The effects of lifelong cognitive lifestyle on executive function in older people with Parkinson's disease

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International Journal of Geriatric Psychiatry

The effects of lifelong cognitive lifestyle on executive function in older people with Parkinson's disease.

Running title- Lifestyle and executive function in Parkinson's

Key words- cognition, dementia, education, occupation, social engagement, motor function

Key points-

1. A lifelong active cognitive lifestyle does not significantly enhance executive function in Parkinson's 2. Age is the factor that has the greatest impact on executive function. 3. Higher cognitive reserve is associated with better motor function. 4. The differential effects of cognitive reserve may reflect the specific cognitive profiles of PD.

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Word count-Abstract 245, Paper 3496 (excluding references)

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1) Research project: A. Conception1,6,7,8. B. Organization1,6,7,8. C. Execution1,2,3,4,5.

2) Statistical Analysis: A. Design1,3,8. B. Execution1. C. Review and Critique 3,8.

3) Manuscript: A. Writing of the first draft 1. B. Review and Critique 2,3,4,5,6,7,8.

Informed Consent- Informed consent was obtained from all participants included in the study. The study received ethical approval from local National Health Service and University ethics committees and complied with the Declaration of Helsinki.

Abstract

Objective

Active lifelong cognitive lifestyles increase cognitive reserve and have beneficial effects on global cognition, cognitive decline and dementia risk in Parkinson's disease (PD). Executive function is particularly impaired even in early PD and this impacts on quality of life. The effects of lifelong cognitive lifestyle on executive function in PD have not been studied previously. This study examined the association between lifelong cognitive lifestyle, as a proxy measure of cognitive reserve, and executive function in people with Parkinson's disease.

Methods

69 people diagnosed with early PD without dementia were recruited as part of the Bilingualism as a protective factor in Age-related Neurodegenerative Conditions (BANC) Study. Participants completed a battery of tests of executive function. The Lifetime of Experiences Questionnaire (LEQ) was completed as a comprehensive assessment of lifelong cognitive lifestyle. Non-parametric correlations compared clinical measures with executive function scores. Cross-sectional analyses of covariance were performed comparing the performance of low and high cognitive reserve groups on executive function tests.

Results

Correlational analyses showed that better executive function scores were associated with younger age, higher levodopa dose, and higher LEQ scores. Higher cognitive reserve was associated with better motor function, but high and low cognitive reserve groups did not differ in executive function.

Conclusions

Cognitive reserve, although associated with global cognition, does not appear to be associated with executive function. This differential effect may reflect the specific cognitive profile of PD. The long-term effects of cognitive reserve on executive function in PD require further exploration.

Introduction

Cognitive impairment in Parkinson's Disease (PD) is manifested in abnormalities of executive function (Kudlicka, Clare, & Hindle, 2011), visuospatial function, attention and memory, with progression over time to dementia (Williams-Gray et al., 2009). More evidence is required about the factors that may be associated with better maintenance of cognitive function and prevention of dementia in PD (Hindle, Martyr, & Clare, 2014; Muslimovic, Schmand, Speelman, & de Haan, 2007). Impairment of executive function is particularly prevalent in PD (Kudlicka, et al., 2011) and may impact on functioning and quality of life for the person with PD and on carer wellbeing (Kudlicka, Clare, & Hindle, 2014), but also may be under-recognised by people with PD (Kudlicka, Clare, & Hindle, 2013). Executive function particularly relates to efficiency of fronto-parietal-striatal (Gawrys et al., 2014) degeneration, which may in part be a function of age (Mufson et al., 2016). In PD executive function may also be affected by deterioration in cholinergic subcortical white matter (Shin et al., 2012), the severity of motor function and depression and by the L-dopa dosage (Ng, Chander, Tan, & Kandiah, 2015).

Cognitive reserve represents individual differences in the processing of cognitive tasks which provide reserve against brain pathology (Tucker & Stern, 2011), reduce age-related decline in cognitive ability, including executive function (Valenzuela & Sachdev, 2006), and delay or prevent the development of dementia (Stern, 2009). The right prefrontal and parietal cortex may mediate the effects of cognitive reserve (Robertson, 2014) enhancing cognitive control and executive function (Bialystok, Craik, & Luk, 2012). Factors associated with cognitive reserve are intelligence, reading ability, education, occupation, socio-occupational class, and lifelong engagement in cognitive, social and physical activities, which is often termed

cognitive lifestyle (Barnett, Salmond, Jones, & Sahakian, 2006; Stern, 2009; Tucker & Stern, 2011) and these factors are used as proxy measures of cognitive reserve. Cognitive reserve promotes protective brain networks (Fischer, Wolf, Scheurich, & Fellgiebel, 2014), protects against hippocampal atrophy (Valenzuela, Sachdev, Wen, Chen, & Brodaty, 2008) and prefrontal neurotrophic changes (Valenzuela et al., 2012) and reduces cognitive decline in later life (Marioni et al., 2014). Higher education may enhance functional capacity in later life, with the effect mediated through executive function (Puente, Lindbergh, & Miller, 2015). There is evidence to suggest that in PD, intelligence (IQ) (Armstrong et al., 2012; Koerts, Tucha, Lange, & Tucha, 2012)and education (Hindle, et al., 2014) as single proxy measures of cognitive reserve contribute to enhancing cognitive performance and possibly slow the progression of global cognitive decline (Hindle, et al., 2014; Muslimovic, et al., 2007). A recent study has shown that higher education may protect cognition through an association with reduced cortical Lewy body pathology in PD (Lucero et al., 2015). Higher educational attainment may also be associated with lower motor impairment, possibly mediated through an extra-nigral effect on white matter integrity (Kotagal et al., 2015).

In a previous study we used separate components of education, socio-occupational class and recent social engagement as proxies for cognitive reserve in PD (Hindle et al., 2016). Higher educational level, socio-economic status and recent social engagement were associated with better cross-sectional global cognition. In those with normal cognition at baseline, higher educational level was associated with better global cognition after 4 years. Increasing age and low levels of a measure of recent social engagement (telephone use) were associated with an increased risk of dementia (Hindle et al., 2016). The study did not however include detailed assessments of executive function in PD. A recent study showed no effect of bilingualism as a single proxy for cognitive reserve on tests of executive function in PD (Hindle et al., 2015).

Researchers have suggested that more evidence is required on the effects of cognitive reserve in PD (Koerts, et al. 2013) and particularly on executive function. Since previous studies have focussed on single proxy measures of cognitive reserve, studies utilising more comprehensive assessments of cognitive reserve are needed. The Lifetime of Experiences Questionnaire (LEQ) has been developed as a more comprehensive tool for the assessment of lifelong cognitive lifestyle, covering education, occupation and social engagement across different stages of the lifespan, and has been used in studies of the effects of cognitive reserve on dementia (Valenzuela & Sachdev, 2007), but has not been used previously in PD.

This study aimed to examine the extent to which lifelong cognitive lifestyle is associated with performance on executive function tasks in people with PD without dementia. The hypothesis was that an active cognitive lifestyle serving as a proxy measure of cognitive reserve would be associated with better performance of executive function tasks in PD.

Method

Design

This was a cross-sectional study of people with PD and part of the Bilingualism as a protective factor in Age-related Neurodegenerative Conditions (BANC Study). The study received ethical approval from local National Health Service and University ethics committees and complied with the Declaration of Helsinki.

Participants

People with PD meeting UK Parkinson's Disease Society Brain Bank criteria (Daniel & Lees, 1993) and diagnosed by specialists were recruited through Movement Disorder Clinics in District Hospitals run by Geriatricians or Neurologists with specific expertise and training in

the assessment and management of PD. A subgroup of participants from the main BANC study was selected who met the criteria for this study. Inclusion criteria for this study were an MMSE (Folstein, Folstein, & McHugh, 1975) of 26 and over, age above 60 years and Hoehn and Yahr stage 1-3 (Hoehn & Yahr, 1967). A cut off of 26 on the MMSE was chosen to clearly exclude those with significant memory problems or dementia which may affect recall relevant to the cognitive reserve assessments. Exclusion criteria were the presence of other significant neurological disease and inability to provide informed consent. In order to minimise the contribution of fluctuations in motor function to performance of some executive tasks all assessments were conducted in participants' best motor "on" state.

As there are no data for minimal clinically significant changes on the executive tasks (Kudlicka, et al., 2011) using the DKEFS, in the original BANC study the sample size was based on an estimate of effect size. It was predicted that, with a sample size of 50, 80% power would be achieved when comparing monolinguals and bilinguals for detecting an effect size of 0.55 when the correlation of the covariates with executive control is 0.3. In this subgroup analysis the predicted effect size based on the final subgroup sample size was considered. With α set at .05 and a power of 80%, 28 participants would be needed to detect a large effect size (0.8) and 85 participants needed to detect a medium effect size (0.5) and 783 to detect a small effect (0.2) (Cohen, 1992). It was predicted that the cohort of ~70 should detect a medium to large effect size. In addition the literature was reviewed for similar studies with evidence of a sample size which would demonstrate a significant effect of lifelong cognitive reserve on executive function in healthy older people. One study, using the DKEFS executive tasks and a composite life-long cognitive reserve score, showed that cognitive reserve accounted for a significant amount of variance in the executive function (adjusted $R2 = .375$, $F(1, 60) = 37.620$, $p < .001$) using a sample of 65 older adults (Puente,

Lindbergh, & Miller, 2015). It was therefore assumed that a sample of ~70 could potentially show a significant relationship between cognitive reserve and executive function.

 Measures

(a) Demographic and clinical characteristics

Baseline demographic information was collected. PD motor severity was measured by the Unified Parkinson's Disease Rating Scale (UPDRS) motor score (Fahn & Elton, 1987) and stage by Hoehn and Yahr (Hoehn & Yahr, 1967). The levodopa equivalent dose was calculated (Tomlinson et al., 2010) and the cholinergic burden of all of the participants' medications included in Campbell's Cholinergic Index was calculated (Campbell et al., 2009). Mood was assessed with the Hospital Anxiety and Depression Scale depression score (HADS) (Snaith & Zigmond, 1994). Global cognition was assessed using the MMSE (Folstein, Folstein, & McHugh, 1975).

(b) Executive function

Tests were selected to cover three sub-domains of executive function. Mental generativity and speed were assessed with the Delis-Kaplan Executive Function System (D-KEFS; Baldo, Shimamura, Delis, Kramer, & Kaplan, 2001) Letter Fluency, Category Fluency, Design Fluency, and Trail Making Tests. Working memory was assessed with the Digit Span and Spatial Span sub-tests of the Wechsler Memory Scale (Wechsler, 1997) and a semantic word recall task, the Keep Track task (Friedman et al., 2008; Yntema, 1963). Set shifting and switching was assessed with the Test of Everyday Attention Elevator Counting with distraction sub-test (TEA; Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994).

(c) Cognitive reserve

Lifelong cognitive lifestyle, as a proxy measure of cognitive reserve, was assessed using the Lifetime of Experiences Questionnaire (LEQ) (Valenzuela & Sachdev, 2007). The LEQ assesses educational, occupational and cognitive activities at different stages through life and is a reliable and valid instrument for assessing complex lifespan mental activity which is protective against cognitive decline. Higher scores indicate a more active cognitive lifestyle, considered to be associated with higher cognitive reserve. A set of general questions is the same for all life stages and assesses the average frequency with which participants engaged in seven activities: visiting family/friends; developing/practicing an artistic pastime such as writing; playing a musical instrument; engaging in physical activity; reading; speaking a foreign language and travel. The general question scores are added to age-specific measures. The young adulthood score assesses the level of education attained prior to the age of 30. The mid-life score comprises scores for occupational complexity and education undertaken between the ages of 30 and 65 (or retirement). The late life section comprises scores for the frequency of engagement in activities more relevant to people over the age of 65 (or after retirement) including frequency of charity/volunteer work, membership of social clubs or groups, methods of seeking information about the world, and number of different types of material read. Additional scores are given for any formal education or paid work undertaken in later life. Each of the young-life, mid-life and late-life stages are weighted to contribute 33.33% to the total score. Reports on the reliability of the measure show Cronbach's alpha ranging from .43 to .84 (Valenzuela & Sachdev, 2007). The LEQ has been utilised in people over 60 years old (Valenzuela & Sachdev, 2007), and has been used to dichotomise research populations into those with high and low cognitive reserve (Valenzuela, et al., 2008).

Planned Analyses

Statistical analyses were conducted using SPSS v22 (IBM Corporation, NY, USA).

Spearman's correlations were conducted between baseline variables, the LEQ total score and sub-scores and tests of EF. The sample was then dichotomised around the mean total LEQ score into high cognitive reserve (H-CR greater than the mean) and low cognitive reserve (L-CR lower than the mean) (Valenzuela, et al., 2008). The H-CR and L-CR groups were compared for the baseline variables of age at the time testing, UPDRS motor score, HADS depression score, LED and cholinergic load using ANOVA, and H&Y stage using the chi-squared test. The General Linear Model tab in SPSS was utilised, with type I sum of squares without the interaction term, to assess the effects of cognitive reserve group on tests of executive function as dependent variables. Baseline variables in which there was a significant difference between H-CR and L-CR groups were included in the model before cognitive reserve groups. Effect sizes were calculated as the difference between the high and low cognitive reserve group mean values divided by the square root of the error mean square from the ANOVA table. This provides the standardised mean difference (SMD) accounting for the effect of motor function. Confidence intervals were calculated using the method described by (Hedges & Olkin 1985). The results were corrected for multiple comparisons using the Bonferroni correction. The participants who met the inclusion criteria but who failed to complete the full LEQ score were compared on demographic and clinical measures with those who completed the full analysis using ANOVA and Chi squared tests.

Results

From the main BANC cohort of 103 participants with PD, 83 met the inclusion criteria for the study (excluded 9 age<60, 9 MMSE <26, 2 H&Y >3). Sixty-nine people who completed all assessments (14 did not complete the full LEQ) were included in the analysis (50 male and 19 female) with a mean age of 73.1 (SD 6.7). There were no significant differences in demographic and clinical measures between those who completed the LEQ and those who

did not (age p=.979, UPDRS p=.549, HADS p=.607, LED p=.659, cholinergic load p=.143, Hoehn and Yahr p=.344). The median Hoehn and Yahr stage was 1 (47 stage 1, 18 stage 2, 4 stage 3), the mean disease duration was 5.8 years (SD 5.4), and the mean age of disease onset was 67.67 (SD 8.6). The mean total LEQ total score was 75.43 (SD 18.04) which compares very well with the mean LEQ score in the original LEQ validation paper (75.5 SD 20) (Valenzuela & Sachdev, 2007) but lower than that found in a more recent study in cognitively intact older people (men 97.9 ± 20.0, women 90.0 ± 24.5) (Valenzuela et al., 2013).

(Insert table 1 here)

Correlational analyses showed that better executive function scores were associated with younger age, higher LED, and higher LEQ scores. Higher LED showed statistically significant correlations with better performance of three tests of executive function (verbal fluency, design fluency and elevator counting). Higher LEQ total score correlated with better performance of design fluency, and higher midlife LEQ correlated with better performance of three tests of executive function.

(Insert table 2 here)

Comparing the cognitive reserve groups on baseline variables showed a significant difference between H-CR and L-CR groups on UPDRS motor scores, with the H-CR group having significantly better motor function. UPDRS was therefore included as a covariate in the model for total LEQ. Although the General Linear Modelling showed a trend to better performance on all executive function tests in the H-CR group compared with the L-CR group, with p<.05 and medium effect sizes on two tests of executive function (category and design fluency), no results were significant after correction for multiple comparisons.

(Insert tables 3 and 4 here)

Discussion

This is the first study to assess the effects of cognitive reserve on executive function in PD using a comprehensive tool specifically designed to assess lifelong cognitive lifestyle as a proxy for cognitive reserve. The overall results show that, comparing a more active lifelong cognitive lifestyle with a less active one, there was no significant difference in performance on tests of executive function in PD. Although performance was higher in all the tests of executive function in the high cognitive reserve group, with two tests having a medium effect size, none reached statistical significance after correction for multiple comparisons. However prior to correction the total LEQ score did correlate significantly with one test of executive function and midlife scores correlated significantly with three tests of executive function. Age at the time of testing was the largest predictor of all tests of executive function in PD. This confirms the importance of ageing for executive function in PD (Hindle, 2010), reflecting age-related degeneration of frontostriatal pathways (Mufson, et al., 2016),.

The results contrast with our previous study published in this journal which showed an effect of individual proxy measures for early, mid and late life cognitive reserve on global cognition and dementia in PD (Hindle, et al., 2016). That study did not however utilise detailed specific test of executive function. The lack of effect of LEQ, which includes intelligence and education, on executive function is surprising and differs from the previous findings which showed that education (Hindle, et al., 2013; Muslimovic, et al., 2007) and intelligence (Armstrong, et al., 2012; Koerts, et al., 2012) play a role in promoting cognitive reserve in PD, with intelligence having the strongest effect on global cognition (Armstrong, et al., 2012), Intelligence is also linked with better performance on executive function tests including design fluency in the general population (Arffa, 2007). It may be that cognitive reserve has a differential effect on global cognition compared with executive function in PD.

This may reflect the nature of the changes seen in cognition in PD, with executive function relating to frontostriatal dopaminergic deficiency and global cognition and dementia relating more to posterior cortical deficits in visuospatial function, memory and language, (Williams-Gray, et al., 2009) and it may be that the latter are more amenable to the beneficial effects of cognitive reserve.

The finding that high cognitive reserve was associated with better motor function fits with previous studies showing that higher education is associated with better motor performance (Kotagal, et al., 2015). Although the effect of cognitive reserve on design fluency was non-significant after correction it may be that in a larger sample with greater power this result would be positive. The correlation of total and midlife LEQ scores with design fluency and the medium effect size (although not statistically significant) of cognitive reserve group are interesting since cognitive reserve may particularly benefit non-verbal fluency (design fluency) which may be linked to right frontal lobe function (Baldo, et al., 2001; Suchy, Kraybill, & Gidley Larson, 2010). The effects of cognitive reserve in general may be in part mediated through enhanced prefrontal cortical function (Valenzuela, et al., 2012), particularly right prefrontal cortical function (Robertson, 2014), and this was thought also to be the case in PD (Suchy, et al., 2010).

The lack of an overall effect of total lifelong cognitive lifestyle on executive function may reflect relative preservation of executive function in this convenience sample of people with early PD. This fits with our previous findings of a lack of effect of bilingualism, as a single proxy for cognitive reserve, on executive function in this cohort (Hindle, et al., 2015). The fact that this is a convenience sample rather than a truly random sample may limit the study, although the mean and range of cognitive reserve is very similar to the validation study of the

LEQ (Valenzuela & Sachdev, 2007). However the majority of previous studies of cognitive reserve in PD have also been based on convenience samples which contributed to a previous meta-analysis of cognitive reserve in PD (Hindle, et al., 2013). The LEQ is quite a long questionnaire (not fully completed or declined by 14 participants) and this may limit its routine use in PD. Although the participants had a higher proportion of males than the general population of people with PD, there is no evidence in the literature that either cognitive reserve or executive function are influenced by gender. Other limitations of the study include the cross-sectional design and the relatively large number of measures used compared with the number of participants. Although this study extends the range of proxies for cognitive reserve in PD it does not examine the relationship between cognitive reserve, executive function, global cognitive decline and dementia. Since the trajectory of cognitive decline in PD may be non-linear (Aarsland, Muniz, & Matthews, 2011) there is a need for longitudinal studies (Hindle, et al., 2014; Muslimovic, et al., 2007). Although all participants were assessed in their best 'on' state, akinesia may possibly have affected some of the tasks which require a motor component (e.g. design fluency) and medication dosage may have been a complicating factor.

In future studies it would be important to estimate the sample size required to demonstrate significant effects of cognitive reserve in cross sectional and longitudinal studies. A much larger study may demonstrate a small effect size which may have been missed by this study, but which may have significant longitudinal effects (Cohen, 1992). In addition the prospective effect of cognitive reserve on the timing and nature of cognitive impairment in PD would be of interest. A prospective study of the effects of cognitive reserve in a large cohort would be required to demonstrate any potential long term benefit of cognitive reserve in PD. This could be linked with studies of other biomarkers and predictors of cognitive

impairment and dementia in PD including the use of neuroimaging. In such large studies it would be important to consider a shorter assessment of lifelong cognitive reserve along with easier to apply clinical assessments of executive function.

Conclusions

Age at the time of testing was the most important predictor of performance on tests of executive function in people with PD. Higher cognitive reserve was associated with better motor function. An active lifelong cognitive lifestyle as a proxy for cognitive reserve was not associated with significantly better performance on tests of executive function in PD. Previous studies have shown a beneficial effect of cognitive reserve on global cognition and dementia in PD. This differential effect, whereby cognitive reserve benefits global cognition but not executive function, may reflect the different cognitive profiles seen in PD (Williams-Gray, et al., 2009). These differential effects of cognitive reserve on executive function compared with global cognitive function, and the long-term effects of cognitive reserve on executive function in PD, should be explored further in larger longitudinal studies.

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Table 1 Participant Characteristics

Demographic and clinical	Mean (range & SD)
Age	73.1 (61-88; 6.74)
UPDRS	21.5 (4-56; 10.92)
H&Y	1 {median}, (1-3)
HADS depression	3.84 (0-18; 2.71)
Levodopa equivalent dose (LED)	487.8 (0-2137; 382.8)
Cholinergic load	0.46 (0-4; 1.28)
MMSE	29 (26-30; 1.071)
LEQ	75.4 (29.-107; 18.04)
D-KEFS verbal fluency total correct raw score	39.29 (13-68; 12.54)
D-KEFS category fluency total correct raw score	36.08 (13-60; 10.04)
D-KEFS design fluency filled + empty + switching total correct raw score	21.51 (7-48; 6.95)
D-KEFS TMT Part 4 raw score (seconds)	143.84 (50-240; 59.50)
Digit span backwards total	6.15 (2-12; 2.10)
Spatial span backwards total	6.26 (2-10; 1.70)
Keep Track task total correct	7.39 (2-11; 2.15)
TEA Elevator counting with distraction raw score	6.97 (2-10; 2.54)

Abbreviations- Delis-Kaplan Executive Function System (D-KEFS), Hoehn and Yahr (H&Y), Hospital Anxiety and Depression Scale (HADS), Lifetime of Experiences Questionnaire total (LEQ), Mini Mental State Examination (MMSE), Tests of Everyday Activity (TEA), Trail Making Test (TMT), Unified Parkinson's Disease Rating Scale (UPDRS)

Table 2

Spearman's correlations (ρ)- clinical and demographic factors and EF

N=69	Age	UPDRS	HADS depression	LED	Cholinergic load	LEQ	LEQ-Y	LEQ-M	LEQ-L
D-KEFS verbal fluency total correct raw score	**-.371****	-.084	.036	**.339****	.074	.151	.097	**.253***	.060
D-KEFS category fluency total correct raw score	**-.406****	-.046	-.109	.177	-.054	.201	.149	.202	.215
D-KEFS design fluency filled + empty + switching total correct raw score	**-.537****	-.152	-.092	**.226***	-.175	**.250***	.150	**.260***	.167
D-KEFS TMT Part 4 raw score (seconds)	**.475****	.121	-.135	.030	.133	-.020	-.016	-.049	-.048
Digit span backwards total	**-.238***	-.214	.013	.083	-.027	.140	.051	.167	.083
Spatial span backwards total	**-.287****	-.177	-.204	-.084	-.122	.069	.031	.055	.021
Keep Track task total correct	**-.328****	-.134	-.128	-.074	-.141	.171	.108	.144	.186
TEA Elevator counting with distraction raw score	**-.371****	-.097	.048	**.235***	-.066	.199	.113	**.254***	.072

Significant results in bold. ** p<.01, *p<.05

Abbreviations: Delis-Kaplan Executive Function System (D-KEFS), Hospital Anxiety and Depression Scale (HADS), Lifetime of Experiences Questionnaire total (LEQ), Levodopa equivalent dose (LED), Lifetime of Experiences Questionnaire for young life (LEQ-Y) midlife (M-LEQ), late life (L-LEQ), Tests of Everyday Activity (TEA), Trail Making Test (TMT), Unified Parkinson's Disease Rating Scale (UPDRS)

Table 3 Comparison High Cognitive Reserve (H-CR) and Low Cognitive Reserve (L-CR) groups

Variable	H-CR Mean (SD) Median for H&Y	L-CR Mean (SD) Median for H&Y	ANOVA F (sig)	Chi squared (sig)
Age	71.97 (7.08)	74.68 (6.83)	2.64 (.111)	
UPDRS	18.56 (9.69)	24.32 (12.09)	**4.36 (.041)***	
H&Y	1 (1= 27, 2=7, 3=1)	1 (1=20, 2=11, 3=3)		2.91 (.233)
HADS depression	3.51 (1.99)	4.32 (3.30)	1.53 (.220)	
LED	560.32 (406.75)	430.39 (359.55)	1.972 (.165)	
Cholinergic load	.34 (.80)	.41 (1.01)	.098 (.756)	

Significant results in bold. *p<.05

Abbreviations- Hoehn and Yahr (H&Y), Hospital Anxiety and Depression Scale (HADS), High cognitive reserve (H-CR), Low Cognitive reserve (L-CR), Levodopa equivalent dose (LED), Unified Parkinson's Disease Rating Scale (UPDRS)

Table 4 Cognitive reserve groups and executive function

N=49 completing all tests	H-CR Mean (SD)	L-CR Mean (SD)	Direction of effect	df	F (sig)	Eta squared ηp2	Effect size (CI)
D-KEFS verbal fluency total correct raw score	44.35 (9.65)	39.30 (13.23)	H-CR > L-CR	2	2.227 (.142)	.046	.436 (.147-.725)
D-KEFS category fluency total correct raw score	38.85 (9.07)	33.39 (9.19)	H-CR > L-CR	2	4.317 (.043)*	.086	.592 (.3-.884
D-KEFS design fluency filled + empty + switching total correct raw score	24.88 (7.66)	20.30 (6.29)	H-CR > L-CR	2	4.890 (.032)*	.096	.644 (.351-.937)
D-KEFS TMT Part 4 raw score (seconds)- lower=better	131.88 (58.01)	145.26 (55.54)	H-CR > L-CR	2	.588 (.447)	.013	.234 (-.053-.521)
Digit span backwards total	6.69 (1.93)	6.13 (2.24)	H-CR > L-CR	2	.828 (.368)	.018	.266 (-.021-.553)
Spatial span backwards total	6.65 (1.57)	6.35 (1.43)	H-CR > L-CR	2	.455 (.503)	.010	.196 (-.09-.482)
Keep Track task total correct	7.81 (2.29)	7.39 (1.64)	H-CR > L-CR	2	.391 (.535)	.008	.211 (-.075-.497)
TEA Elevator counting with distraction raw score	7.77 (2.26)	6.57 (2.74)	H-CR > L-CR	2	2.862 (.097)	.059	.475 (.185-.765)

* Not significant after Bonferroni correction

Abbreviations: Confidence interval (CI), Delis-Kaplan Executive Function System (D-KEFS), Hospital Anxiety and Depression Scale (HADS),High cognitive reserve (H-CR), Low Cognitive reserve (L-CR), Lifetime of Experiences Questionnaire (LEQ), Tests of Everyday Activity (TEA), Trail Making Test (TMT), Unified Parkinson's Disease Rating Scale (UPDRS)