Semantic Fluency Deficits and Associated Brain Activity in Parkinson's Disease Patients With Mild Cognitive Impairment

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Research Article

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Abstract

Parkinson's disease (PD) patients with poor verbal fluency have an increased risk of developing dementia. This study examines the neural mechanisms underpinning semantic fluency deficits in PD patients with mild cognitive impairment (PD-MCI) compared to patients without MCI (PD-NC) and healthy controls (HC). Thirty-seven (37) PD patients completed a cognitive assessment battery to identify MCI (13 PD-MCI). Gender- and age-matched 20 HC also participated. Participants were scanned (3T Siemens PRISMA) whilst performing semantic fluency, semantic switching, and automatic speech tasks. The number of responses, error rate, and fMRI data for semantic generation and semantic switching were analyzed. Participants also completed a series of verbal fluency tests outside the scanner, including letter fluency. Patients with PD-MCI performed significantly worse than PD-NC and HC during semantic fluency and semantic switching tasks. Patients with PD-MCI showed greater activity in the right angular gyrus compared to PD-NC and HC during semantic switching. Increased right angular activity correlated with worse verbal fluency performance outside the scanner. Our study showed that PD-MCI patients perform more poorly on semantic fluency than either PD-NC or HC groups. Increased right angular gyrus activity in patients with PD-MCI during semantic switching suggests early compensatory mechanisms predicting the risk of future dementia in PD.

Introduction

There is a growing interest in language impairment in patients with Parkinson's disease (PD). Notably, verbal fluency tasks have been widely used to further understand cognitive impairment in PD (Dujardin et al, 2004; Pagonabarraga and Kulisevsky, 2012; Rodriguez-Porcel et al, 2020). Verbal fluency tasks involve generating words that begin with a particular letter (letter fluency) or from a particular semantic category (semantic fluency) within a given period of time. Semantic fluency is strongly linked to semantic memory, whereas letter fluency relies less on semantic memory and more on executive functioning (Greenaway et al, 2009). Semantic switching, which requires switching between two semantic categories, is linked to frontal-executive control for alternating attention and inhibiting irrelevant responses (Ellfolk et al, 2014). Not only are PD patients with semantic fluency deficits more susceptible to dementia than those without semantic fluency deficits (Janvin et al, 2006; Williams-Gray et al, 2009; Williams-Gray et al, 2007), but they also report poorer quality of life and increased carer burden (Rosenthal et al, 2017). Given the clinical significance of semantic fluency impairment in PD, the present study investigates the neural underpinnings of semantic fluency deficits in PD patients with early cognitive deficits (i.e. mild cognitive impairment (MCI)) to identify functional neural markers prior to development of dementia.

It has been suggested that early semantic fluency deficits in PD that increases the risk of dementia may be associated with posterior cortical and temporal lobe dysfunction (Williams-Gray et al, 2009). To date, however, there are no fMRI studies empirically investigating brain regions constituting this link in PD patients with MCI (PD-MCI). The present study is novel in examining deficits in semantic fluency and associated neural activity in PD-MCI compared to PD patients without MCI (PD-NC) and healthy controls (HC). It is predicted that a greater impairment in semantic and semantic switching fluency will be

observed in PD-MCI patients compared to other groups and impaired posterior cortical and temporal lobe activity will be related to semantic fluency deficits in PD-MCI patients.

Methods

Participants

Thirty-seven (37) non-demented PD patients (13 PD-MCI, 24 PD-NC) and 20 age- and gender-matched HC were included in this study (Table 1). The inclusion criterion for PD was the fulfilment of the UK PD Society Brain Bank diagnostic criteria. Exclusion criteria for both PD and HC were the presence of: 1) dementia (diagnosed by neurologist or < 19 in the Montreal Cognitive Assessment (MoCA)); 2) other neurological diseases; 3) major depression and/or significant anxiety screened by Mini International Neuropsychiatric Interview (MINI-plus); 4) contraindications for MRI; 5) abnormal brain finding or 6) excessive head movement > 1 voxel (2.6mm^3). All assessments in PD patients were performed in their 'ON' state. Written informed consent was collected from each participant prior to their participation. This study was approved by the human research ethics committees of the University of Queensland and the Royal Brisbane and Women's Hospital.

Table 1
Demographics and clinical characteristics of participants

	PD-MCI (N = 13)	PD-NC (N = 24)	HC (N = 20)	p-value	Post-hoc analysis
Sex (M/F) ^a	8/4	13/11	12/9	ns	
Age (years) ^c	70.38 (8.61)	67.75 (9.29)	64.00(8.08)	ns	
Education (years) ^b	12.31 (3.54)	13.22 (3.67)	14.66(3.36)	ns	
Disease Duration (Year) ^d	6.00 (3.70)	4.29 (3.38)		ns	
HY Stage ^e	1.62 (0.65)	1.50 (0.66)		ns	
LEDD (mg) ^d	368.27 (220.36)	509.7 3(273.38)		ns	
MDS-UPDRS Total ^e	34.85 (12.05)	32.96 (15.01)		ns	
UPDRS-III ^e	20.46 (8.24)	14.92 (9.12)		ns	
MoCA ^c	23.00 (2.24)	26.08 (2.21)	26.52 (1.83)	.0001	PD-MCI < PD-NC***, < HC***
PDCRS ^d	88.08 (11.32)	104.38 (11.11)		.0001	
CCRT ^b	37.08 (8.46)	38.08 (6.16)	40.57 (6.87)	ns	
HAM-A ^b	4.23 (3.72)	5.00 (4.18)	0.94 (1.34)	.003	HC < PD-MCI*, < PD-NC**
PAS ^e	7.46 (5.47)	8.00 (7.05)		ns	
HAM-D ^b	4.38 (3.69)	4.58 (3.34)	1.94 (2.16)	.014	HC < PD-NC*
SAS ^b	11.31 (4.99)	10.09 (5.15)	9.40 (3.58)	ns	

^a Chi-square Test; ^bKruskal-Wallis H Test; ^cANOVA (Analysis of Variance) Test; ^d Independent T-Test; ^e Mann Whitney Test Results are presented as mean (SD). Statistically significant results for post-hoc analysis are indicated as * $p < .05$, ** $p < .001$, *** $p < .0001$. *Note.* PD-MCI = Parkinson's disease patients with mild cognitive impairment; PD-NC = Parkinson's disease patients with no cognitive impairment; HC = age-and sex-matched healthy controls; HY Stage = Hoehn and Yahr Stage (1–5); LEDD = Levodopa Equivalent Daily Dose; MDS-UPDRS = Movement Disorder Society Unified Parkinson's Disease Rating Scale; MoCA = Montreal Cognitive Assessment; PDCRS = Parkinson's Disease Cognitive Rating Scale; CCRT = Cambridge Contextual Reading Test; HAM-A = Hamilton Anxiety Scale, PAS = Parkinson's disease Anxiety Scale, HAM-D = Hamilton Depression Scale, SAS = Starkstein Apathy Scale, IADL = Instrumental Activities of Daily Living, IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), ns = Non statistically significant.

	PD-MCI (N = 13)	PD-NC (N = 24)	HC (N = 20)	p-value	Post-hoc analysis
IADL ^e	8.58 (.90)	8.91 (1.28)		ns	
IQCODE ^e	3.01(.45)	3.28(.33)			
^a Chi-square Test; ^b Kruskal-Wallis H Test; ^c ANOVA (Analysis of Variance) Test; ^d Independent T-Test; ^e Mann Whitney Test Results are presented as mean (SD). Statistically significant results for post-hoc analysis are indicated as * $p < .05$, ** $p < .001$, *** $p < .0001$. <i>Note.</i> PD-MCI = Parkinson's disease patients with mild cognitive impairment; PD-NC = Parkinson's disease patients with no cognitive impairment; HC = age-and sex-matched healthy controls; HY Stage = Hoehn and Yahr Stage (1–5); LEDD = Levodopa Equivalent Daily Dose; MDS-UPDRS = Movement Disorder Society Unified Parkinson's Disease Rating Scale; MoCA = Montreal Cognitive Assessment; PDCRS = Parkinson's Disease Cognitive Rating Scale; CCRT = Cambridge Contextual Reading Test; HAM-A = Hamilton Anxiety Scale, PAS = Parkinson's disease Anxiety Scale, HAM-D = Hamilton Depression Scale, SAS = Starkstein Apathy Scale, IADL = Instrumental Activities of Daily Living, IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), ns = Non statistically significant.					

Clinical and cognitive measures

All participants were administered the MoCA for global cognition (Gill et al, 2008); Hamilton Depression Scale (HAM-D) (Hamilton, 1960), Hamilton Anxiety Scale (HAM-A) (Maier et al, 1988) for depression and anxiety; MINI-plus (Sheehan et al, 1998), for psychological symptoms; and Edinburgh Handedness Inventory (EHI) for handedness (Oldfield, 1971). PD patients also completed the Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) for PD symptom severity (Goetz et al, 2008), and the Lawton Instrumental Activities of Daily Living (IADL) for functional ability (Graf, 2008).

A comprehensive neuropsychological battery of tests was administered to identify PD-MCI according to the level 2 Movement Disorder Society (MDS) task force criteria (Litvan et al, 2012). Further details of this test battery can be found in our previously published study (Yang et al, 2021). PD-MCI was diagnosed when PD patients performed 1.5 *SD* below the normative mean score on at least two neuropsychological tests in one or more cognitive domains out of five cognitive domains recommended to include for testing in PD (Litvan et al, 2012).

Semantic fluency task

During the in-scanner task, each participant was prompted with different instructions aligned to the following four conditions with a timing of 15 seconds per condition: 1. Rest ("Think of nothing"), 2. Automatic Speech (e.g., "Name the months of the year"), 3. Overt unpaced semantic fluency (e.g., "Name musical instruments") and 4. Overt unpaced semantic switching (e.g., "Name colours and male first names (switch)"). The categories used for the semantic fluency and semantic switching conditions were selected from category norms (Van Overschelde et al, 2004). The task consisted of a total of 64 trials (16 per condition) and for each trial, the instructions were first displayed on the screen (4000ms), and then a green dot appeared on screen during which participants were asked to provide their responses loudly and clearly (except during rest) until the dot disappeared (11500ms). Responses were recorded through the

MR compatible optoactive acoustic microphone (Optoacoustics, www.optoacoustics.com). The task was presented using Cogent 2000 (Wellcome Laboratory of Neurobiology) and MATLAB 2018a (The MathWorks Inc., Natick, MA).

MRI Acquisition

MRI scans were performed on a Siemens 3T Prisma (Siemens, Erlangen) using a 20-channel head coil. 125 BOLD sensitive gradient echo-planar images (EPI) were acquired during each block with 3 dummy scans at the start of each session (TE = 30ms, TR = 2050ms, flip angle = 80°, axial slices = 50, slice thickness = 2.6mm, contiguous slices, field of view = 190). Three-dimensional high resolution structural T1-weighted MP2RAGE scans were also obtained (TE = 2.05ms, TI = 700ms, FA = 3, field of view = 256 x 240 x 176 mm³).

MRI Processing

All fMRI pre-processing and analyzes were conducted using SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK) and MATLAB 2018a (The Mathworks Inc., Natick, MA). The first three functional volumes were discarded to allow for steady-state magnetisation. The EPI images were realigned and unwarped (Andersson et al, 2001). The derived six-motion fingerprint parameters using Motion Fingerprint Toolbox (Wilke, 2012) were used as regressors. Each participant's EPI and T1 images were co-registered, then the T1 was normalised to a Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra (DARTEL) template created from all participants (Ashburner, 2007). Normalised functional volumes were smoothed with a Gaussian Kernel of 6.5mm³ (FWHM). The grey matter mask based on the structural template was overlaid to focus on the regions within the grey matter.

Statistical analysis

For all clinical characteristic variables, assessment of normality was performed with the Shapiro-Wilk test. Missing data were handled by using complete case analysis as recommended by Kang et al. (2013). We performed the ANOVA/Kruskal-Wallis H test to compare the difference between PD-MCI, PD-NC and HC in SPSS v25 (IMBL Armonk, New York, USA). Repeated measure ANOVA was used to analyze the effect of group and condition. A significance level of $p < 0.05$ was used. For the fMRI analysis, GLM were created with realignment parameters using the six motion fingerprint parameters (Wilke, 2012, 2014). Three attentional components were created as a contrast at the first level and were compared between the groups. An uncorrected significance level of $p < .001$ and cluster size FWE of $p < .05$ in SPM12 was accepted. The association between significant clusters and verbal fluency cognitive measures were examined using correlation analyzes. A significance value adjusted using the Bonferroni correction.

Results

Clinical characteristics

PD-MCI and PD-NC groups did not differ significantly on demographic and clinical characteristics (Table 1), nor on PD-specific measures. As expected, patients in the PD-MCI group performed significantly worse on the MoCA ($\chi^2(2) = 17.309, p < .001$) compared to PD-NC and HC groups, while there was no difference between PD-NC and HC.

Behavioral Results

The mean number of correct responses for semantic fluency ($\chi^2(2) = 11.53, p = .003$), semantic switching ($\chi^2(2) = 14.148, p = .001$) significantly differed between PD-MCI, PD-NC and HC (Table 2). Automatic responses did not differ between the three groups. Using post-hoc analysis, a significantly lower mean number of correct responses during semantic fluency was identified in the PD-MCI group compared to the PD-NC and HC ($p < .01$) groups. During semantic switching, the PD-MCI group also produced a lower mean number of correct responses compared to the PD-NC ($p < .05$) and HC ($p = .001$) groups, whilst did not differ between the PD-NC and HC. Lastly, the PD-MCI group failed to respond to 1.77 ± 1.30 trials, which was significantly higher ($\chi^2(2) = 12.68, p = .002$) than the PD-NC (0.38 ± 0.71) and HC (0.85 ± 1.90) groups.

Table 2
Average number of responses for each condition per group during fMRI

	PD-MCI (N = 13)	PD-NC (N = 24)	HC (N = 20)	p-value	Post-hoc analysis
Automatic ^a	13.01(3.49)	15.53(5.52)	14.03(4.01)	ns	
Semantic ^b	5.09 (.73)	6.21(.92)	6.21(1.25)	.003	PD-MCI < PD-NC**, PD-MCI < HC**
Semantic Switching ^b	2.40(1.08)	3.49 (1.03)	4.07(1.24)	.001	PD-MCI < PD-NC*, PD-MCI < HC**

^aANOVA (Analysis of Variance) Test; ^bKruskal-Wallis H Test

Table of average number of responses (SD) for automatic, semantic, semantic switching during the semantic fluency fMRI task for 15s. Statistically significant results for post-hoc analysis are indicated as * $p < .05$, ** $p < .01$, *** $p < .001$. *Note.* PD-MCI = Parkinson's disease patients with mild cognitive impairment; PD-NC = Parkinson's disease patients with no cognitive impairment; HC = age- and sex-matched healthy controls.

Imaging Results

The main effect of group for semantic switching compared to the rest condition showed a significantly different activation in the right angular gyrus (Fig. 1). Post-hoc analysis indicated that right angular gyrus activity was up-regulated in the PD-MCI group relative to both the PD-NC group ($p < .001$) and the HC group ($p < .001$) (Fig. 1), whilst no difference was evident between the PD-NC and HC group. There was also a main effect of group for semantic switching compared to the automatic condition in the right

angular gyrus (Fig. 1). A follow-up analysis demonstrated that the right angular gyrus was significantly up-regulated in the PD-MCI group compared to PD-NC ($p < .001$) and HC ($p < .001$) groups (Fig. 2). There was no significant difference between PD-NC and HC.

Correlation analysis

Correlation analysis was performed between the activity of the right angular gyrus observed during the semantic switching task compared to the automated condition inside the scanner and performance in semantic, semantic switching, and letter fluency tasks conducted outside the scanner in PD patients (Fig. 3). Significant negative correlations were found for all verbal fluency tasks performed outside the scanner; letter ($r = -.43$, $N = 37$, $p = .001$), semantic ($r = -.37$, $N = 37$, $p = .02$), and semantic switching ($r = -.41$, $N = 37$, $p = 0.02$).

Discussion

The present study was the first to examine the neural correlates of semantic fluency deficits in PD-MCI. At a behavioral level, patients with PD-MCI performed significantly worse than PD-NC and HC on semantic and semantic switching fluency, whereas PD-NC performed comparably to HC. Our findings therefore support previous literature suggesting that verbal fluency deficits as a defining feature of PD-MCI and thus a potential predictor of PDD (Galtier et al, 2017; Williams-Gray et al, 2007). The results also support suggestions that verbal fluency deficits are associated with an increased risk of dementia more broadly (e.g., Sutin et al (2019)).

PD-MCI patients demonstrated increased activation in the right angular gyrus compared to PD-NC and HC groups during the semantic switching task. Interestingly, no differences in brain activation were revealed during the semantic fluency task across groups. This may be due to the fact that the semantic fluency task is less cognitively demanding than the semantic switching task, which places more substantial demands on executive functions compared to semantic fluency (Baddeley et al, 2001). It is perhaps the taxing combination of executive control and semantic memory that results in the increased activation of the right angular gyrus and decreased task performance in PD-MCI compared to PD-NC and HC. Increased activation was also revealed in the right angular gyrus of PD-MCI patients during semantic switching compared to both the rest and automatic speech conditions, further indicating task-specific hyperactivation in PD-MCI during semantic switching.

When the relationship of the right angular gyrus brain activity to broader fluency performance was considered, there was a significant negative correlation between the activation of the right angular gyrus and verbal fluency tasks including letter (F, A, S), semantic (e.g. animals, boys' names) and semantic switching (e.g. fruits and furniture). That is, the greater the number of correct responses produced for each task, the less activity in the right angular gyrus was observed. Therefore, it is apparent that the increased right angular gyrus activity is a predictor of increased verbal fluency deficits identified outside the scanner.

The angular gyrus is located at the junction between the occipital, temporal and parietal lobes, and is interconnected bilaterally via the dorsal region of the corpus callosum (Park et al, 2008; Seghier, 2013). It is known to play a significant role in semantic processing, language, complex information integration, memory retrieval, default mode network (DMN) and social cognition (Binder et al, 2009; Seghier, 2013). Semantic processing, in particular, is a function consistently associated with the angular gyrus, with stronger activation typically observed in the left hemisphere (Binder et al, 2009). However, in the present study an increased activation was observed in the right, but not left, angular gyrus with impaired semantic switching in PD-MCI.

While our finding of right as opposed to left angular gyrus activity was unexpected, the involvement of the right angular gyrus in PD-related changes in neural activity is not without precedent. Of note, a recent meta-analysis of whole-brain resting state connectivity in PD found that the most consistent disturbances relative to healthy controls were evident within the posterior inferior parietal lobe (IPL) (Tahmasian et al, 2017). This finding was driven by observations of increased functional connectivity within the bilateral IPL for patients off dopaminergic medication, and decreased connectivity for those on medication. The authors suggested the findings may reflect compensatory mechanisms relating to basal ganglia dysfunction associated with the disease. Similarly, Manes et al (2018) observed increased resting state functional connectivity between the internal globus-pallidus and the angular gyrus bilaterally for PD patients with speech impairments relative to those without speech impairments. The authors attributed these findings to a potential compensatory mechanism, and also suggested that the findings may reflect increased semantic processing deficits in those with speech impairment given that impaired semantic verbal fluency has previously been shown to correlate with impaired speech (Gago et al, 2009). In a similar way, our findings may reflect a compensatory up-regulation of activity within the right angular gyrus in order to compensate for the increasing compromise of cognitive-linguistic function in patients with MCI.

Our findings of increased recruitment of a contralateral non-task-dominant region is also supported by previous lesion, aging, and clinical studies (Isaacs et al, 2019; Meinzer et al, 2009; Tinaz et al, 2008). Meinzer et al (2009) reported increased right inferior/middle frontal activity with worse semantic performance in older adults compared to young adults. Isaacs et al (2019) reported that PD patients compared to HC showed increased right hemisphere activity during a verbal production task related to verbal fluency. Another study demonstrated an increased recruitment of the right hemisphere in PD patients compared to age-matched and younger healthy controls during the semantic sequencing task (Peran et al, 2009). Compensation for the progressive loss of language function may therefore be reflected by the switch from the left to the right hemisphere, as observed in the present study. This switch may be exacerbated by increased task demands, particularly during the semantic switching task which requires both semantic memory and executive control. Considering the language function is typically dominated in the left hemisphere, the increased activation for additional recruitment can be related to the inefficient activation of the region in the dominant hemisphere (Braver et al, 2001).

The angular gyrus is also reported to be a part of the DMN which is highly active while at rest and decreases its activity during task performance (Buckner et al, 2008; Vatansever et al, 2017). DMN dysfunction in PD, particularly in patients with MCI, has been reported previously (Baggio et al, 2015; Gorges et al, 2015; Hou et al, 2016). Therefore, over-activated right angular gyrus in PD-MCI compared to decreased activity in PD-NC and HC may suggest disrupted connectivity of the DMN in PD-MCI.

A longitudinal study from the CamPaIGN cohort highlighted that impairment in semantic fluency is a key predictors of PDD, which was assumed to be related to posterior temporal-parietal regions (Williams-Gray et al, 2009). The present study confirmed that the increased activity in the parietal region was associated with worse semantic switching fluency in PD-MCI patients. Therefore, our results in PD-MCI patients indicate that the activation of the right angular gyrus may be a critical indicator of predicting PDD, and a possible target for future therapeutic interventions.

Strengths and Limitations

Stratifying PD-MCI from PD-NC was a great strength of this study, as it allowed for a more in-depth exploration of verbal fluency deficits related to cognitive impairment in PD. For example, Henry and Crawford (2004) found in their meta-analysis that PD patients were impaired on semantic fluency compared to HC. However, the results from the present investigation suggest that only PD-MCI patients exhibit impaired semantic fluency compared to HC, while verbal fluency in PD-NC is unimpaired. Furthermore, PD-MCI showed greater deficits during letter fluency compared to semantic fluency, which is contrary to Henry and Crawford (2004) meta-analysis, which reported the opposite pattern. This finding highlights the importance of looking at PD-MCI when exploring cognition in PD, particularly for the identification of those at risk of dementia. Another strength was the use of the automated speech as a control. The automatic speech condition requires over-learned responses without difficulty, therefore, this is used as a baseline for language production and to control for motion artifacts (Birn et al, 2010). Comparing the automatic speech condition to the semantic switching condition enabled us to isolate lexical-semantic processing from speech production.

It is important to consider that the verbal fluency assessments (outside the scanner) used to compare between groups were also used to separate patients into PD-MCI and PD-NC. However, PD-MCI is not defined solely by the performance of verbal fluency but rather is defined on a comprehensive cognitive testing. There were also many PD-MCI patients who were not impaired on semantic fluency.

Conclusion

To our knowledge, this is the first fMRI study to investigate neural mechanisms of semantic fluency impairment in patients with PD-MCI. The present study showed that increased functional activity in the right angular gyrus is associated with impaired verbal fluency in PD-MCI. This finding supports the view that verbal fluency deficits may be a substantial predictor of cognitive decline related to premorbid PDD.

Our results warrant further investigations to understand the progressive cognitive impairment associated with alterations in brain function outlined in this study, and its relationship to the development of PDD.

Declarations

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Compliance with Ethical Standards

Conflict of interest: The authors declare that there was no potential conflict of interest.

Ethical approval: This study was approved. The present study was performed in agreement with the Declaration of Helsinki and its further amendments, by the human research ethics committees of the University of Queensland and the Royal Brisbane and Women's Hospital.

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

Data availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Code availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Author contributions included conception and study design (J.Y., D.A.C., G.J.B., N.N.D); data acquisition and design statistical analysis (J.Y., K.L.M.); recruitment (J.D.O., J.Y., D.P); data collection (J.Y., D.P); interpretation of results (all authors); drafting the manuscript and revision of subsequent drafts (J.Y.); critical revision, and approval of final version to be published and agreement to be accountable for the integrity and accuracy of all aspects of the work (all authors)

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Figures

Region	Condition	Coordinate			z	Cluster extent (voxels)	P _{FWE-corr}
		x	y	z			
R Angular Gyrus	Rest	42	-58	34	4.29	983	0.0027
	Automated	54	-57	34	4.30	1265	0.009

Figure 1

Axial view of main effect of group in category switching greater than rest (top) and category switching compared to automated (bottom) at significance level of $p < .001$ uncorrected, cluster size familywise error (FWE) $p < .05$

Figure 2

Post-hoc analysis of the category switching > rest (left) and category switching > automated (right) Post-hoc analysis in the right angular gyrus. Bar graph displays mean (SE) beta weighted values. Significant level ** $p < .01$. Note. PD-MCI = Parkinson's disease patients with mild cognitive impairment; PD-NC = Parkinson's disease patients with no cognitive impairment; HC = age- and sex-matched healthy controls

Figure 3

Correlation matrix of scatter plots showing Pearson's correlation for activation of the right angular gyrus (R Ang) during the category switching > automated and performance of verbal fluency outside the scanner including letter (L), semantic (S) and semantic switching (SS) in patients with Parkinson's disease (PD).

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