The Influence of Contextual Constraint on Verbal Selection Mechanisms and its Neural Correlates in Parkinson's Disease

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Abstract

A small number of studies have described verbal selection deficits in Parkinson's disease (PD) when selection must occur among competing alternatives. However, these studies have largely focused on single-word processing, or have utilised sentence stems that carry high contextual constraint, thus reducing selection demands. The present study aimed to determine the influence of variable contextual constraint on the selection of a verbal response in PD. This was achieved using an adaption of the Hayling Sentence Completion Task whereby PD participants and matched controls were required to provide a single word to complete a cloze probability sentence stem that carried a low, medium, or high degree of contextual constraint. Results revealed no main effect of group in terms of response time or accuracy, though a group-by-condition interaction in accuracy was noted. This was characterised by a significant difference in accuracy between low and medium levels of constraint for control participants, but no significant difference for the PD group. Functional MRI data revealed marked between-group differences in underlying neural activity. The control group showed increased recruitment of the dorsal striatum and the vlPFC under conditions that placed greater demands upon selection (i.e. low and medium constraint), and greater activity overall in the left dlPFC and right vlPFC. However, in the PD group, behavioural performance appeared to be maintained despite underlying decreases in frontostriatal activity, suggesting other compensatory mechanisms that may include changes in functional connectivity or an over-medication effect in frontal networks in response to loss of signalling in cortico-subcortical pathways.

Keywords

verbal selection, Parkinson's disease, lexical-semantics, fMRI, cognitive control, prefrontal cortex

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1. Introduction

Individuals with Parkinson's disease (PD) demonstrate impairment across a vast catalogue of language tasks (for reviews see Altmann & Troche 2011; Murray 2007; Smith & Caplan 2018), however the precise locus of these deficits has yet to be fully described. The characterising pathology of PD is the depletion of dopaminergic projections within the basal ganglia (Bartels and Leenders 2009; Kish et al.1988). Current understanding holds that while the basal ganglia do not appear to play a primary role in language functions, these nuclei may support linguistic processing via their participation in cognitive operations (Crosson et al. 2007). Specifically, the basal ganglia appear to be integral to the dynamic process of *cognitive control* - the selective facilitation and inhibition of motor or cognitive actions (Frank, Loughry, & O'Reilly 2001; Mestres-Missé, Turner, & Friederici 2012; Redgrave et al. 1999). In the context of spoken language production, cognitive control is thought to facilitate the production of an appropriate response (single word) in the face of increased competition from multiple alternatives – a process termed *verbal selection*.

Notably, language disturbances in PD appear to manifest when the task at hand places increased demand upon verbal selection. For example, individuals with PD have demonstrated decreased performance on measures of ambiguity resolution (Copland et al. 2009; Ketteler et al. 2014), verbal fluency (for review see Henry and Crawford 2004), and verb generation (Boulenger et al. 2008; Colman et al. 2009; Cotelli et al. 2007; Peran et al. 2003; Rodríguez-Ferreiro et al. 2009) – all of which are tasks that inherently involve selection among multiple alternatives. In particular, verb generation is thought to necessitate the recruitment of additional executive resources, due to the increased number of competing alternatives associated with verbs relative to nouns (Matzig et al. 2009; Silveri et al. 2012).

Crescentini et al. (2008) compared performance on verb and noun generation tasks in PD participants and healthy controls. The PD group demonstrated impaired verb production relative to controls as a function of both retrieval demands (stimulus-response association strength) and selection demands (number of alternatives). An effect of association was also detected in the PD group during noun generation, wherein participants responded less accurately when stimulus-response association was weak. The authors concluded that these findings supported a role for the basal ganglia in mediating the processes of semantic retrieval and selection among competing alternatives. Similarly, Silveri et al. (2018) utilised a series of morphological tasks in which participants with PD and healthy controls generated nouns, verbs or adjectives from various word classes,. This study confirmed that the deficits observed in PD are not specific to verbs, demonstrating that the number of competing alternatives and the number of alternatives with higher frequency than the target (thus potent competitors) are also critical modulators of performance.

Further support for the hypothesis that a deficit in verbal selection underlies the language impairments observed in PD can be drawn from imaging literature. The basal ganglia share reciprocal connections with the prefrontal cortex (PFC) - the anatomical locus of cognitive control (Braver et al. 2009; Koechlin et al. 2003; Macdonald et al., 2000; Miller and Cohen 2001; Miller 2000; Norman and Shallice 1986; Ridderinkhof et al. 2004). Importantly, it has been demonstrated that a number of these pathways, those arising from the striatal nuclei (caudate and putamen), terminate in those regions of the PFC thought to participate specifically in verbal selection: namely, the ventrolateral prefrontal cortex (vlPFC, encompassing Brodmann Areas [BA] 44, 45, 47; Di Martino et al. 2008; Ford et al. 2013; Leh et al. 2007; Ullman, 2006). In healthy controls, caudate activity has been identified in studies of word generation (Crosson et al. 2003) and ambiguity resolution (Ketteler et al. 2008), both of which are tasks that inherently involve selection among multiple alternatives. The vlPFC has been consistently implicated in semantic retrieval and selection (Moss et al., 2005; Poldrack et al. 1999;

Thompson-Schill et al.1999; Thompson-Schill et al.1997; Wagner et al. 2001; for review see Nozari & Thompson-Schill 2016), and it is activated during verb generation tasks and other paradigms involving words with multiple possible alternatives (Nagel et al. 2008; Nelson et al. 2009; Persson et al. 2004). Furthermore, activation of the vlPFC increases when subjects are asked to name pictures with lower naming agreement, or generate items from larger categories (Kan and Thompson-Schill 2004; Tremblay and Gracco 2006) – conditions which increase selection demands. Badre et al. (2005) proposed a model of the vlPFC's participation in semantic processes, wherein the anterior vlPFC (BA 45) meditates controlled semantic retrieval, and the mid vlPFC (BA47) mediates post-retrieval selection. The former allows for controlled retrieval of semantic knowledge when the cues made available by stimuli are insufficient to drive bottom-up activation. In contrast, the latter is a domain-general selection mechanism that allows a single response to be selected from among several task-relevant representations, each of which was activated in response to the stimulus. If compromised verbal selection processes do underlie the language impairments observed in PD it follows that behavioural differences should be accompanied by altered neural activity in the aforementioned frontostriatal networks. To date, such investigations have been limited in the PD literature. Di Tella et al. (2018) replicated and extended the findings of Silveri et al. (2018) by utilising structural MRI in a PD cohort in combination with noun derivation and verb generation. Their study demonstrated that in both tasks the number of competing alternatives and the number of alternatives with higher frequency than the target have an inhibitory effect on response time and accuracy, for both PD and control groups. However, participants with right-sided onset of PD symptoms (and hence left hemisphere neuronal loss) were less accurate in the derivation task (associated with a greater number of alternatives), and their accuracy and response time data was partially correlated with cortical thickness in the left pars triangularis (consistent with left vlPFC).

Interestingly, most of the studies described above have only considered selection mechanisms in the context of single word processing. However, if the language impairments observed in PD reflect a deficit in controlled retrieval and selection as a result of disrupted frontostriatal signalling, it could be suggested that any condition that places sufficient demands upon these mechanisms will likewise be affected. In healthy controls, fronto-striatal activity has been detected in studies of verbal selection that utilise contextually loaded sentences in order to bias meaning selection. For example, Argyropoulos et al. (2013) reported strong activation of the caudate during overt sentence generation, in contrast with no activation during sentence repetition - interpreted as evidence of the caudate's role in semantic selection processes. Similarly, in studies of word learning, the caudate has been observed to activate in association with the left vlPFC (BA 44 and 45) when new meaning must be derived from sentence context (Mestres-Missé et al. 2008).

Limited studies have explored verbal selection performance in PD beyond the level of single word processing. A small number of authors have administered The Hayling Sentence Completion Task (HSCT; Burgess and Shallice 1996) in this population (Bouquet et al. 2003; O'Callaghan et al. 2013a; O'Callaghan et al. 2013b; Obeso et al. 2011). The HSCT involves presentation of sentence stems with the final word removed, and participants are asked to either provide a word that completes the sentence correctly (measuring verbal selection) or provide a word that is unrelated to the sentence (measuring verbal suppression). These studies have generally reported minimal differences in performance on Part A between PD and control groups. However, it is noted that the HSCT traditionally involves only sentence stems with a high level of contextual constraint, and therefore few competing alternatives and strong association between the stem and the likely response. It is assumed that sentences with low contextual constraint may carry both greater selection demands and controlled retrieval demands, and therefore require increased input from cognitive control facilities. The

capacity of individuals with PD to generate an appropriate response for a sentence with low contextual constraint is yet to be explored.

Such a paradigm has been administered in healthy adults. Nathaniel-James and Frith (2002) designed a novel variation on the HSCT that manipulated contextual constraint. Sentence stems were classified as either high, medium, or low constraint, and effects were observed across both selection and suppression conditions, whilst participants underwent Positron Emission Tomography. Activation of the left dorsolateral prefrontal cortex (dlPFC) was observed during the suppression condition, however most intriguingly, this region was also recruited during the low constraint condition of the selection task. Activation in the medial orbital frontal cortex, a region contained within the ventromedial PFC, was also observed during selection conditions. Based on these results, Nathaniel-James and Frith (2002) concluded that the dlPFC was involved in generating a set of possible responses from which an alternative can be selected. This description appears to overlap significantly with the aforementioned accounts of the vlPFC's role, and indeed the putative roles of the dlPFC and vlPFC have been contended in the literature for some time without definitive resolution (Kerns et al. 2004; Nagel et al. 2008; Wagner et al. 2001). Nathaniel-James and Frith (2002) did not report activation of subcortical nuclei, however their study only included six participants, and thus may not have possessed sufficient sensitivity to detect activity in these smaller anatomical regions.

The present study sought to clarify the involvement of frontostriatal circuitry in verbal selection beyond the limitations of a single-word based generation task, and determine whether impaired verbal selection processes underlie the language deficits observed in PD. The task drew upon the design elements of Nathaniel-James and Frith's (2002) sentence completion study combined with fMRI in order to observe the influence of contextual constraint on verbal selection in PD and identify underlying substrates. Based on converging evidence from studies of word production in PD (see above), it was hypothesised that the PD group would experience greater difficulty selecting items when selection demands are high (i.e. cloze sentences with low contextual constraint) and this would correlate with decreased activity in frontostriatal networks encompassing the subcortex and vlPFC.

2. Materials and Methods

2.1. Participants

Fourteen individuals with diagnosed idiopathic PD were recruited to participate in the study (9 female). All participants in the PD group were required to meet the following inclusion criteria: (1) confirmed diagnosis of idiopathic PD according to the Calne et al. (1992) criteria; (2) right-handed, confirmed with the Annett Hand Preference Questionnaire (Annett 1970); (3) English as a first language; (4) Hoehn and Yahr (1967/2001) rating of 1-3. Potential applicants were excluded if: (1) they reported a history of substance and/or alcohol abuse, head trauma, stereotaxic surgery and/or neurological disease other than PD; (2) they achieved a score on the Montreal Cognitive Assessment (MoCA v7.1/7.2; Nasreddine et al. 2005) that was > 1 *SD* below the expected range for their age group and level of education (Rossetti et al. 2011); (3) they presented with moderate-severe dysarthria (in order to minimise variation in response transcription due to poor intelligibility of speech); or (4) they reported an uncorrected hearing or visual impairment that could affect the validity of task performance. Finally, the Geriatric Depression Scale (GDS; Sheikh and Yesavage 1986) was administered to screen for untreated clinical depression. A score greater than 8 was considered indicative of major clinical depression and participants scoring in this range were excluded (Dissanayaka et al. 2011; Dissanayaka et al. 2007). Total years of education (YOE) was calculated for each participant and included years spent in primary, secondary, bachelor, post-graduate, and diploma or certificate studies. Levodopa equivalent daily dosage

(LEDD) was calculated for each patient based on the procedures outlined by Tomlinson et al. (2010). One participant was not taking medicinal treatment at the time of testing. Demographic and neurological data for PD participants was collected via self-completed questionnaires and is presented in Table 1.

>Insert Table 1 here<

Fifteen neurologically healthy individuals were recruited to serve as a control group (9 females, mean age = 67.7 [5.84], mean YOE = 15.5 [3.9]). Controls were required to: (1) be right-handed (Annett 1970); (2) have English as their first language; (3) have no self-reported history of alcohol and/or substance abuse; (4) have no significant neurological disease or history of trauma /surgery; and (5) have normal or corrected-to-normal vision and hearing. Controls were excluded if they achieved a score on the MoCA (v7.1/7.2; Nasreddine et al. 2005) that was > 1 *SD* below the expected range for their age group (Rossetti et al. 2011). The mean total MoCA score for the control group was 26.5 [1.8].

Participants in both groups completed a battery of neurocognitive and linguistic assessments, comprising the Boston Naming Test 2nd Edition (BNT; Kaplan et al. 2001), selected subtests of the Test of Everyday Attention (TEA; Robertson et al.1994) including Elevator Counting and Elevator Counting with Distraction, the National Adult Reading Test (NART; Nelson and Willison, 1991), digits forwards and backwards, and verbal fluency (phonemic, semantic, and cued). The study was approved by the Human Research Ethics Committee of the University of Queensland and was therefore in accordance with the ethical standards laid down in the 2007 NHMRC National Statement on Ethical Conduct in Human Research. Participants provided informed written consent and were financially compensated for their participation in the study.

2.2 Experimental Design and Stimuli

The study employed a variation on the HSCT (Burgess and Shallice 1996), similar to that described by Nathaniel-James and Frith (2002), and required participants to provide a single word that correctly completed a given sentence stem. The cloze-probability of the sentence stem was systematically manipulated, in order to allow for observation of verbal response selection as a function of contextual constraint. Sentence stems (120 in total), 6-8 words in length *(M* = 7.2 [0.8]) were selected from a database of 400 sentence completion norms (Block and Baldwin 2010). This database comprises 400 high cloze probability sentences that expand upon the norms compiled by Bloom and Fischler (1980) and were standardised against an undergraduate student population. N-Watch software (Davis 2005) was employed to determine the CELEX spoken word frequency of the most probable response for each sentence stem.

Three conditions were constructed based on the level of contextual constraint associated with sentences. Constraint is here defined as the cloze probability of a particular word being provided to complete a sentence stem. This was calculated based on the frequency with which responses were given in a sampled cohort and may be viewed as relating to the number of competing alternatives that could plausibly complete the sentence accurately (Block and Baldwin 2010). A sentence stem that activates a limited number of possible responses would be described as possessing a high level of constraint (e.g., He loosened the tie around his…"neck"). In contrast, a sentence stem that could be completed by a large number of words would be considered to generate low level constraint (e.g., The boy asked his teacher for extra… "credit" or "help" or "work" or "marks"). Each condition consisted of 30 sentence stems with either (a) high close probability (0.83 or above); (b) medium constraint (0.56 - 0.76); or (c) low constraint (0.5 or less). A baseline condition (read) was also employed in order to control for neural activation related to orthographic and syntactic processing, and motor execution. In this condition, the final word of the sentence was provided, and participants were required

to read this single word aloud. The cloze probabilities of stimuli in the baseline condition were all of a medium constraint level (0.56 - 0.76). A one-way Welch's ANOVA confirmed that cloze probability was significantly different between conditions, Welch's $F(3, 62.404) = 334.88$, $p < .001$. Post-Hoc Games-Howell tests further demonstrated that a significant difference in cloze probability was present between all pairwise comparisons ($p<0.001$) with the exception of read vs. medium, which did not differ significantly ($p=0.999$). This was as expected given that both of these conditions contained sentence stems with a cloze probability that fell within the range defined as medium. Each condition contained 30 trials, which did not significantly differ with respect to sentence stem length ($p = .357$), or spoken word frequency of the most probable response ($p = .808$).

The experiment was completed across two runs, each containing 60 trials, with a short break in between. Six pseudorandomisations were created in order to control for trial order effects across these blocks. Baseline read trials were presented in blocks of five, followed by five consecutive complete trials in an A – B – A –B design. Condition (low, medium, high) was varied within the complete blocks.

2.3 Procedure

In order to ensure adequate understating of the task requirements, ten practice trials (five read and five complete) were administered prior to testing. Corrective feedback was given as required during practice trials only, in line with the instructions provided in the original HSCT manual (see Burgess and Shallice 1996).

Behavioural testing was conducted in-scanner. The experiment was created using Cogent 2000 software (Wellcome Department of Imaging Neuroscience 2013) operating via a Matlab R2011b platform (MathWorks 2011) with a screen resolution of 1024 x 768, Arial font in size 50. This display was projected onto a large screen visible to the participants via a mirror positioned on the roof of the scanner. Participants were equipped with an MRI-safe microphone to capture overt verbal responses.

Each trial began with a fixation cross which appeared for 250 ms. Sentence stems were then presented visually, one word at a time (500 ms between each word). Once presented, each word remained on screen, such that the sentence stem became visible in its entirety. The final word of the sentence was replaced with a blank line "_____", and a written instruction simultaneously appeared below that informed participants of the nature of the required response (i.e. "read" or "complete"). The entire sentence stems and instruction remained on screen for 5000 ms before automatically progressing to the next trial. During this time, participants were required to overtly provide a single word that completed the preceding sentence stem as accurately as possible (complete condition), or read the final word of the sentence (read baseline condition). Verbal responses were only recorded if they were produced during this 5000 ms temporal window.

2.4 Image Acquisition

Images were acquired across two runs using a Siemens Trio (3T; Siemens AG, Germany) with a gradient echo EPI sequence (echo time [TE] = 36 ms, repetition time [TR] = 2500 ms, field of view [FOV] = 210 x 210 mm, flip angle 80°, in-plane resolution of 3.6 x 3.6 mm, and 36 slices x 3 mm, with a 0.6 mm gap). During each run, 232 image volumes were acquired. Three-dimensional T1-weighteed images were also acquired using a magnetization-prepared rapid acquisition with gradient echo sequence (TE = 2.99 ms, TR = 2200 ms, TI = 900 ms, FOV = 256 x 256 x 192 mm, 192 phase encodings in the slice direction, isotropic voxel size of 1 mm^3). A FLAIR sequence was included in the same session in order to remove signal from cerebrospinal fluid from resulting images (FLAIR TE/TR 93/7000 ms, TI [inversion time] = 2500 ms, resolution = 0.86 x 0.86 x 4mm, FOV = 220 mm).

2.5 Imaging Data Processing

Raw imaging data was processed using Statistical Parametric Mapping software (SPM v12; Wellcome Trust Centre for Neuroimaging 2014) operating via a Matlab R2013b platform (MathWorks 2013). Pre-processing included realignment and unwarping of the fMRI time series and slice-time correct. Functional images were then co-registered to a within-session, high resolution T1 structural image. A motion-fingerprinting tool was used to automatically assess and correct for the effects of motion within the fMRI time series. Motion-finger printing (Wilke 2012) pulls out the maximal motion of total displacement from scan to scan, and detects motion in the brain, whilst incorporating changes resulting from motion by B0 interaction. This generates multiple motion fingerprint time-courses that can be included as regressors of no interest. Regressors are unique to individual participants and include the three most independent representations of motion. Following this procedure, a DARTEL template of high-resolution images was created, then normalisation applied to coregistered EPI images (Ashburner 2007). T1 images were segmented into grey matter, white matter, and cerebrospinal fluid using a tissue classification method. Resulting images were smoothed using an 8mm, full-width, half maximum Gaussian kernel.

An exploratory whole brain analysis was conducted with findings masked to the grey matter. At the group level, a GLM ANOVA was constructed to model conditions (low, medium, high, read) by group (PD and control). Independent t-tests were also developed to observe group differences in activation between Low and High conditions, and between a general complete condition (collapsed across low, medium, and high) and the read condition. Anatomical labels for significant clusters were retrieved using the Neuromorphometrics software in SPM12 (Wellcome Trust Centre for Neuroimaging 2014).

Mean % blood-oxygen-level-dependent (BOLD) signal change was examined in regions of interest (ROI) that were developed a priori based on the hypotheses outlined above and included seed regions within frontostriatal circuits known to participate in cognitive control functions (Dirnberger and Jahashini 2013; Lewis et al.2003; Owen 2004; Middleton and Strick 2000). ROIs were developed using the Marsbar ROI toolbox (Brett et al. 2002) in SPM12 (Wellcome Trust Centre for Neuroimaging 2014). The WFU Pickatalas toolbox (Maldjian et al.2003) was used to derive anatomical ROIs. These included the left and right vlPFC (built by combining BA 45 and BA 47 as per Nagel et al.'s [2008] findings), and the left dorsal striatum (caudate and putamen nuclei). The left dlPFC was also included as an ROI (-38 30 32) due to its participation in frontostriatal circuitry and implication in previous administrations of the HSCT (Nathaniel-James and Frith 2002).

2.6 Scoring of Behavioural Data

Audio files were digitally filtered in order to reduce interference from scanner noise using Audacity (v2.1.2) software. Response times were manually extracted and measured with millisecond accuracy from the onset of the written instruction indicating required response (e.g. "complete", "read") to the onset of the participant's response so as to avoid contamination from non-verbal artifacts (e.g., coughing or throat clearing). Two independent markers scored each participant's responses based on predetermined criteria. A correct response was required to consist of a single word (though responses containing two lexical units representing a single semantic concept were accepted e.g., washing machine, swimming pool) that completed the sentence in a way that was conceptually and grammatically correct. Responses containing *excessive* interjections, false starts, self-corrections, or multiple words were scored as incorrect. Cohen's kappa was run to determine the level of inter-rater agreement, and this was found to be acceptable, $\kappa = .819$ (95% CI 0.803, 0.835), $p < .001$.

3. Results

Initial exploration of ROI data (see Section 3.2.1) revealed three participants (2 PD, 1 control) who were significant outliers in the included ROIs. Outliers were identified based on interquartile range (IQR). Specifically, a data point (representing the mean percentage BOLD signal change) was considered to be an outlier if its value met one of the following conditions: < 25th percentile – 1.5*ICR, or > 75th percentile + 1.5*IQR. These three participants were excluded from all subsequent analyses. The final results of the study therefore include 12 PD participants and 14 control participants. There was no significant difference between groups included in this analysis in terms of gender (x^2 = 1.0), age (p = .051), or YOE (p = .326).

Analysis of behavioural data was undertaken using SPSS software (Version 22). Of the total trials administered, 3.1% in the PD group and 2.8% in the control group were recorded as non-responses (no response given) and subsequently discarded from statistical analysis.

3.1 Behavioural Results

3.1.1 Neurocognitive battery.

A series of independent t-tests were conducted in order to identify group differences in the mean performance of each measure in the neurocognitive battery. Results are presented in Table 2. No significant differences in performance were detected between groups for any measure. Note that participants excluded due to outlying ROI data were also excluded from analysis of neurocognitive battery data. In some cases, participants were unable to complete selected assessment items due to fatigue, reducing the sample size reported in Table 2.

>Insert Table 2 here<

3.1.2 Response time.

Analysis of response time data only considered those responses that were scored as correct. Further, responses were required to be provided within a temporal window of 250 ms to 2500 ms in order to be included. Any responses provided outside this threshold were discarded, resulting in the loss of 5.97% of trials in the PD group, and 4.43% in the control group. The between-group difference in number of trials discarded was not significant (p = 0.069).

Initial exploration of the distribution of response time data indicated a departure from normality. A log10 transformation was performed and the resulting distribution satisfied requirements for parametric analysis. These transformed data were submitted to a random intercept Linear Mixed Model (LMM) analysis with the two groups (PD, control) and the four conditions (*high constraint*, *medium constraint*, *low constraint*, *read*) included as fixed effects and participant included as a random effect. Results are presented in Figure 1 in their untransformed state (ms) for ease of interpretation. The analysis revealed a significant effect of condition (F [3, 2575] = 73.2, p < .001) but no effect of group (F [1, 25.97] = 0.25, p = 0.618) or group by condition interaction (F [3, 2575] = 2.12, p = 0.095). Bonferroni-corrected pairwise comparisons collapsed across group revealed significant differences between all conditions (p<.01), with the exception of the low versus medium comparison (p = 1.0). Response time increased in a step-wise progression from the high constraint condition, to the read baseline, and to low and medium constraint conditions (slowest response time).

>Insert Fig.1<

Fig.1 Mean response time (ms) as a function of degree of contextual constraint (high, medium, low). The read condition served as a baseline. Error bars represent mean standard error. A main effect of condition was detected, characterised by significant differences between all conditions (p < .05), with the exception of the low vs. medium constraint comparison, which did not reach significance.

3.1.3 Accuracy.

Accuracy data for each participant was extracted in the form of the total percentage correct so that it could be analysed as continuous data. Distribution of this data was found to satisfy normality requirements for parametric analysis. A random intercept LMM was conducted with the two groups (PD and control) and four conditions (*high constraint*, *medium constraint*, *low constraint*, and *read*) modelled as fixed effects and participant modeled as a random effect. These results are presented in Figure 2. The analysis indicated a significant main effect of condition (F [3, 78] = 91.47, $p < .001$) that was characterised by a significant difference between all pairwise comparisons of condition, when collapsed for group (with Bonferroni adjustment for multiple comparisons). In addition, the LMM also revealed a significant group by condition interaction (F [3, 78] = 3.17, $p = .029$). Paired sample t-tests conducted independently within each group revealed the nature of this interaction. The PD group showed no significant difference between low and medium constraints ($p = 0.073$), whereas the control group showed significant differences between all conditions. There was no main effect of group (F [1, 26] = 0.107, $p = 0.746$).

>Insert Fig.2<

Fig.2 Mean accuracy (percentage correct responses) as a function of degree of contextual constraint (high, medium, low). The read condition served as a baseline. Errors bars represent standard error of the mean. In the control group, significant differences were present across all pairwise comparisons of condition ($p < .05$). This was also the case in the PD group, with the exception of low vs. medium constraint, which did not reach significance. No main effect of group was detected.

3.2 Imaging Results

3.2.1 Region of interest analysis.

Mean percentage signal change for the read condition in each ROI was subtracted from each experimental condition (e.g., low minus read), thus controlling for the common processes of sentence comprehension and speech production. These subtraction figures were submitted to independent repeated measures ANOVAs. Independent t-tests were also conducted in order to determine whether read baseline activation was equivalent across groups for each ROI. These tests revealed no significant differences in baseline activation between groups for the left vlPFC and left striatum. Baseline activation was found to be significantly different between groups in the left dlPFC (t [24] = 2.53, $p = .018$) and right vlPFC (t [24] = 2.45, $p = .022$). Further analysis of ROI data obtained from these regions was therefore not undertaken.

A main effect of condition was detected in the left striatum (F [2, 48] = 8.36, $p = .001$). Paired sample t-tests in the control group revealed significant differences between the medium vs. high conditions ($p = .004$), and low vs. high condition ($p = .005$). In contrast, the PD group did not modulate recruitment of this region as a function of condition, with no significant differences recorded for any pairwise comparison ($p > .1$ for all). These results are plotted in Figure 3.

>Insert Fig3. (a&b) here (colour)<

Fig.3 Region of interest analysis for the left striatum. Bar graph indicates relative mean percentage change in BOLD signal in left striatum as a function of degree of contextual constraint (high, medium, low). Brackets indicate significant within-group differences in activation ($p < .05$). Error bars indicate standard error of the mean. Figure displays render of a priori defined anatomical ROI for left dorsal striatum (caudate and putamen).

A main effect of condition was detected in the left vlPFC (F [2, 48] = 8.79, $p = .001$). Paired sample t-tests revealed that this effect of condition was characterised in the control group by significant differences between medium vs. high conditions ($p = .006$, respectively) and low vs. high conditions ($p = .001$). However, the PD group only recorded a significant change in activation in the medium vs. high comparison ($p = .028$). These results are plotted in Figure 4.

>Insert Fig4. (a&b) here (colour)<

Fig.4 Region of interest analysis for the left vlPFC. Bar graph indicates relative mean percentage change in BOLD signal in left vlPFC as a function of degree of contextual constraint (high, medium, low). Brackets indicate significant within-group differences in activation ($p < .05$). Error bars indicate standard error of the mean. Figure displays render of a priori defined anatomical ROI for left vlPFC.

3.2.2 Whole brain analysis.

Results are reported for a height threshold of $p < .001$ uncorrected and clusters corrected at the voxel level for FWE ($p < .05$). No main effect of condition or group-by-condition interaction was detected. A main effect of group was detected in the following regions: right triangular portion of the IFG (BA 45, equivalent to right vlPFC), left caudate, left dlPFC, left angular gyrus, right medial superior frontal gyrus (SFG), right posterior cingulate gyrus (PCgC) and the right superior marginal gyrus (SMG). This effect was characterised by significantly increased activity in these regions in the control group relative to the PD group when collapsed across condition. An independent t-test revealed that the control group recorded increased recruitment of the right central operculum relative to the PD group, when all experimental conditions were collapsed into one condition called complete and compared to the baseline read condition ($p<0.001$). Independent t-tests revealed no significant differences between groups when comparing high and low constraint conditions ($p>0.05$). These results are presented in Table 3 and Figure 5.

>Insert Table 3 here <

>Insert Fig5. here (colour) <

Fig.5 Whole-brain analysis - main effect of group (Control > PD). Significant activations are overlayed on a rendered template brain surface in MNI space. Activations are shown at a height threshold of $p < .001$ uncorrected with clusters corrected at the voxel level for FWE ($p < .05$).

4. Discussion

The present study aimed to determine the influence of contextual constraint on verbal selection and identify its underlying neural substrates in a PD cohort. A sentence completion task was employed that manipulated the contextual constraint of the sentence stem across three conditions (low, medium, and high constraint). The primary finding of the study was largely commensurate behavioural performance in the PD and control groups in terms of response time and accuracy (with the exception of no significant difference between low and medium constraint accuracy in the PD group), accompanied by significant group differences in underlying neural activity. Such differences were characterised by increased overall activity across a distributed network of frontal and subcortical regions in the control group relative to the PD group. Several key regions were identified in line with the aforementioned hypotheses, including the left caudate and bilateral vlPFC. The control group relied heavily upon recruitment of these regions during the low and medium constraint conditions relative to the high constraint condition, while the PD group demonstrated minimal modulation of activity as a function of condition.

Relative to controls, the PD group demonstrated significantly decreased overall activity in a number of regions across the frontal cortex and subcortex, including the right vlPFC, left dlPFC, and the caudate nucleus. Numerous imaging studies of PD have demonstrated that decreased signalling in these networks accompanies impairments in cognitive and linguistic function (Dirnberger and Jahashini 2013; Grossman et al. 2003;

Hanganu et al. 2015; Ketteler et al. 2008; Lewis et al. 2003; Owen 2004; Zgaljardic et al. 2006). In the present study it was therefore hypothesised that decreased activation would be observed within these regions in the PD group. However, unexpectedly, although this difference in neural activity was indeed observed it was not accompanied by impaired behavioural performance. Rather, the PD group was able to maintain their behavioural output at a level commensurate with the control group, despite this significant decrease in frontostriatal activity.

Possible explanations for the discrepancy between the findings of the present study and pre-existing evidence will be discussed further below. The results for the healthy control group will be considered first, providing the contextual framework necessary to support subsequent inferences regarding the performance of the PD group.

4.1 Involvement of the Lateral Prefrontal Cortex

ROI analysis revealed increased activation of the left vlPFC during conditions with increased selection demands (i.e. low contextual constraint). A recent meta-analysis conducted by Noonan et al. (2013) examined neuroimaging data from 53 studies of semantic control in healthy adults and semantically-impaired stroke patients, as a means of confirming the neural substrates of this process. The analysis identified a bilateral network extending beyond the left and right lateral PFC (dorsal and ventral), to include the left posterior MTG, angular gyrus, and ACC. In particular, the left PFC and angular gyrus were significantly activated as a function of semantic control across a variety of tasks (e.g., categorization, comparison, and ambiguity processing), irrespective of expressive versus receptive processes. In contrast, though the present study identified increased activity in both the right vlPFC (triangular portion of IFG or BA 45) and left vlPFC (BA 45/47) during conditions of low and medium constraint, whole brain analysis did not reveal evidence of activation in the MTG.

Given Badre et al.'s (2005) distinction between controlled retrieval and post-retrieval demands in the vlPFC, this lack of MTG activation may be inferred as indirect evidence of limited controlled retrieval demands in this task. Instead, the observed vlPFC activation may be more representative of post-retrieval selection demands, which may not necessitate the recruitment of the MTG. This may be conceivable considering the design of the task. Low and medium constraint sentences can be completed by a large number of alternatives presumed to be activated by the contextual information. For example, the low constraint sentence stem "The two opposing families had an ongoing ____" may be reasonably completed by a number of words including "feud", "argument", "disagreement", etc. The semantic similarity of these linguistic units suggests that sufficient information is provided by the sentence to drive bottom-up activation of relevant concepts. However, a large number of equally appropriate words are activated. In this way, it could be surmised that post-retrieval selection mechanisms are of greater importance when completing this task than controlled retrieval mechanisms.

Irrespective of the specific mechanisms, the present study does provide evidence to substantiate prior claims of a role for the vlPFC in the controlled selection of contextually appropriate words. Interestingly, the Nathaniel-James and Frith (2002) study upon which the present study is based did not find evidence of vlPFC activity during the completion component of their task. However a number of factors may account for this discrepancy, as the study only assessed six healthy males (aged 32 to 63), and did not include a baseline measure. These limitations may have masked any effects in the vlPFC from reaching significance.

Nathaniel-James and Frith (2002) did identify significant dlPFC activity across all levels of constraint during the suppression condition (generation of an unrelated word) as well as during the low constraint

condition of the completion task, and attributed this to 'sculpting of the response space'. As described previously, this refers to the process of generating a set of possible responses (when no single response is prepotently appropriate) and appears to overlap somewhat with the concept of selection among competing alternatives. In the present study, a significant difference between groups in activation of the left dlPFC was also identified at the whole brain level, characterised by increased recruitment in the control group relative to the PD group. However, this effect could not be examined further with ROI analysis due to group differences in the baseline condition. Activation of the dlPFC during a selection task does appear to raise the question of whether these regions have unique, overlapping, or shared roles.

Kerns et al. (2004) had previously noted this contention surrounding the differential roles of the dlPFC and vlPFC, and suggested that both may contribute to a similar goal via complementary mechanisms. They framed their investigation in the context of guided activation theory (Miller and Cohen 2001); a widely endorsed model of how the PFC performs its role as the instigator of cognitive control. It proposes that the PFC exerts top-down influence over more posterior regions of the cortex responsible for task execution in order to bias task-relevant responses. Such guidance is particularly necessary when a task introduces the need for novel responses, selection among competing alternatives, or selection of a task-relevant response in the face of a strongly prepotent but task-irrelevant response. Previous applications of the model in language-processing paradigms have suggested that the PFC represents and maintains the contextual information conveyed by a syntactic structure and uses this information to bias the selection of a context-appropriate response in posterior language regions (Cohen et al. 1999; Cohen and Servan-Schreiber 1992). In this way, selection of the most appropriate response can occur. The model therefore posits that context maintenance and selection of a response are the same mechanism.

Kerns et al. (2004) interpret this notion as suggesting that maintenance and selection would be subserved by the same region of the PFC, and tested this assumption with a missing letter paradigm. In this task, participants were asked to fill in the blank in order to create a complete word, and this took place following presentation of sentences designed to provide contextual priming for the probing words. Whole brain analysis found that activity in both the dlPFC and the vlPFC during encoding and maintenance phases was associated with the provision of context-appropriate verbal response. Such a relationship was not observed elsewhere. Furthermore, these same regions demonstrated increased activation during the provision of a verbal response that was context-inappropriate. Kerns et al. (2004) interpreted their findings as evidence for guided activation theory. They inferred that both the dlPFC and vlPFC were involved in representing and maintaining contextual information derived from sentence processing in order to bias the selection of an appropriate response. When this process failed, the selective activation of the appropriate response did not occur, and as a result participants were required to generate a response presumably from multiple competing alternatives. At this point a selection mechanism (likened to the post-retrieval selection mechanisms of Badre et al. [2005]) was required to choose one response from among these alternatives. Kerns et al. (2004) suggested that this accounted for the increased activity observed in the dlPFC and vlPFC during the response phase and conclude that maintenance of context and selection of a response during language processing are subserved by a unitary mechanism, presumably involving both dlPFC and vlPFC. This account does not functionally segregate these two regions (BA 9/46 and BA45). The present study appears to provide support for the conclusions of Kern et al. (2004), as activity in both the vlPFC and dlPFC was detected.

Importantly, it is noted that the present study identified prefrontal activity in both left and right hemispheres. Noonan et al. (2013) similarly identified a bilateral network hypothesised to subserve semantic

control. This is a departure from earlier findings that have largely implicated left hemisphere structures (Badre et al. 2005; Nagel et al. 2008; Snyder et al. 2011; Souza et al. 2009) however it is possible that the bilateral activity noted in our cohort and Noonan et al.'s cohort relate to the older age of these participants relative to previously studied cohorts and reflect typical age-related hemispheric compensation (Berlingeri et al. 2013; Cabeza et al. 2008). Indeed, this phenomenon has been specifically reported in studies of age-related changes in semantic processes (Diaz et al. 2014; Wierenga et al. 2008).

4.2 Involvement of the Striatum in Verbal Selection

In the present study, whole brain analysis also identified significantly increased activation in the left caudate for the control group, relative to the PD group. ROI analysis of the left striatum further revealed that this effect was characterised by increased recruitment during low and medium constraint conditions, and a decrease during the high constraint condition. This pattern of recruitment suggests that striatal participation in verbal selection is necessitated when either selection and/or controlled retrieval demands are increased. As hypothesised, this pattern of engagement mirrors that observed bilaterally in the lateral PFC, suggesting the existence of a frontostriatal network recruited to mediate processing when selection demands are increased. This is in line with previous studies that have identified activity in the caudate during the execution of tasks with a verbal selection component (Argyropoulos et al. 2013; Crosson et al. 2003; Ketteler et al. 2008; Mestres-Missé et al. 2008).

Taken together with the parallel activation in the lateral prefrontal cortex, this finding corroborates and extends the proposals of Chatham et al. (2014), who noted that cognitive control requires achieving a balance between the need to flexibly update goals and the need to maintain them over time. Consistent with guided activation theory (Miller and Cohen 2001), they suggest that in order to maintain task-relevant representations in the PFC, selective updating of these representations must occur in response to dynamic changes in the contextual environment. This, they claim, must be supported by two distinct mechanisms. The PFC is responsible for the maintenance of contextual information in working memory, while the basal ganglia provides an input gating mechanism, reliant upon dopamine-driven frontostriatal networks, that exercises selective control over the updating of this information, in line with internal goals. This maintained information is then available to exert top-down control over activity in more posterior regions of the cortex, in order to bias task-relevant responding. Furthermore, Chatham et al. (2014) also propose an output gating system that acts to allow only selected representations to exert this top-down bias. This output mechanism is likewise thought to be controlled by structures within the basal ganglia which amplify selected representations received from the PFC via frontostriatal pathways.

This model may be extrapolated and applied to the results of the present study. Previous accounts have suggested that reciprocal connections exist between the head of the caudate and the vlPFC (di Martino et al. 2008; Leh et al. 2007). Ford et al. (2103) utilised a novel diffusion-weighted imaging fibre tracking method to identify a connection between the anterior aspect of the putamen and the vlPFC (Ford et al. 2013). In the present study, striatal nuclei appear to be co-activated under conditions of increased selection demand, suggesting the presence of a distributed network. It may be hypothesised that the lateral PFC structures were responsible for maintaining the contextual representations during sentence stem processing, and the caudate selectively updated these representations as contextual information dynamically altered with the addition of each word in the string. Output gating co-ordinated by the caudate then amplified specific representations in order to bias selection from among the multiple competing alternatives activated by the maintained contextual information. These selected representations in the PFC were then able to exert top-down influence over

posterior language regions, allowing for production of a single, relevant response. Such a coordinated network is similar to a proposal by Canini et al. (2016), who investigated the neural networks associated with semantic control through the administration of a cumulative semantic interference task in healthy adults. These authors that both the left IFG (commensurate with the vlPFC) and left caudate were recruited as semantic competition increased, and suggested that the left IFG may be primarily responsible for responding to increased demands during selection and retrieval, while the left caudate serves an overarching role in guiding the left IFG during this process.

Returning to our findings in the PD cohort, despite the differences in activation detected between the groups in frontostriatal networks thought to be critical to verbal selection processes, the present study did not identify any difference in behavioural performance between groups. The question of how the PD group were able to maintain response times and accuracy commensurate with controls, in the face of significantly decreased recruitment in these networks, must therefore be addressed. Given that whole brain and ROI analysis did not identify possible compensatory activity, any hypotheses here can only be speculative in nature. One explanation may be that compensatory mechanisms were at play in regions where there was not sufficient power to detect significant activity in the whole brain analysis, or that were not included in our set of pre-determined ROIs. Previous studies have described equivalent behavioural performance in PD participants in the face of altered neural recruitment during cognitively-loaded tasks including set-shifting (Gerrits et al. 2015; Poston et al. 2016) or semantic event sequencing (Tinaz et al. 2008). However, unlike the present study, the compensatory activity observed in these cohorts has been largely characterised by the presence of hyperactivity in task relevant areas, or their right hemispheres analogues.

Alternatively, behavioural performance in this group may have been maintained via increased functional connectivity between task-relevant regions. Though the present study was unable to address this possibility, emerging evidence of this phenomenon has been identified in the realm of cognition. In their 2017 review, Hilary and Grafman described accumulated evidence of a compensatory hyperconnectivity response following neural injury, including numerous accounts in individuals with early stage Parkinson's disease. More specifically, Gorges et al. (2015) demonstrated hyperconnectivity in cortical, limbic, and basal-thalamic areas in individuals with PD who were cognitively intact relative to healthy controls. Further, individuals with PD who were cognitively impaired were observed to have decreased connectivity between these regions relative to controls in these regions. Gorges et al. suggest that this increase in connectivity in the cognitively intact PD cohort may represent a compensatory mechanism. In addition, Yang et al. (2016) demonstrated that levodopa medication can alter resting-state functional connectivity in the striatum, with differential effects upon dorsal and ventral pathways. Given that the participants recruited for the present study were considered to be in a mild-moderate stage of the disease and were medicated at the time of testing, this may also have played some role in bolstering behavioural performance.

Another alternative explanation may also be drawn from consideration of medication effects in this cohort. A number of authors have suggested that dopamine has a modulatory effect upon activation in semantic networks. In their placebo-controlled study of semantic priming in healthy adults, Kischka et al. (1996) concluded that dopamine exerted a "focusing effect" over the automatic spread of lexical activation through semantic networks, limiting this activation to only those concepts closely related to the target word. Subsequent studies have furthered this notion with several finding evidence of decreased indirect priming (reduced activation of distantly related concepts) and decreased activation of weaker representations when participants had ingested levodopa versus a placebo (Copland et al. 2003; Roesch-Ely et al. 2006). However, alternative

findings suggest that dopamine may act to modulate the speed with which the spread and decay of semantic activation occurs (Angwin et al. 2004). Specifically, Angwin et al. suggest that increased levels of dopamine will result in the absence of direct or indirect priming at long SOAs (i.e. when controlled processing is invoked). Subsequent investigations in a PD population described a relationship between the increasing magnitude of the semantic processing impairment, and the degree of dopaminergic depletion (Angwin et al. 2009).

It is well established that the depletion of dopaminergic projections progresses through the striatum in a dorsal-to-ventral pattern (Kish et al. 1988). Cools (2006) has further demonstrated that those structures that receive output from the dorsal striatum are therefore affected earlier in the course of the disease, relative to those that receive output from the ventral striatum. The pre-SMA and premotor cortex are therefore the earliest affected, and this can account for the earlier onset of motor symptoms relative to manifestation of cognitive impairment. Prefrontal regions, including the vlPFC and dlPFC, are affected later in the course of the disease. As a result, levodopa medication can induce a hyperdopaminergic state in these as yet unaffected areas in the early stages of the disease.

With respect to the present study, decreased activation of critical selection substrates may have been observed in the medicated PD group because activation of possible responses during sentence processing resulted in limited spreading activation or faster decay of activated concepts. As a result, fewer competing alternatives were available for selection to this group, reducing the need for frontostriatal mechanisms of controlled retrieval and selection. This tentative suggestion may offer some support in the results of the whole brain analysis, which detected significant group differences in the pars triangularis. According to Badre et al.'s (2005) model, this is the region of the vlPFC associated with post-retrieval selection (choosing among multiple competing alternatives). The fact that activation in this region was reduced in PD participants relevant to controls may therefore further demonstrate that the PD group did not require engagement of post-retrieval selection mechanisms to the same degree, as a result of more focused activation within the semantic network. In addition to greater sample sizes, future investigations in this field should strive to include on and off medication testing of PD participants, in order to observe the differential effects of dopaminergic medication upon controlled semantic retrieval and selection mechanisms and resulting influence on underlying neural recruitment.

An interesting effect that can be noted is the absence of significant differences in the activation of the vlPFC in low vs. medium conditions for the PD group, in turn with no difference in accuracy between these conditions. Given that the control group did show reduced accuracy between these conditions, and that statistical analysis confirmed a significant difference in the degree of contextual constraint carried by stimuli in these conditions, this insensitivity to increasing selection demands is presently unclear and would require further exploration in a larger sample size. Of note, Di Tella et al. (2018) observed a lack of sensitivity to the number of higher frequency competitors in a PD cohort, however these individuals were defined as having left-sided onset of symptoms, and thus (presumably) right hemisphere neuronal loss. The comparator cohort with right-sided onset did show variation in accuracy as a function of the number of high frequency competitors. In the present study we were unable to verify side of onset, and thus cannot speak to the possibility of a similar phenomenon, however this should be considered in future investigations.

With respect to the work of Di Tell et al. (2018), a limitation of the present study may be that we did not account for the frequency of competitors, only the frequency of the target response. As Di Tella et al. demonstrated, this psycholinguistic variable can have an inhibitory effect upon response time and accuracy in a

selection task (in both PD and control cohorts), and any further study should attempt to account for its influence. It must also be acknowledged that the small sample size included in the present work places considerable limitation upon the generalisation of findings, and indeed Paul et al. (2017) have demonstrated that small sample sizes are detrimental to the reproducibility of ROI analysis in task-based fMRI. However, it can be noted that significant changes in activation were detected in the striatum in both ROI and whole-brain analyses, lending some support to their validity.

In conclusion, the results of the present study suggest that in older adults, the capacity to select a contextually appropriate linguistic unit under conditions of increased contextual constraint is subserved by a number of frontal and subcortical regions related to cognitive control. These primarily include the left dlPFC and bilateral vlPFC, and the left striatum. Furthermore, in the early stages of PD the behavioural efficiency of this linguistic process appears to be maintained, despite underlying decreases in frontostriatal activity. While this behavioural performance does not appear to be facilitated by up-regulation of activity in task-relevant regions, it may be hypothesised that increased functional connectivity between critical structures, or an over-medication effect in frontal networks act to compensate for disease-driven loss of signalling along cortico-subcortical pathways.

Compliance with Ethical Standards

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Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

References

Altmann, L. J., & Troche, M. S. (2011). High-level language production in Parkinson's disease: A review. *Parkinson's Disease, 2011*, 238956. doi:10.4061/2011/238956

Angwin, A. J., Chenery, H. J., Copland, D. A., Murdoch, B. E., & Silburn, P. A. (2004). The time course of semantic activation in Parkinson's disease (Vol. 91, pp. 145-146).

Angwin, A., Arnott, W., Copland, D., Haire, M., Murdoch, B., Silburn, P. A. et al. (2009). Semantic activation in Parkinson's disease patients on and off levodopa. *Cortex, 45*(8), 950-959. doi:10.1016/j.cortex.2009.02.012

Annett, M. (1970). A classification of hand preference by association analysis. *British Journal of Psychology, 61*(3), 303-321.

Argyropoulos, G., Tremblay, P., & Small, S. (2013). The neostriatum and response selection in overt sentence production: An fMRI study. *Neuroimage, 82*, 53-60. doi:10.1016/j.neuroimage.2013.05.064

Ashburner, J. (2007). A fast diffeomorphic image registration algorithm. *Neuroimage, 38*(1), 95-113. doi:10.1016/j.neuroimage.2007.07.007

Badre, D., Poldrack, R. A., Pare-Blagoev, E. J., Insler, R. Z., & Wagner, A. D. (2005). Dissociable controlled retrieval and generalized selection mechanisms in ventrolateral prefrontal cortex. *Neuron, 47*(6), 907-918. doi:10.1016/j.neuron.2005.07.023

Bartels, A. L., & Leenders, K. L. (2009). Parkinson's disease: The syndrome, the pathogenesis and pathophysiology. *Cortex, 45*(8), 915-921. doi:10.1016/j.cortex.2008.11.010

Berlingeri, M., Danelli, L., Bottini, G., Sberna, M., & Paulesu, E. (2013). Reassessing the HAROLD model: Is the hemispheric asymmetry reduction in older adults a special case of compensatory-related utilisation of neural circuits? *Experimental Brain Research, 224*(3), 393-410. doi:10.1007/s00221-012-3319-x

Block, C. K., & Baldwin, C. L. (2010). Cloze probability and completion norms for 498 sentences: Behavioral and neural validation using event-related potentials. *Behavior Research Methods, 42*(3), 665-670. doi:10.3758/BRM.42.3.665
Bloom, P. A., & Fischler, I. (1980). Completion norms for 329 sentence contexts. *Memory and Cognition, 8*(6), 631-642. doi:10.3758/BF03213783
Boulenger, V., Mechtouff, L., Thobois, S., Broussolle, E., Jeannerod, M., & Nazir, T. A. (2008). Word processing in Parkinson's disease is impaired for action verbs but not for concrete nouns. *Neuropsychologia, 46*(2), 743-756. doi:10.1016/j.neuropsychologia.2007.10.007
Bouquet, C. A., Bonnaud, V., & Gil, R. (2003). Investigation of supervisory attentional system functions in patients with Parkinson's disease using the Hayling task. *Journal of Clinical and Experimental Neuropsychology, 25*(6), 751-760. doi:10.1076/jcen.25.6.751.16478
Braver, T. S., Paxton, J. L., Locke, H. S., Barch, D. M., & Smith, E. E. (2009). Flexible Neural Mechanisms of Cognitive Control within Human Prefrontal Cortex. *Proceedings of the National Academy of Sciences of the United States of America, 106*(18), 7351-7356. doi:10.1073/pnas.0808187106
Brett, M., Anton, J., Valabregue, R., & Poline, J. (2002). *Region of interest analysis using an SPM toolbox [abstract]*. Paper presented at the 8th International Conference on Functional Mapping of the Human Brain, Sendai, Japan.
Burgess, P. W., & Shallice, T. (1996). Response suppression, initiation and strategy use following frontal lobe lesions. *Neuropsychologia, 34*(4), 263-272. doi:10.1016/0028-3932(95)00104-2
Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: The HAROLD Model. *Psychology and Aging, 17*(1), 85-100. doi:10.1037/0882-7974.17.1.85
Calne, D. B., Snow, B. J., & Lee, C. (1992). Criteria for diagnosing Parkinson's disease. *Annals of Neurology, 32*(S1), S125-S127. doi:10.1002/ana.410320721
Canini, M., Della Rosa, P. A., Catricalà, E., Strijkers, K., Branzi, F. M., Costa, A., et al. (2016). Semantic interference and its control: A functional neuroimaging and connectivity study. *Human Brain Mapping, 37*(11), 4179-4196, doi:10.1002/hbm.23304.
Chatham, C. H., Frank, M. J., & Badre, D. (2014). Corticostriatal output gating during selection from working memory. *Neuron, 81*(4), 930-942. doi:10.1016/j.neuron.2014.01.002
Cohen, J. D., & Servan-Schreiber, D. (1992). Context, cortex, and dopamine: A connectionist approach to behavior and biology in schizophrenia. *Psychological Review, 99*(1), 45-77. doi:10.1037/0033-295X.99.1.45
Cohen, J. D., Barch, D. M., Carter, C., & Servan-Schreiber, D. (1999). Context-processing deficits in schizophrenia: Converging evidence from three theoretically motivated cognitive tasks. *Journal of Abnormal Psychology, 108*(1), 120-133. doi: 10.1037//0021-843X.108.1.120
Colman, K. S., Koerts, J., van Beilen, M., Leenders, K. L., Post, W. J., & Bastiaanse, R. (2009). The impact of executive functions on verb production in patients with Parkinson's disease. *Cortex, 45*(8), 930-942. doi:10.1016/j.cortex.2008.12.010
Cools, R. (2006). Dopaminergic modulation of cognitive function-implications for l-DOPA treatment in Parkinson's disease. *Neuroscience and Biobehavioral Reviews, 30*(1), 1-23. doi:10.1016/j.neubiorev.2005.03.024
Copland, D. A., Chenery, H. J., Murdoch, B. E., Arnott, W. L., & Silburn, P. A. (2003). Dopamine enhances semantic salience: Semantic priming evidence from healthy individuals. *Brain and Language, 87*(1), 103-104. doi: http://dx.doi.org/10.1016/S0093-934X(03)00220-7
Copland, D. A., Sefe, G., Ashley, J., Hudson, C., & Chenery, H. J. (2009). Impaired semantic inhibition during lexical ambiguity repetition in Parkinson's disease. *Cortex, 45*(8), 943-949. doi:10.1016/j.cortex.2009.02.023
Cotelli, M., Borroni, B., Manenti, R., Zanetti, M., Arévalo, A., Cappa, S. F., et al. (2007). Action and object naming in Parkinson's disease without dementia. *European Journal of Neurology, 14*(6), 632-637. doi:10.1111/j.1468-1331.2007.01797.x
Crescentini, C., Mondolo, F., Biasutti, E., & Shallice, T. (2008). Supervisory and routine processes in noun and verb generation in nondemented patients with Parkinson's disease. *Neuropsychologia, 46*(2), 434-447. doi:10.1016/j.neuropsychologia.2007.08.021
Crosson, B., Benefield, H., Cato, M. A., Sadek, J. R., Moore, A. B., Wierenga, C. E., et al. (2003). Left and right basal ganglia and frontal activity during language generation: Contributions to lexical, semantic, and phonological processes. *Journal of the International Neuropsychological Society, 9*(7), 1061-1077. doi:10.1017/S135561770397010X
Crosson, B., Benjamin, M., & Levy, I. (2007). Role of the basal ganglia in language and semantics: Supporting cast. In J. Hart, Jr. & M. Kraut (Eds.), *Neural Basis of Semantic Memory* (pp. 219-244). New York: Cambridge.
Davis, C. (2005). N-Watch: A program for deriving neighborhood size and other psycholinguistic statistics. *Behavior Research Methods, 37*(1), 65-70. doi:10.3758/BF03206399

Di Martino, A., Scheres, A., Margulies, D. S., Kelly, A. M. C., Uddin, L. Q., Shehzad, Z., et al. (2008). Functional connectivity of human striatum: A resting state fMRI study. *Cerebral Cortex, 18*(12), 2735-2747. doi:10.1093/cercor/bhn041

Di Tella, S., Baglio, F., Cabinio, M., Nemni, R., Traficante, D., & Silveri, M. C. (2018). Selection Processing in Noun and Verb Production in Left- and Right-Sided Parkinson's Disease Patients. *Frontiers in Psychology, 9*, 1241-1241, doi:10.3389/fpsyg.2018.01241.

Diaz, M. T., Johnson, M. A., Burke, D. M., & Madden, D. J. (2014). Age-related differences in the neural bases of phonological and semantic processes. *Journal of Cognitive Neuroscience, 26*(12), 2798-2811. doi:10.1162/jocn_a_00665

Dirnberger, G., & Jahanshahi, M. (2013). Executive dysfunction in Parkinson's disease: A review. *Journal of Neuropsychology, 7*(2), 193-224. doi:10.1111/jnp.12028

Dissanayaka, N. N., O'Sullivan, J. D., Silburn, P. A., & Mellick, G. D. (2011). Assessment methods and factors associated with depression in Parkinson's disease. *Journal of the Neurological Sciences, 310*(1-2), 208-210. doi:10.1016/j.jns.2011.06.031

Dissanayaka, N. N., Sellbach, A., Matheson, S., Marsh, R., Silburn, P. A., O'Sullivan, J. D., et al. (2007). Validity of Hamilton Depression Inventory in Parkinson's disease. *Movement Disorders, 22*(3), 399-403. doi:10.1002/mds.21309

Ford, A., Triplett, W., Sudhyadhom, A., Gullett, J., McGregor, K., FitzGerald, D., et al. (2013). Broca's area and its striatal and thalamic connections: A diffusion-MRI tractography study. *Frontiers in Neuroanatomy*, 7, article 8, 1-12. doi: 10.3389/fnana.2013.00008

Frank, M., Loughry, B., & O'Reilly, R. (2001). Interactions between frontal cortex and basal ganglia in working memory: A computational model. *Cognitive, Affective, & Behavioral Neuroscience, 1*(2), 137-160, doi:10.3758/CABN.1.2.137.

Gerrits, N. J., van der Werf, Y. D., Verhoef, K. M., Veltman, D. J., Groenewegen, H. J., Berendse, H. W., et al. (2015). Compensatory fronto-parietal hyperactivation during set-shifting in unmedicated patients with Parkinson's disease. *Neuropsychologia, 68*, 107-116. doi:10.1016/j.neuropsychologia.2014.12.022

Gorges, M., Muller, H. P., Lule, D., Pinkhardt, E. H., Ludolph, A. C., & Kassubek, J. (2015). To rise and to fall: Functional connectivity in cognitively normal and cognitively impaired patients with Parkinson's disease. *Neurobiology of Aging, 36*(4), 1727-1735. doi:10.1016/j.neurobiolaging.2014.12.026

Grossman, M., Cooke, A., Devita, C., Lee, C., Alsop, D., Detre, J., et al. (2003). Grammatical and resource components of sentence processing in Parkinson's disease: An fMRI study. *Neurology, 60*(5), 775.

Hanganu, A., Provost, J. S., & Monchi, O. (2015). Neuroimaging studies of striatum in cognition part II: Parkinson's disease. *Frontiers in Systems Neuroscience, 9*, 138. doi:10.3389/fnsys.2015.00138

Henry, J. D., & Crawford, J. R. (2004). Verbal fluency deficits in Parkinsons disease: A meta-analysis. *J Inter Neuropsych Soc, 10*(4), 608-622. doi:10.1017/S1355617704104141

Hillary, F. G., & Grafman, J. H. (2017). Injured Brains and Adaptive Networks: The Benefits and Costs of Hyperconnectivity. *Trends in Cognitive Sciences, 21*(5), 385-401, doi:10.1016/j.tics.2017.03.003.

Hoehn, M. M., & Yahr, M. D. (2001). Parkinsonism: onset, progression, and mortality. 1967. *Neurology, 57*(10 Suppl 3), S11.

Kan, I. P., & Thompson-Schill, S. L. (2004). Effect of name agreement on prefrontal activity during overt and covert picture naming. *Cognitive, Affective & Behavioral Neuroscience, 4*(1), 43-57.

Kaplan, E., Goodglass, H., & Weintraub, S. (2001). *Boston naming test* (2nd ed.). Philadelphia: Lippincott, Williams, & Wilkins.

Kerns, J. G., Cohen, J. D., Stenger, V. A., & Carter, C. S. (2004). Prefrontal cortex guides context-appropriate responding during language production. *Neuron, 43*(2), 283-291. doi:10.1016/j.neuron.2004.06.032

Ketteler, D., Kastrau, F., Vohn, R., & Huber, W. (2008). The subcortical role of language processing. High level linguistic features such as ambiguity-resolution and the human brain; an fMRI study. *Neuroimage, 39*(4), 2002-2009. doi:10.1016/j.neuroimage.2007.10.023

Ketteler, S., Ketteler, D., Vohn, R., Kastrau, F., Schulz, J. B., Reetz, K., et al. (2014). The processing of lexical ambiguity in healthy ageing and Parkinsons disease: role of cortico-subcortical networks. *Brain Research, 1581*, 51-63. doi:10.1016/j.brainres.2014.06.030

Kischka, U., Kammer, T., Maier, S., Weisbrod, M., Thimm, M., & Spitzer, M. (1996). Dopaminergic modulation of semantic network activation. *Neuropsychologia, 34*(11), 1107-1113.

Kish, S. J., Shannak, K., & Hornykiewicz, O. (1988). Uneven pattern of dopamine loss in the striatum of patients with idiopathic Parkinson's disease. Pathophysiologic and clinical implications. *New England Journal of Medicine, 318*(14), 876-880. doi:10.1056/nejm198804073181402

Koechlin, E., Ody, C., & Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. *Science, 302*(5648), 1181-1185. doi:10.1126/science.1088545

Leh, S. E., Ptito, A., Chakravarty, M. M., & Strafella, A. P. (2007). Fronto-striatal connections in the human brain: A probabilistic diffusion tractography study. *Neuroscience Letters, 419*(2), 113-118. doi:10.1016/j.neulet.2007.04.049

Lewis, S., Dove, A., Robbins, T., Barker, R., & Owen, A. (2003). Cognitive Impairments in Early Parkinson's Disease Are Accompanied by Reductions in Activity in Frontostriatal Neural Circuitry. *Journal of*

Neuroscience, 23(15), 6351-6356.
MacDonald, A. W., Cohen, J. D., Stenger, V. A., & Carter, C. S. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science, 288*(5472), 1835-1838.
Maldjian, J.A., Laurienti, P.J., Kraft, R.A., & Burdette, J.H. (2003). An automated method for neuroanatomic and cytoarhcitectonic atlas-based interrogation of fmri data sets. *Neuroimage, 19*, 1233-1239.
MathWorks. (2011). MatLab (R2011b) [Software]. Retrieved from http://www.mathworks.com.au/products/new_products/release2011b.html
MathWorks. (2013). MatLab (R2013b) [Software]. Retrieved from https://au.mathworks.com/products/new_products/release2013b.html
Matzig, S., Druks, J., Masterson, J., & Vigliocco, G. (2009). Noun and verb differences in picture naming: past studies and new evidence. *Cortex, 45*(6), 738-758, doi:10.1016/j.cortex.2008.10.003.
Mestres-Missé, A., Camara, E., Rodriguez-Fornells, A., Rotte, M., & Munte, T. F. (2008). Functional neuroanatomy of meaning acquisition from context. *Journal of Cognitive Neuroscience, 20*(12), 2153-2166. doi:10.1162/jocn.2008.20150
Mestres-Missé, A., Turner, R., & Friederici, A. D. (2012). An anterior–posterior gradient of cognitive control within the dorsomedial striatum. *Neuroimage, 62*(1), 41-47.
Miller, E. K. (2000). The prefrontal cortex: No simple matter. *Neuroimage, 11*(5 Pt 1), 447-450. doi:10.1006/nimg.2000.0574
Miller, E., & Cohen, J. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*, 167-202.
Moss, H. E., Abdallah, S., Fletcher, P., Bright, P., Pilgrim, L., Acres, K., et al. (2005). Selecting among competing alternatives: selection and retrieval in the left inferior frontal gyrus. *Cerebral Cortex, 15*(11), 1723-1735, doi:10.1093/cercor/bhi049.
Murray, L. L. (2008). Language and Parkinson's Disease. *Annual Review of Applied Linguistics, 28*, 113, doi:10.1017/s0267190508080100.
Nagel, I. E., Schumacher, E. H., Goebel, R., & D'Esposito, M. (2008). Functional MRI investigation of verbal selection mechanisms in lateral prefrontal cortex. *Neuroimage, 43*(4), 801-807. doi:10.1016/j.neuroimage.2008.07.017
Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., et al. (2005). The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. *Journal of the American Geriatrics Society, 53*(4), 695-699. doi:10.1111/j.1532-5415.2005.53221.x
Nathaniel-James, D. F., C. D. (2002). The Role of the Dorsolateral Prefrontal Cortex: Evidence from the Effects of Contextual Constraint in a Sentence Completion Task. *Neuroimage, 16*(4), 1094-1102. doi:10.1006/nimg.2002.1167
Nelson, H. E., & Willison, J. (1991). *The revised national adult reading test – test manual*. Windsor, UK: NFER-Nelson.
Nelson, J. K., Reuter-Lorenz, P. A., Persson, J., Sylvester, C.-Y. C., & Jonides, J. (2009). Mapping interference resolution across task domains: A shared control process in left inferior frontal gyrus. *Brain Research, 1256*, 92-100. doi:10.1016/j.brainres.2008.12.001
Noonan, K. A., Jefferies, E., Visser, M., & Lambon Ralph, M. A. (2013). Going beyond inferior prefrontal involvement in semantic control: evidence for the additional contribution of dorsal angular gyrus and posterior middle temporal cortex. *Journal of Cognitive Neuroscience, 25*(11), 1824-1850. doi:10.1162/jocn_a_00442
Norman, D. A., & Shallice, T. (1986). Attention to Action. In R. J. Davidson, G. E. Schwartz, & D. Shapiro (Eds.), *Consciousness and Self-Regulation: Advances in Research and Theory Volume 4* (pp. 1-18). Boston, MA: Springer US.
Nozari, N., & Thompson-Schill, S. L. (2016). Chapter 46 - Left Ventrolateral Prefrontal Cortex in Processing of Words and Sentences. In G. Hickok, & S. L. Small (Eds.), *Neurobiology of Language* (pp. 569-584). San Diego: Academic Press.
O'Callaghan, C., Naismith, S. L., Hodges, J. R., Lewis, S. J., & Hornberger, M. (2013a). Fronto-striatal atrophy correlates of inhibitory dysfunction in Parkinson's disease versus behavioural variant frontotemporal dementia. *Cortex, 49*(7), 1833-1843. doi:10.1016/j.cortex.2012.12.003
O'Callaghan, C., Naismith, S. L., Shine, J. M., Bertoux, M., Lewis, S. J., & Hornberger, M. (2013b). A novel bedside task to tap inhibitory dysfunction and fronto-striatal atrophy in Parkinson's disease. *Parkinsonism & Related Disorders, 19*(9), 827-830. doi:10.1016/j.parkreldis.2013.04.020
Obeso, I., Wilkinson, L., Casabona, E., Bringas, M. L., Alvarez, M., Alvarez, L., et al. (2011). Deficits in inhibitory control and conflict resolution on cognitive and motor tasks in Parkinson's disease. *Experimental Brain Research, 212*(3), 371-384. doi:10.1007/s00221-011-2736-6
Owen, A. M. (2004). Cognitive dysfunction in Parkinson's disease: The role of frontostriatal circuitry. *The Neuroscientist, 10*(6), 525-537. doi:10.1177/1073858404266776
Paul, E. J., Turner, B., Miller, M. B., & Barbey, A. K. (2017). How Sample Size Influences The Reproducibility Of Task-Based fMRI. *bioRxiv*, doi:10.1101/136259.

Peran, P., Rascol, O., Demonet, J. F., Celsis, P., Nespoulous, J. L., Dubois, B., & Cardebat, D. (2003). Deficit of verb generation in nondemented patients with Parkinson's disease. *Movement Disorders, 18*(2), 150-156. doi:10.1002/mds.10306

Persson, J., Sylvester, C.-Y. C., Nelson, J. K., Welsh, K. M., Jonides, J., & Reuter-Lorenz, P. A. (2004). Selection requirements during verb generation: Differential recruitment in older and younger adults. *Neuroimage, 23*(4), 1382-1390. doi:10.1016/j.neuroimage.2004.08.004

Poldrack, R. A., Wagner, A. D., Prull, M. W., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. E. (1999). Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. *Neuroimage, 10*(1), 15-35. doi:10.1006/nimg.1999.0441

Poston, K. L., YorkWilliams, S., Zhang, K., Cai, W., Everling, D., Tayim, F. M., et al. (2016). Compensatory neural mechanisms in cognitively unimpaired Parkinson disease. *Annals of Neurology, 79*(3), 448-463. doi:10.1002/ana.24585

Redgrave, P., Prescott, T. J., & Gurney, K. (1999). The basal ganglia: A vertebrate solution to the selection problem? *Neuroscience, 89*(4), 1009-1023. doi:10.1016/S0306-4522(98)00319-4

Ridderinkhof, K. R., van den Wildenberg, W. P., Segalowitz, S. J., & Carter, C. S. (2004). Neurocognitive mechanisms of cognitive control: the role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. *Brain and Cognition, 56*(2), 129-140. doi:10.1016/j.bandc.2004.09.016

Robertson, I. H., Ward, T., Ridgeway, V., & Nimmo-Smith, I. (1994). *The test of everyday attention*. Bury St. Edmunds, UK: Thames Valley Test Company.

Roesch-Ely, D., Weiland, S., Scheffel, H., Schwaninger, M., Hundemer, H. P., Kolter, T., et al. (2006). Dopaminergic modulation of semantic priming in healthy volunteers. *Biological Psychiatry, 60*(6), 604-611. doi:10.1016/j.biopsych.2006.01.004

Rossetti, H. C., Lacritz, L. H., Cullum, C. M., & Weiner, M. F. (2011). Normative data for the Montreal Cognitive Assessment (MoCA) in a population-based sample. *Neurology, 77*(13), 1272. doi:10.1212/WNL.0b013e318230208a

Sheikh, J. I., & Yesavage, J. A. (1986). Geriatric Depression Scale (GDS): Recent evidence and development of a shorter version. *Clinical Gerontologist, 5*(1-2), 165-173.

Silveri, M. C., Ciccarelli, N., Baldonero, E., Piano, C., Zinno, M., Soleti, F., et al. (2012). Effects of stimulation of the subthalamic nucleus on naming and reading nouns and verbs in Parkinson's disease. *Neuropsychologia, 50*(8), 1980-1989. doi:10.1016/j.neuropsychologia.2012.04.023

Silveri, M. C., Traficante, D., Lo Monaco, M. R., Iori, L., Sarchioni, F., & Burani, C. (2018). Word selection processing in Parkinson's disease: When nouns are more difficult than verbs. *Cortex, 100*, 8-20, doi:10.1016/j.cortex.2017.05.023.

Smith, K. M., & Caplan, D. N. (2018). Communication impairment in Parkinson's disease: Impact of motor and cognitive symptoms on speech and language. *Brain and Language, 185*, 38-46.

Snyder, H. R. B., Marie, T.; Munakata, Yuko. . (2011). Choosing Our Words: Retrieval and Selection Processes Recruit Shared Neural Substrates in Left Ventrolateral Prefrontal Cortex. *Journal of Cognitive Neuroscience, 23*(11), 3470-3482.

Souza, M. J., Donohue, S. E., & Bunge, S. A. (2009). Controlled retrieval and selection of action-relevant knowledge mediated by partially overlapping regions in left ventrolateral prefrontal cortex. *Neuroimage, 46*(1), 299-307. doi:10.1016/j.neuroimage.2009.01.046

Thompson-Schill, S. L., Amp, Apos, Esposito, M., & Kan, I. P. (1999). Effects of repetition and competition on activity in left prefrontal cortex during word generation. *Neuron, 23*(3), 513-522. doi:10.1016/S0896-6273(00)80804-1

Thompson-Schill, S. L., D'esposito, M., Aguirre, G. K., & Farah, M. J. (1997). Role of left inferior prefrontal cortex in retrieval of semantic knowledge: A reevaluation. *Proceedings of the National Academy of Sciences of the United States of America, 94*(26), 14792. doi:10.1073/pnas.94.26.14792

Tinaz, S., Schendan, H. E., & Stern, C. E. (2008). Fronto-striatal deficit in Parkinson's disease during semantic event sequencing. *Neurobiology of Aging, 29*(3), 397-407. doi:10.1016/j.neurobiolaging.2006.10.025

Tomlinson, C. L., Stowe, R., Patel, S., Rick, C., Gray, R., & Clarke, C. E. (2010). Systematic review of levodopa dose equivalency reporting in Parkinson's disease. *Movement disorders : Official journal of the Movement Disorder Society, 25*(15), 2649. doi:10.1002/mds.23429

Tremblay, P., & Gracco, V. L. (2006). Contribution of the frontal lobe to externally and internally specified verbal responses: fMRI evidence. *Neuroimage, 33*(3), 947-957. doi:10.1016/j.neuroimage.2006.07.041

Tröster, A. I., Fields, J. A., Testa, J. A., Paul, R. H., Blanco, C. R., Hames, K. A., et al. (1998). Cortical and subcortical influences on clustering and switching in the performance of verbal fluency tasks. *Neuropsychologia, 36*(4), 295-304. doi:10.1016/S0028-3932(97)00153-X

Ullman, M. T. (2006). Is Broca's area part of a basal ganglia thalamocortical circuit? *Cortex, 42*(4), 480-485.

Wagner, A. D., Maril, A., Bjork, R. A., & Schacter, D. L. (2001). Prefrontal contributions to executive control: fMRI evidence for functional distinctions within lateral prefrontal cortex. *Neuroimage, 14*(6), 1337-1347. doi:10.1006/nimg.2001.0936

Wellcome Department of Imaging Neuroscience. (2013). Cogent (2000) [Software]. Retrieved from http://www.vislab.ucl.ac.uk/cogent.php

Wellcome Trust Centre for Neuroimaging. (2014). Statistical parametric mapping (Version 12) [Software]. Retrieved from http://www.fil.ion.ucl.ac.uk/spm/

Wierenga, C. E., Benjamin, M., Gopinath, K., Perlstein, W. M., Leonard, C. M., Rothi, L. J. G., et al. (2008). Age-related changes in word retrieval: Role of bilateral frontal and subcortical networks. *Neurobiology of Aging, 29*(3), 436-451.

Wilke, M. (2012). An alternative approach towards assessing and accounting for individual motion in fMRI timeseries. *Neuroimage, 59*(3), 2062-2072, doi:10.1016/j.neuroimage.2011.10.043.

Yang, W., Liu, B., Huang, B., Huang, R., Wang, L., Zhang, Y., et al. (2016). Altered resting-state functional connectivity of the striatum in Parkinson's disease after levodopa administration. *PloS One, 11*(9), e0161935. doi:10.1371/journal.pone.0161935

Zgaljardic, D. J., Borod, J. C., Foldi, N. S., Mattis, P. J., Gordon, M. F., Feigin, A., et al. (2006). An examination of executive dysfunction associated with frontostriatal circuitry in Parkinson's disease. *Journal of Clinical and Experimental Neuropsychology, 28*(7), 1127-1144. doi:10.1080/13803390500246910