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	Residual Variance
HVTOT_2	0.993	0.001	868.591	0.000	
SWT8_2	0.998	0.000	2435.128	0.000	
Latent Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	
SWM	0.001	0.001	0.642	0.521	
VWM	0.003	0.004	0.656	0.512	

Group PIGD

Observed Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	Residual Variance
HVTOT_2	0.993	0.001	876.795	0.000	
SWT8_2	0.998	0.000	2452.010	0.000	
Latent Variable	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value	
SWM	0.004	0.005	0.871	0.384	
VWM	0.020	0.022	0.905	0.365	

QUALITY OF NUMERICAL RESULTS

Condition Number for the Information Matrix
(ratio of smallest to largest eigenvalue) 0.529E-03

DIAGRAM INFORMATION

Use View Diagram under the Diagram menu in the Mplus Editor to view the diagram.
If running Mplus from the Mplus Diagrammer, the diagram opens automatically.

Diagram output
c:\users\andrew johnson\dropbox\uni\y4s2\honours\analysis\results - initial\m1w2\mgroup.dgm

Beginning Time: 23:22:58
Ending Time: 23:22:58
Elapsed Time: 00:00:00

Mplus VERSION 7.2 DEMO has the following limitations:
Maximum number of dependent variables: 6
Maximum number of independent variables: 2
Maximum number of between variables: 2

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Supplementary Material L

Statistical Consultation Advice**STATISTICAL CONSULTATION FOR PSYCHOLOGY HONOURS
STUDENTS 2014**

Please complete this form, then email the form to Dr Robert (Bob) Kane and make an appointment time for you and your supervisor(s).

Student Name: Andrew Johnson

Thesis Title: Working Memory Decline in Parkinson's Disease

Supervisors: Dr. Andrea Loftus, Dr. Natalie Gasson

Research Question

Can the motor subtypes of PD predict decline in verbal working memory (VWM) or spatial working memory (SWM)?

Hypotheses

The motor subtype of the individual will account for a significant amount of variance in their VWM scores.

The motor subtype of the individual will account for a significant amount of variance in their SWM scores.

The motor subtype will continue to account for a significant amount of variance at a two year follow-up.

Sample Size Required Based on Power Analysis

85 Participants

- F test, Multiple Regression – Increase of R^2
- 4 predictors
- $f^2 = .15$

Sampling Strategy:

Analysis using existing database

- ParkC database
 - 4 years of collected data
 - 3 waves, data collected every two years

Measures (include number of factors and alpha reliability where applicable)**Motor Subtypes**

- Unified Parkinson's Disease Rating Scale, Parts 2 & 3
 - $\alpha = .92, .93$
 - Part 2: 3 Factors, Part 3: 7 factors
 - Using select items from parts, not entire measure

Verbal Working Memory

- Hopkins Verbal Learning Test – Revised
 - $\alpha = .82$

Spatial Working Memory

- CANTAB SWM Test
 - $\alpha = .95$

Planned Analyses

Four Hierarchical Multiple Regressions, two regressions per time point

- Control variables (age and gender) entered on step 1, motor subtype entered on step 2
- One regression with VWM as the criterion and one with SWM as the criterion
- Repeated for Time 2

Specific Questions for Statistical Consultant

Four analyses seem to be an inefficient approach and increases the risk of error, is there a better form of analysis for this?

I'm attempting to see if the motor subtypes can predict decline in either type of working memory, then to use the data from Time 2 to validate this.

Previous research into this has found contradicting results, so I cannot confidently say that VWM and SWM are independently affected.

TO BE COMPLETED BY STATISTICAL ADVISOR

- No changes required**
- The following changes are required**

✓**The following comments should be taken on board**

Hypotheses

You formulate two cross-sectional hypotheses.

After controlling for age and gender:

- H1a: Motor subtype (a binary variable derived from the UPDRS) will account for a significant amount of variance in *concurrent* verbal working memory (as measured by the HVLT-R).
- H1b: Motor subtype will predict a significant amount of variance in *concurrent* spatial working memory scores (as measured by the CANTAB SWM).

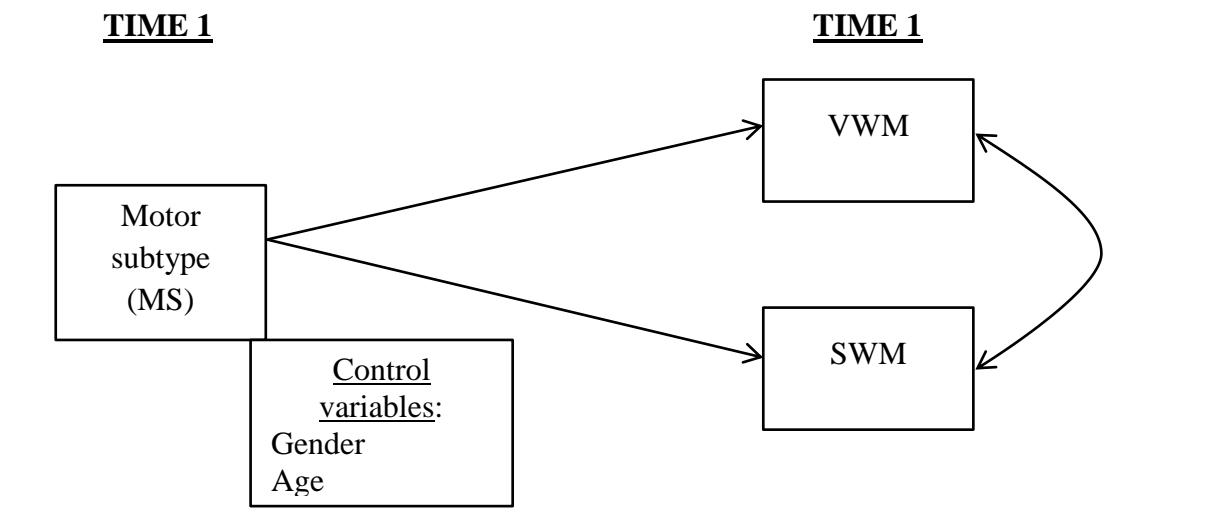
And two longitudinal hypotheses.

After controlling for age and gender:

- H2a: Motor subtype will continue to account for a significant amount of variance in verbal working memory *assessed at a two-year follow-up*.
- H2b: Motor subtype will continue to account for a significant amount of variance in the spatial working memory *assessed at a two-year follow-up*.

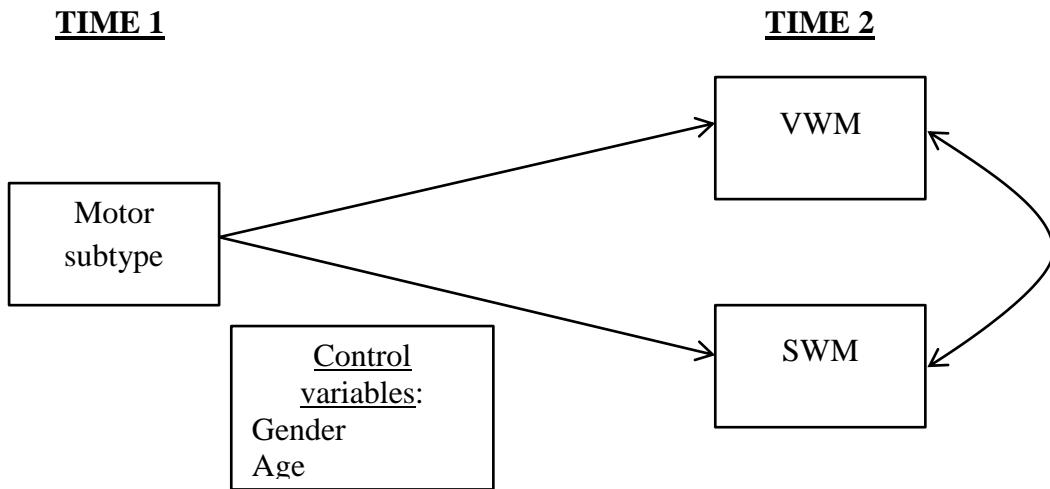
Hypothesis testing

H1a & H1b can be formulated in terms of the following path diagram.



There is no need to test model fit because the path model is saturated and will therefore fit the data perfectly. H1a predicts a significant MS→VWM path coefficient; H1b predicts a significant MS→SWM path coefficient. The direction of the path coefficients (positive or negative) will depend on how the binary MS variable has been coded. The double headed arrow represents the correlation between VWM & SWM – would we expect this to be positive significant?

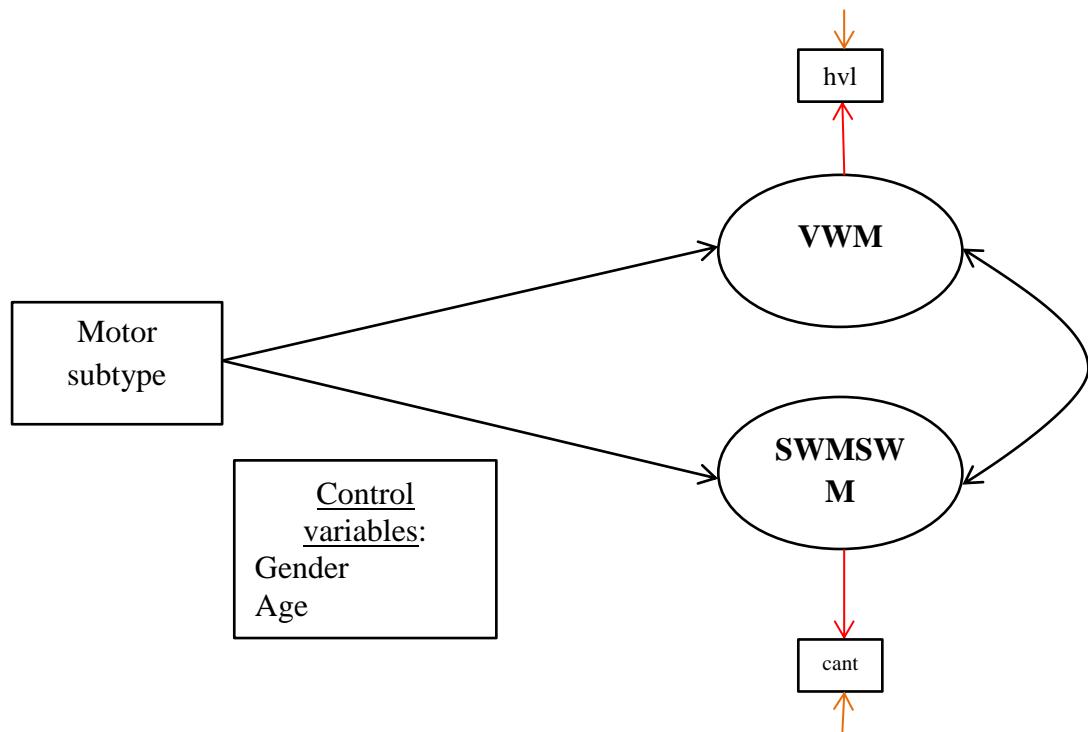
H2a & H2b can be formulated in terms of a similar path diagram:



Once again, there is no need to test model fit because the path model is saturated and will therefore fit the data perfectly. H2a predicts a significant MS→VWM path coefficient; H2b predicts a significant MS→SWM path coefficient. Once again, the direction of the path coefficients (positive or negative) will depend on how the binary MS variable has been coded. The double headed arrow represents the correlation between VWM & SWM.

Controlling measurement error

You could compute test-retest (T1-T2) reliabilities for VWM and SWM, and include these in both path models to control for measurement error. When we control for measurement error, the path model is more appropriately referred to as a structural equation model (SEM). Your SEMs would look like this.



The SEM assumes that each of the *observed* variables (represented by the small boxes in the above model) is driven by the *latent* variable that it's trying to capture (represented by the ovals in the above model). The measurement error associated with an observed variable (represented by the orange arrow) is set to one minus the reliability coefficient of the variable, and we set its factor loading (represented by the red arrow) to the square root of its reliability coefficient. *Incidentally, no additional participants are required to test the more sophisticated SEM model.*

Assumption testing

Multivariate normality

Path analysis & SEM assume that the measures being analysed (HVLT-R, CANTAB SWM) are *bivariate normal* (Kline, 2005). LISREL will test for bivariate normality.

Linearity

Path analysis & SEM assume that the bivariate relationship between HVLT-R and CANTAB SWM is *linear* rather than *curvilinear*. The most straight-forward way to test for linearity is to examine the scatterplot of the bivariate relationship. If there is no obvious curvilinear trend, then we can assume that the linearity assumption has been met.

Sample size

In order to reliably test path and SEM models, Kline has recommended that we have at least 10 participants for each free parameter in the structural model - although 20 participants per free parameter would once again be the ideal. A *free* parameter is a parameter that must be estimated from the data. Generally speaking, the free parameters in your models include the

path coefficients (2), the disturbances of the endogenous variables (2), the variance of the exogenous variable (1), and the correlation between the endogenous variables (1). Each of your models therefore has six free parameters. An ideal sample size for testing your models would therefore be $20 \times 6 = 120$. If the two groups could be of roughly equal size and homogeneous in terms of their variances on the HVLT-R and CANTAB , the analysis will have optimal power.

Note: This advice was updated on 8/10/2014, further information can be obtained from Dr. Robert Kane