Investigating the relationship between impulsivity and executive function in Parkinson's disease, and healthy older and younger participants: A quantitative database and real-world study.

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ABSTRACT

Executive function (EF) in this study will be explored in older healthy controls and Parkinson's Disease patients, with regards to working memory (WM) in younger healthy controls. Past literature suggests a lack of understanding between EF, WM and impulsivity despite vast research that shows the relationship between these concepts are related to a multitude of negative behaviours such as substance abuse (Moeller et al., 2004), addiction (Zhou et al., 2014; 2016), and the development of impulsive-compulsive disorders (ICDs) in neurodegenerative diseases such as Parkinson's (Foster et al., 2013).

The present study intends to build on previous literature by investigating the relationship between the two variables in 102 younger healthy controls, 196 older healthy controls, and 498 PD patients.

Correlation analyses supported literature that suggests impulsivity is higher in younger participants and that the relationship between impulsivity and EF is different across age groups; however, previous assumptions that PD patients who have not yet begun medication will be less impulsive than age-matched controls and therefore exhibit an altered relationship between their EF scores were not met. Future research should expand on data using unmedicated PD patients to better understand the relationship between impulsivity and EF, and the development of ICDs.

KEY WORDS:	EXECUTIVE FUNCTIONS	WORKING MEMORY	IMPULSIVITY	PARKINSON'S DISEASE	IMPULSIVE-COMPULSIVE DISORDER

Introduction

Executive function refers to a collection of top-down mental processes that are required for goal-directed behaviour (Shallice, 1982) and encompasses a group of cognitive skills that control inhibition, attention, working memory, and cognitive flexibility (Diamond, 2013). Due to the diverse nature of executive functions, the focus of research outside of Parkinson's disease will largely be on working memory and its role in temporarily storing and managing incoming sensory information to carry out complex cognitive tasks (Baddeley and Hitch, 1974). Impulsivity, defined as swift action without forethought of conscious judgement (Hinslie, 1940), and its relationship with working memory is a widely researched concept within a range of clinical disorders such as substance abuse or addiction with a focus on the relationship between impulsivity and the deterioration of cognitive functions (Kalenscher et al., 2006; Verdejo-García, 2008).

Within addiction research, evidence supports the current hypothesis that long-term drug use of cocaine and other psychostimulants that are dopamine agonists impair executive functions, specifically working memory and inhibition control – functions of which are mediated by the prefrontal cortex and limbic system (Dalley et al., 2007). Further evidence for cocaine and other stimulants such as methamphetamine affecting impulsivity and working memory is supported in reports of higher impulsivity scores on the Barratt Impulsivity Scale-11 (BIS-11) associated with decreased results on working memory tasks (Moeller et al, 2004; Albein-Urios et al., 2012; Sleigh et al., 2014; Minozzi et al., 2015). Additionally, the impact of methadone and ketamine use groups self-reporting higher impulsivity scores correlates with significantly lower working memory task results than a non-drug using control group (Zang et al., 2016), however research in this area also shows impulsivity acts as a vulnerability factor for engaging in substance abuse (von Diemen et al., 2008; Jentsch, 2009) so the true nature of whether impulsivity is a symptom or an effect of substance abuse is unclear and requires further research.

Furthermore, impulsivity and working memory are explored within areas of addiction other than narcotic abuse. Alcohol-dependent patients and internet addictive individuals both tested similar scores in increased impulsivity and decreased working memory scores on the BIS-11, Wisconsin Card Sorting test and Digit Span (Zhou et al., 2014), while pathological gamblers presented with significantly higher scores of impulsivity and cognitive dysfunction than the control group (Zhou et al., 2016). Gunn and Finn (2013) theorised that reduced working memory capacity in any form may promote impulsivity, which in turn predisposes the participant to addiction.

Despite the prominence of measuring impulsivity and working memory in addiction, the emphasis of research is based on how the two variables have a negative effect following substance abuse and how further research can inform vulnerability factors on people with impulsive characteristics (von Diemen et al., 2008; Stautz et al., 2016). Research lacks the understanding of how impulsivity may affect working memory prior to the onset of an addiction.

Another aspect of research that is often overlooked in this area is age and how impulsivity levels may affect working memory in different age ranges, and how impulsivity may change over the course of a lifetime. Focus of the research in this area is mainly concentrated on younger samples and discovering a relationship

between impulsive traits and related life outcomes (Tsukayama et al., 2013), health behaviours (Stautz et al., 2016), and substance use disorders (von Diemen et al., 2008). Research that does offer perspective on impulsivity across the lifespan disregards the impact of working memory but offers a divided opinion on whether age impacts impulsivity. The majority of findings in this area suggest impulsivity levels start gradually decreasing in a linear pattern after preadolescence (Steinberg et al., 2008; Fino et al., 2014) and are supported by literature that infers dopamine (DA) gradually declines across the lifespan, and thus impulsive behaviours decline likewise (Nagel et al., 2008; Li et al., 2010; Rutledge et al., 2016; Abdulrahman et al., 2017). However, both Nagel et al. (2008) and Li et al. (2010) only look at DA decline in regard to variations in DA gene signalling; while Rutledge et al. (2016) look at decreasing levels of DA in the hippocampus of their participants, ergo do not fully explore the declining dopamine hypothesis that suggests lower levels of impulsivity has a negative effect on working memory and executive function. Furthermore, a study that explores functional and dysfunctional impulsivity in a sample of older adults, aged 65 and above, found that elder participants had higher levels of dysfunctional impulsivity than young adults (Morales-Vives and Vigil-Colet, 2012). This inconsistency within the research supports further analysis of the effects of ageing on both impulsivity, working memory and executive function.

Previous literature that explores the neurobiological basis of impulsivity holds inconclusive results as to which areas of the brain correlate with impulsive behaviours. Bickel et al (2007; 2012) argue that there are overlapping brain areas associated with an impulsive decision system embodied within the limbic and paralimbic brain regions that, within addiction, exhibit more control than the prefrontal cortex that is associated with executive function. However, Dichter et al. (2012) suggest a dysfunctional output of the nigrostriatal dopamine pathway that mediates the processing of rewards. Furthermore, the mesolimbic pathway that transports dopamine from the ventral tegmental area to the nucleus accumbens in the ventral striatum (Ikemoto, 2010) is attributed to detecting rewarding stimuli and reward hypersensitivity, both recognised as features of impulsivity (Martin and Potts, 2004; Adinoff, 2007). Additionally, clinical research has associated damage to the orbital frontolimbic system with increased results in self-reported and behavioural measures of impulsivity in borderline personality disorder (Lieb et al., 2004; Berlin, 2005; Kahnt and Tobler, 2017).

Seemingly the specific neuroanatomy for impulsivity is still in question, as evidence suggests impulsivity is associated with a wide range of areas such as the nigrostriatal and mesolimbic pathways (Ikemoto, 2010; Dichter et al., 2012) and orbital frontolimbic cortex (Lieb et al., 2004; Berlin, 2005; Kahnt and Tobler, 2017). However, research agrees that underpinning each of the structures and pathways discussed is the neurotransmitter dopamine.

In Parkinson's disease (PD) research, a neurodegenerative disorder characterised by progressive nigrostriatal dopamine depletion (Callesen et al., 2014), the importance of DA is highlighted within impulsivity as using DA agonist replacement therapy exacerbates impulsive-compulsive behaviour in some patients (Pine et al., 2010). Following the administration of medications such as Levodopa, that act as a precursor for dopamine, and Carbidopa, a DA agonist, literature shows a small percentage of patients are seen to develop impulse-control problems that extend to

compulsive gambling, shopping, eating, and hypersexuality (Weintraub et al., 2014). The use of DA precursor and agonist medications has shown to be largely successful in reducing the motor symptoms that are debilitating in PD that include bradykinesia, the slowness of muscle movement; tremors; rigidity; and gait issues (Vijverman and Fox, 2014). However, manipulating levels of DA within the ventral striatum is associated with an increased interest in obtaining rewards and novelty seeking (Leyton et al., 2002), and inducing the previously denervated nigrostriatal and mesolimbic systems with DA agonists accounts for increased behavioural fluctuations, including impulsivity (Thobias et al., 2010). Furthermore, prior to the onset of DA agonist medication use, results shows decreased levels of novelty seeking behaviour in PD patients potentially due to decreased dopamine volume (Raja and Bentivoglio, 2012). This association between impulsivity levels prior to dopamine medication administration suggests that the increase of impulsive behaviours is related directly to DA manipulation in some PD patients.

In Parkinson's disease research the focus of impulsivity is on the prevalence of impulsive-compulsive disorders (ICDs) that can be exhibited in a range of patients with limited understanding as to why. ICD figures range from 6% of Parkinson's patients without, and 16-35% with, a dopamine agonist treatment (Papay et al., 2011; Weintraub et al., 2012; Okai et al., 2016), yet despite knowledge of impulsive-compulsive behaviours affecting approximately 10% of patients, it remains to be examined as to whether Parkinson's disease itself is associated with impulsivity, or if it is the dopamine medication causing impulsivity issues.

Past research has found the administration of dopamine agonists in young PD patients (average age of 45) who had never previously been medicated resulted in increased temperament changes in novelty seeking and reward dependence (Bódi et al., 2009). Impulsive decisions based on good outcomes also increased in medicated Parkinson's patients compared to unmedicated (Frank et al., 2004) which suggests that if impulsivity increases after DA manipulation, those with higher levels of impulsivity prior to medication may be at risk of developing ICD's.

With respect to executive function in PD, assessment involves testing a patient's cognitive performance throughout the duration of the disease from onset. The emphasis of research that is aimed at impulsivity and executive function in Parkinson's patients is involved in locating the cognitive deficits a patient is experiencing and using progressive initiatives to assist patients and carers as the disease progresses (Woods and Tröster, 2003; Kudlicka et al., 2011) rather than understanding the relationship between the two constructs.

The cognitive deficits known to correlate with PD prior to medication are executive function tasks such as task-set switching, visuospatial tasks, concept-formation, verbal fluency, memory recall and problem solving - all linked to fronto-executive activations mediated by the dorsal striatum (Balleine et al., 2007; Broeders et al., 2013; Goldman et al., 2014). This disturbance has been suggested that mesocortical DA neurons originating from the ventral tegmental area affected in PD are not innervating the prefrontal cortex that is associated with executive function (Tassin, 1997). Executive function capacity is also decreased following the use of dopamine medication in tasks such as inhibiting interfering stimuli and digit span tasks (Woods and Tröster, 2003) also due to the depletion of dopamine in the striatonigral and mesocortical DA systems of the frontal lobes (Sawamoto et al., 2008; Foster et al.,

2013). This research supports how a dopamine deficiency effects executive function in PD patients, and with impulsivity also being underlined by DA, it solidifies the need for further research into how the two interact within PD patients who are on and off medication.

Furthermore, cognitive deficits can be detected in early unmedicated patients (Santengelo et al., 2015), however, the means of testing these deficits are mixed. Research suggests that the sensitivity of cognitive tests such as the Letter-Number Sequencing and Digit Span tasks are unable to detect cognitive dysfunction in early PD patients (Schneider et al., 2010) with research advising clinicians to apply further tests before drawing conclusions of impaired executive function from these tasks (Egeland, 2015). However, information processing speed tested by the Symbol Digit Modality task has been appraised for its detected of impaired performance in PD (Benedict et al., 2017; Silva et al., 2018). The contrast in results for cognitive testing in PD shows that development into using tasks that detect dysfunction needs to be equal across all realms to aid diagnosis.

Additionally, research in this area rarely evaluates the relationship between impulsivity and executive functions as a whole in Parkinson's disease, unless combined with another factor such as depression (Foster et al., 2013), personality (Poletti and Bonuccelli, 2012), or the results of dopaminergic medication (Djamshidian et al., 2011; Papay et al., 2011), and there is no research on exploring executive function in impulsivity with Parkinson's patients off medication. Furthermore, cognitive decline is common in elderly people (Winblad et al., 2004; Curerri et al., 2018), with deficits in executive function showing a consistent decline in both PD and older healthy controls (Leung et al., 2015), and an increase in cognitive impairments in baseline measures of PD patients diagnosed at an older age (Chaudhuri et al., 2005; Chaudhuri et al., 2006). These findings, along with Morales-Vives and Vigil-Colet's (2012) impulsivity research in an increase of dysfunctional impulsivity in the elderly discussed above, highlights the need for an increase in research surrounding executive function and impulsivity in older healthy controls. Research is needed to better understand how these variables develop with age as added benefits to understanding how these variables interlink prior to the effects of Parkinson's would aid average baseline results for a multitude of neurodegenerative diseases that involve cognitive testing, and in a non-clinical sample would build on previous recommendations of providing an index of age-dependent cognitive performance in the elderly (Abdulrahman et al., 2017).

Rationale

Evidence throughout has highlighted the need for further research into how impulsivity and working memory interact pertaining to both advancing age and PD patients who are both on and off medication. Impulsivity has been significantly explored in addiction research, but its role is unclear as to whether it is a vulnerability factor for substance abuse or a symptom (von Diemen et al., 2008; Zang et al., 2016), and lacks an understanding of how impulsivity may affect working memory prior to the onset of substance abuse.

Likewise, in Parkinson's research a consensus has still not been met as to whether impulsivity is associated as a symptom of PD or due to the dopaminergic medication (Djamshidian et al., 2011; Papay et al., 2011). There is also no research specifically

aimed at PD patients off medication with regards to the relationship between impulsivity and executive function.

Furthermore, age in impulsivity and working memory research is explored in a limited capacity in that participants are usually of a younger age and is often studied without consideration for working memory. Despite inconsistencies within impulsivity levels in older age (Steinberg et al., 2008; Morales-Vives and Vigil-Colet, 2012) research is still limited in the area, and research that does consider working memory in age focuses on cognitive impairments (Leung et al., 2015) despite previous recommendations of providing an age-dependent cognitive performance index in the elderly (Abdulrahman et al., 2017).

Aims

To build on gaps in the research critiqued above, the aims of these study are three-fold:

- Assess whether impulsivity is altered in unmedicated, early-stage Parkinson's disease patients.
- Assess any changes in the relationship between impulsivity and executive functions in older Parkinson's patients and healthy controls.
- Assess the relationship between impulsivity and working memory in younger and older healthy controls to establish the link between the variables in an age-varying non-clinical sample.

Hypothesis

- H1: Participants with Parkinson's disease who have not yet begun medication will be less impulsive than age-matched controls
- H2: There will be an altered relationship between executive function ability and impulsivity in the PD group compared to the older healthy control group
- H3: Younger participants will be more impulsive than older participants
- H4: The relationship between executive function and impulsivity will be different across the age groups

Methods

Due to this study utilising data from the Parkinson's Progression Markers Initiative (PPMI) quantitative database and real-world data collected, two methods sections have been created to give greater clarity on each aspect of the project. Methods I will inform the collection of real-world data, whilst Methods II will follow PPMI data collection regulations.

Methods I

Design

This is a correlational study assessing impulsivity and working memory in a group of participants recruited through opportunity sampling in Manchester Metropolitan's Research Participation Pool and from an announcement made on the researcher's behalf in a Manchester Metropolitan Psychology society meeting. A modified online

digit span (Wechsler, 1997) was used to measure working memory, and impulsivity was tested on the Barratt Impulsivity Scale (Stanford et al., 2009).

Participants

A total of 118 participants, aged between 18-63, completed the online questionnaire and digit span. 16 participants were removed to reduce the maximum age to 29 for comparisons against the older healthy controls from the quantitative database, who's ages started at 30. This left 102 participants aged 18-29, all of whom were healthy, with no known cognitive impairments.

Measures

Barratt Impulsivity Scale-11

The Barratt Impulsivity Scale-11 (BIS-11) (APPX 1) consisted of 30 questions on a Likert scale of 'Rarely/Never' to 'Almost Always/Always' and was used to determine participant's impulsivity score that included questions such as 'I plan tasks carefully' and 'I say things without thinking'. These scores were totalled for overall impulsivity. The BIS-11was found to have high internal reliability ($\alpha = .83$).

Digit Span

Executive function was, in this instance, tested on working memory through a modified online digit span (APPX 2). Participants were presented with instructions on how to answer and were given two attempts at a 3-digit forward practise, and 3-digit reverse practise, before beginning each marked attempt.

Each sequence of digits was generated using an online random number generator (Hedges, 2018). Using Qualtrics (2018), 3 digits were first presented to participants '7-3-9', followed by a series of 4 digits that increased by 1 number each correct answer until it reached a sequence of 9 digits altogether. During the first round of sequences the participants were asked to report the digits exactly as they appeared and would be sent to the reverse digit span section if two incorrect attempts were made.

Following the first round of digits, participants were then asked to repeat the process but report the digits in reverse to the sequence they had seen, so the correct answer for '3-9-6' would be '6-9-3', and so on until 9 digits. The total score for digit span results were points for the highest number sequenced reached, with 2 points awarded per digit for a correct answer on the first attempt, and 1 point awarded per digit for a correct answer on the second attempt.

Permission was sought through email for the use of the BIS-11 and digit span test.

Procedure

Participants who applied through the MMU participation pool and MMU Psychology Society were provided with an invitation letter (APPX 3) and those who proceeded to the study were provided with further information in the participant information sheet (APPX 4) and agreed to terms of a consent form (APPX 5) that detailed what the study entailed. Age was recorded as a measure for later analysing the results, followed by the BIS-11, and then the forward and reverse digit span. Once all tasks were completed, a debrief sheet (APPX 6) was provided to reiterate aims of the

study to participants and provide an anonymous code generator which they were required to fill in if they wished to withdraw from the study at a later date, or request research details.

Analysis

All analysis was completed using SPSS (Version 24). On the younger healthy controls, a correlation analysis was carried out to test the relationship between impulsivity and working memory using total scores from the BIS-11 and total digit span, and a Fisher's r-to-z test was carried out to compare correlations between impulsivity and working memory from the younger healthy control to their older healthy control equivalents. Lastly, a Fisher's exact test was used to calculate the difference in impulsivity scores between younger and older healthy controls. (APPX 11)

Ethical considerations

The research conducted in this study adhered to the guidelines stated by the British Psychological Society (2009) and was reviewed by the Department of Psychology Ethics Panel and approved by the Faculty of Health and Social Care Research Ethics Committee at Manchester Metropolitan University, ergo following all correct procedures with regard to consent, confidentiality, debriefing, and deception (APPX 7).

Vulnerable participants were not involved in this study as all were over the age of 18 and were of sound mind and ability to give consent following the provision of study information. Each participant was provided with the necessary information prior to completion of the study, agreed to the terms of a consent form which listed the study's aims and their right to withdraw, and a debrief was provided upon completion of the questionnaires and test. A code generator was provided for anonymity in the data, all of which was stored in compliance with the Data Protection Act (1998).

Methods II

Data used in the preparation of this article were obtained from the Parkinson's Progression Markers Initiative (PPMI) database (www.ppmi-info.org/data). For up-to-date information on the study, visit www.ppmi-info.org.

Design

The PPMI study is a 5-year longitudinal study funded by the Michael J. Fox Foundation (MJFF) and industry partners with an overarching aim to identify one or more biomarkers of Parkinson's disease progression using brain imaging, clinical evaluations, and biospecimen data (PPMI, 2017).

Participants

A total of 694 participants were collected in the PPMI database; 498 Parkinson's disease patients (PD) and 196 older healthy controls, aged between 30-84 years old.

Measures

Tests used from the PPMI database included the following tests: Questionnaire for Impulsive-Compulsive Disorders (QUIP) (APPX 8), Letter-Number Sequencing (APPX 9), and Symbol Digit Modalities (APPX 10).

Procedure

Each procedure was carried out subject to the guidelines highlighted in the study protocol, available to read at http://www.ppmi-info.org/study-design/research-documents-and-sops/.

Analysis

A correlation analysis was carried out in both the older healthy controls and PD patients to test the relationship between impulsivity using the QUIP and executive function using Letter-Number Sequencing and Symbol Digit modality scores.

An analysis of variance was performed on older healthy controls and PD patients following the creation of two groups from QUIP scores – those who showed evidence of an impulsive issue and those who did not – in both Letter-Number Sequencing and Symbol Digit modality scores. A Fisher's Z-test was carried out on older healthy controls and PD patients to compare the correlation between each group's impulsivity scores on the QUIP and executive function scores on Letter-Number Sequencing and Symbol Digit modality tasks.

Finally, an independent t-test was performed on older healthy controls and PD patient to test for differences in impulsivity between the groups.

Ethical Consideration

The data collected in this study was performed in accordance with the Good Clinical Practise and the International Conference on Harmonization guidelines, as well as any applicable national and local regulations (Parkinson's Progression Markers Initiative, 2017). Each participant gave informed consent, and anonymity is enforced through patient code numbers.

Results

Descriptive statistics were created for the participants in both the younger healthy control sample, and data collected from the Parkinson's Progression Markers Initiative (PPMI) database. Table 1 summarises the demographics of younger controls with their scores on the digit span and impulsivity test. The average age of younger healthy controls was 24 years old.

Table 1

Age and Cognitive Scores in Younger Healthy Controls

	Mean (n=118)	**Standard Deviation** (n=118)
Age (years)	24.00	8.74
Forward Digit Span*	9.26	3.09
Reverse Digit Span*	6.90	4.34
Total Digit Span**	16.16	6.41
Barratt Impulsivity Scale-11	76.36	11.06

*Total correct out of 14

**Total correct out of 28

Table 2 summarises the demographics of older healthy controls and patients with Parkinson's disease (PD) with impulsivity scores, and two executive functions tasks. The average age for age for older healthy controls was 60 years old, and average age for PD patients was 61.

Table 2

Age, Impulsivity and Cognitive Scores in Older Healthy Controls and PD Patients

	Older Healthy controls (n=196)	**PD** (n=498)
Age (years)	60.00 (*11.17*)	61.00 (*9.83*)
Questionnaire for Impulsive-Compulsive Disorders	0.32 (*0.78*)	0.40 (*2.72*)
Letter-Number Sequencing*	11.76 (*2.73*)	11.37 (*10.04*)
Symbol-Digit Modality**	46.75 (*10.50*)	41.16 (*9.83*)

*Total score out of 21

**Total score out of 110

Correlational analysis

Multiple bivariate Spearman's correlations were carried out to test for relationships between impulsivity and executive function. In younger healthy controls, correlations were tested between impulsivity and digit span scores, the results of which can be seen in Table 3.

Table 3

Correlation analysis

Control variable		**Forward Digit Span**	**Reverse Digit Span**	**Total Digit Span**
Barratt Impulsivity Scale-11 (BIS-11) Total	*p*	0.85	0.48	0.69
	Rho	0.02	-0.07	-0.04

For older healthy controls and PD, correlations were tested between impulsivity, Letter-Number Sequencing and Symbol Digit modality scores. The results of which can be seen in Table 4.

Table 4

Correlation analysis

Control variables			**Letter Number Sequencing**	**Symbol Digit Modality**
Questionnaire for Impulsive-Compulsive Disorders Total	Older HC	*p*	0.15	0.50
		Rho	-0.10	-0.05
	PD Patients	*p*	0.34	0.51
		Rho	-0.04	-0.03

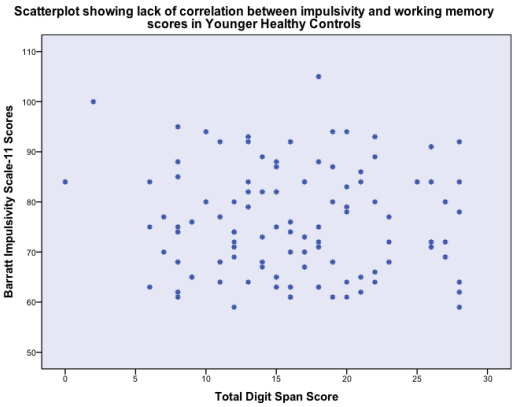

Figure 1.1: Scatterplot showing the correlation in younger healthy controls impulsivity and executive functions

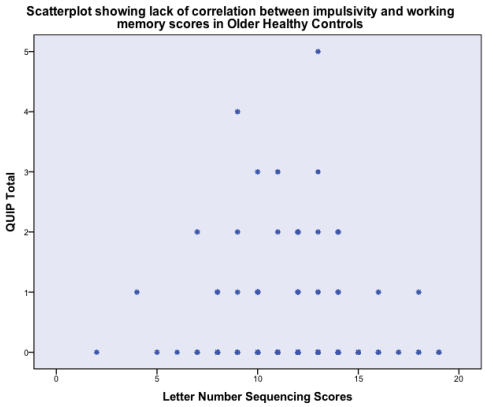

Figure 1.2: Scatterplot showing the correlation in older healthy controls impulsivity and Letter-Number sequencing scores

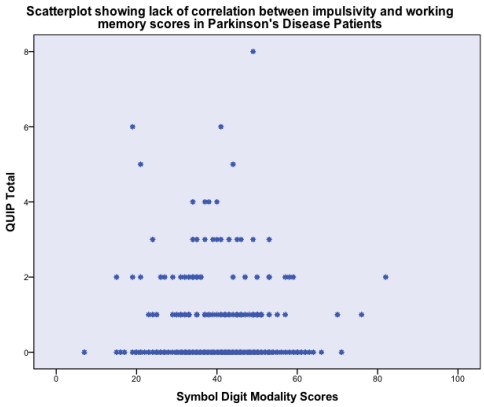

Figure 1.3: Scatterplot showing the correlation in PD patients impulsivity and Symbol Digit modality scores

The scatter diagrams above have been provided as an example of the lack of correlation between test scores in younger healthy controls, older healthy controls and PD patients. The results from the correlations revealed that the relationships between impulsivity and executive function were not significant for either younger healthy controls ($r_s(118) = -0.04$, $p = 0.69$), older healthy control's Letter Number Sequencing scores ($r_s(195) = -0.10$, $p = 0.15$), older healthy controls Symbol Digit Modality scores ($r_s(195) = -0.05$, $p = 0.50$), PD patient's Letter Number Sequencing scores ($r_s(493) = -0.04$, $p = 0.34$) or PD patient's Symbol Digit Modality scores ($r_s(493) = -0.03$, $p = 0.51$).

Fisher's Z-tests were carried out on the correlation coefficients that resulted from the correlations between impulsivity and executive function scores in the three groups (YHC, OHC and PD) in order to test whether these were significantly stronger in any of the groups compared with the others. The coefficients on the correlation computed between younger healthy controls Letter-Number Sequencing and Symbol Digit modality scores were significantly higher than those in older healthy controls (Letter-Number Sequencing: z = 2.69, $p<0.001$; Symbol Digit modality: z = 3.14, $p<0.001$) and PD patients Letter-Number Sequencing: z = -0.01, p = 0.99; Symbol Digit modality: z = -0.10, $p = 0.92$). Comparisons between older healthy controls and PD patients were not significant (Letter-Number Sequencing: z = -1.74, $p = 0.08$; Symbol Digit modality: z = -0.02, $p = 0.83$).

Furthermore, an independent t-test was performed on older healthy controls and PD patients to test whether there was a difference in impulsivity between the two groups, with no significant difference found ($t(432.84) = -1.06$, $p = 0.29$: 95% CI: -0.74-0.07).

Finally, to compute impulsivity scores between younger and older healthy controls, BIS-11 scores ≥ 74 (Patton et al., 1995; Stanford et al., 2009) and QUIP scores ≥ 8 (Weintraub et al., 2009) were coded '1' for high impulsivity, and anything below these scores were '0' for no impulsivity. A Fisher's exact test was used to calculate differences in impulsivity between the two groups; there was a significantly greater proportion of younger healthy controls with high impulsivity (measured by the BIS-11) than older healthy controls with high impulsivity (measured by the QUIP), $p>0.001$: 95% CI 0.12-0.21.

Comparison between PD patients with and without evidence of an impulsivity issue

The PD and older healthy controls groups were classified as either with impulsivity issues (QUIP > 1) or without (QUIP = 0). The subsequent bar charts illustrate the comparisons of whether participants exhibited impulsivity issues in older healthy controls and Parkinson's disease patient's in executive functioning task scores.

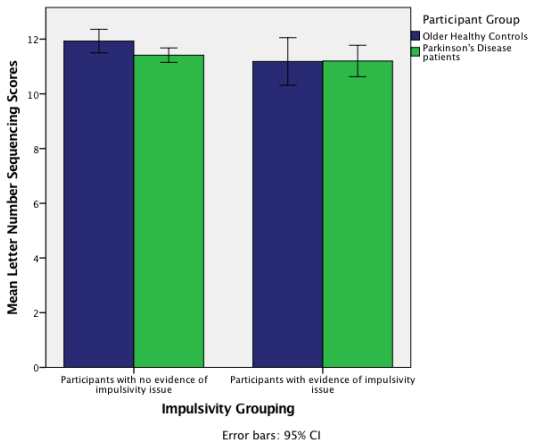

Figure 2.1: Bar Chart illustrating mean Letter Number Sequencing scores across older participants impulsivity grouping

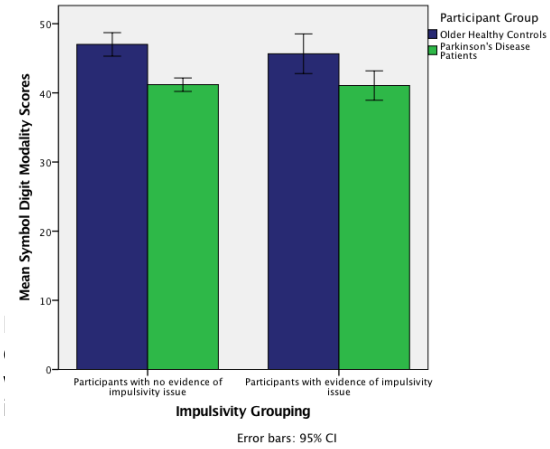

Figure 2.1: Bar Chart illustrating mean Symbol Digit Modality scores across older participants impulsivity grouping

Analysis of Variance

Two 2x2 independent ANOVA's were conducted; Letter-Number sequencing scores were used as the first dependent variable, and Symbol Digit modality scores as the second. The two independent variables were patient grouping: older healthy control or PD patient; and whether or not there was evidence of impulsivity issues as the second variable.

Results showed there were no significant differences in Letter-Number Sequencing scores between PD and older healthy controls ($F(1, 680) = 0.76$, $p = 0.38$) nor were results of those between participants with and without evidence of an impulsivity issue ($F(1,680) = 2.79$, $p = 0.10$).

Symbol Digit modality scores between PD patients and older healthy controls were significantly different ($F(1,680) = 23.68$, $p<0.001$), however differences between participants with and without evidence of an impulsivity issue were not significant ($F(1, 680) = 0.47$, $p = 0.49$).

Furthermore, interactions between participant grouping (PD and older healthy controls) and evidence of impulsivity issues (QUIP>1 with, QUIP=0 without) were insignificant in both Letter-Number Sequencing test ($F(1,680) = 0.87$, $p = 0.35$) and Symbol Digit Modality ($F(1,680) = 0.33$, $p = 0.57$).

Discussion

The current study aimed to investigate the relationship between impulsivity and scores on tasks measuring working memory in younger healthy controls, and

executive function in older healthy controls, and Parkinson's disease (PD) patients. The results of this study did not support the aim of assessing whether impulsivity is altered in unmedicated PD patients following an insignificant t-test between PD and older healthy controls impulsivity scores. Analysis of Fisher's Z-tests showed no significant relationship between executive function scores and impulsivity in PD patients, contrary to previous research that showed cognitive deficits could be identified in early unmedicated patients (Santengelo et al., 2015). Therefore, the two hypotheses that predicted PD patients would be less impulsive than age-matched controls and that there would be an altered relationship between executive function ability and impulsivity in the PD group compared to the older healthy control group were rejected.

Conversely the hypothesis that younger healthy controls would be more impulsive than older participants was accepted as there was a significantly greater proportion of younger healthy controls with high impulsivity (measured by the BIS-11) than older healthy controls with high impulsivity (measured by the QUIP) that supported previous research (Steinberg et al., 2008; Fino et al., 2014). Fisher's Z-test between younger and older healthy controls supported the third aim of assessing the relationship between impulsivity and executive function in younger and older healthy controls to establish the link between the variables in an age-varying non-clinical sample, as well as adding to previous impulsivity research by including executive function scores within this. Consequently, the hypothesis that the relationship between executive function and impulsivity would be different across the age groups was accepted following Fisher's Z-tests between younger and older healthy controls impulsivity and working memory correlations that showed significant variances in executive function and impulsivity between younger and older healthy controls.

Limitations

Limitations in this study arose predominantly from the differences between data collection from the younger healthy control sample, and data collated from the Parkinson's Progression Markers Initiative's quantitative database. Large differences in sample size between younger (n=102) and older (n=196) healthy controls, and PD patients (n=498) meant equal representation for all participants was unavailable. Additionally, impulsivity measures for both groups were based on self-report scales that meant there was no objective measure for impulsivity, and response bias may have occurred depending on whether participants considered impulsivity a positive or negative attribute.

Evidence of working memory being attributed to higher learning (Ghani and Gathercole, 2013; Cowan, 2014) may also have influenced working memory results in the younger healthy controls as the majority of participants were recruited through Manchester Metropolitan University's student participation pool.

In addition to sample bias, executive function tests administrated to the younger healthy control group, older healthy controls and PD patient group were different due to time restrictions on the collection of data for younger healthy controls. Older healthy controls and PD patients completed the Letter-Number Sequencing and Symbol Digit Modality to test for executive function, whereas younger healthy controls completed the Digit Span. Although all the tasks test executive function, Digit Span specifically tests working memory, whilst the Letter-Number Sequencing

and Symbol Digit modality do not test the same areas of executive function equally. Furthermore, research highlighted in the introduction suggests the Letter-Number Sequencing and Digit Span tasks specifically require further development and additional tests before conclusions regarding impaired executive function can be drawn (Schneider et al., 2010; Egeland, 2015).

A final restriction on results is attribution of causality. Throughout this study it has been implied that executive function deficits stem from impulsivity due to past literature (Moeller et al, 2004; Albein-Urios et al., 2012; Sleigh et al., 2014; Minozzi et al., 2015), however impulsivity may stem from executive function deficits.

Applied Implications

Despite the limitations discussed above, the present study adds to current developing research in an area presently lacking in data. Results have added to understanding the dynamic nature of the relationship between impulsivity and executive function by highlighting a greater correlation in younger healthy samples outside of current addiction literature (von Diemen et al., 2008; Stautz et al., 2016). The data collected can also be used to add to recommendations of an age-dependent cognitive performance index in the elderly (Abdulrahman et al., 2017) and potentially drive an initiative of examining data in unmedicated PD patients to better understand the relationship between impulsivity and executive function.

Future Research

The results of this study provide a good foundation for a number of directions for future research. The literature on impulsivity in PD patient's notes a lack of understanding in how impulsive-compulsive disorders develop, so further research from the data of unmedicated PD patients in this study could involve a longitudinal study with a specific focus on how impulsive behaviours develop in unmedicated PD to impulsive-compulsive disorders. Alongside this, healthy controls could be used to add to research in how impulsivity changes across the lifespan, especially in the elderly.

With regards to the previous critique of sample size differences, an increase of healthy control participants would be of benefit in the collection of data for the recommendation of age-matched cognitive scores in elderly participants (Abdulrahman et al., 2017).

Future work in the sensitivity of tests in executive function and working memory, taking into account the limitations acknowledged in Letter-Number Sequencing and Digit Span tasks (Schneider et al., 2010; Egeland, 2015) has potential to aid diagnosis in numerous neurodegenerative diseases, aside from Parkinson's, as cognitive deficits would be noticed earlier.

Additionally, addiction research highlighted the lack of understanding of how impulsivity and working memory relate to one another prior to substance abuse. Given that results in this study support higher levels of impulsivity in younger healthy controls (Tsukayama et al., 2013), future work in addiction has the supporting evidence to cultivate preventative initiatives aimed at targeting younger impulsive individual's that are vulnerable to developing addictive behaviours (von Diemen et al., 2008; Gunn and Finn, 2013).

Lastly, research into dopaminergic pathways relating to impulsivity were unable to be studied in this piece of work due to methodological restrictions, however literature shows extensive contradictions in the neurobiological underpinnings of impulsivity. Building on from this study's supporting results of impulsivity changing across the lifespan, knowledge of the neurological basis of impulsivity can assist in understanding the development of impulsive-compulsive disorders.

Conclusion

To conclude, the present study has explored the relationship between impulsivity and executive function in relation to age and Parkinson's disease. The current findings from both samples that belong to real-world collected data and the PPMI quantitative database support aspects of current research that indicates impulsivity is higher in a younger age and that the relationship between impulsivity and executive function is altered across age groups. On the contrary, findings did not support lower levels of impulsivity in early stage unmedicated Parkinson's patients or differences in the relationship between impulsivity and executive function in PD patients or age-matched controls. This highlights the need for further development of cognitive dysfunction sensitivity in assessment tools for PD diagnosis as recommended by past research (Leung et al., 2015), as well as adding to previous literature on providing data for an age-dependent cognitive performance index in the elderly (Abdulrahman et al., 2017). Additionally, suggestions have been made for future research to improve our understanding of the relationship between impulsivity and executive function, and how this can benefit primarily older healthy adults and early unmedicated Parkinson's disease patients.

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