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Cognitive and cortical thinning patterns of subjective cognitive decline in patients with and without Parkinson's disease

Jin Yong Hong [a], Hyuk Jin Yun [b], Mun Kyung Sunwoo [c], Jee Hyun Ham [d], Jong-Min Lee [b], Young H. Sohn [d], Phil Hyu Lee [d, e, *]

[a] Department of Neurology, Yonsei University Wonju College of Medicine, Wonju, Republic of Korea
[b] Department of Biomedical Engineering, Hanyang University, Seoul, Republic of Korea
[c] Department of Neurology, Bundang Jesaeng General Hospital, Kwandong University College of Medicine, Seongnam, Republic of Korea
[d] Department of Neurology and Brain Research Institute, Yonsei University College of Medicine, Seoul, Republic of Korea
[e] Severance Biomedical Science Institute, Yonsei University College of Medicine, Seoul, Republic of Korea

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ABSTRACT

Background: Subjective cognitive decline (SCD) has gained attention as a predictor of future cognitive decline in neurodegenerative diseases. Based on the hypothesis that different pathologies may distinctly contribute to SCD, we investigated the cognitive profiles and cortical thickness of patients with SCD, with and without Parkinson's disease (PD).

Methods: In total, 96 patients experiencing SCD were classified as having PD (SCD-PD$^+$, $n = 49$) or no neurological disease (SCD-PD$^-$, $n = 47$); cognitively normal subjects without SCD ($n = 23$) were included as controls. Neurocognitive profiles and cortical thickness were examined using standardized neuropsychological tests and magnetic resonance imaging-based analysis.

Results: No significant differences in demographic characteristics were found among the three groups. Neuropsychological tests demonstrated that the SCD-PD$^+$ patients had lower semantic fluency than SCD-PD$^-$ patients and controls, and showed poorer performance in visual memory and confrontational naming than controls, whereas no significant difference in cognitive performance was observed between the SCD-PD$^-$ patients and controls. Cortical thickness analysis revealed that the SCD-PD$^+$ patients had focal cortical thinning in the dorsolateral prefrontal, orbitofrontal, parietal, and parahippocampal areas compared with controls. Compared with SCD-PD$^-$ patients, SCD-PD$^+$ patients had cortical thinning in the frontal, parahippocampal, and posterior cortical areas.

Conclusion: Our data show that cortical thinning and cognitive performance in patients with SCD may differ based on the presence of PD, suggesting that SCD in patients with PD reflects disease-related cortical thinning and cognitive dysfunctions more closely than SCD without PD.

1. Introduction

Mild cognitive impairment (MCI) is a transitional state between normal aging and dementia that has been used for the early detection and treatment of dementia. Amnestic MCI, a subtype of MCI, has 10–15% annual conversion rate to Alzheimer's disease (AD) [1]. Several studies have reported that amyloid burden and cortical atrophy at the diagnosis of MCI are already extensive, which is comparable to AD stage [2]. More recently, subjective cognitive decline (SCD) has gained attention as a predictor of future dementia. Although the predictive value is controversial, increasing evidence suggests SCD to be a possible predictor of AD [3–7].

In patients with Parkinson's disease (PD), the cumulative incidence of dementia is up to 80% [8], and thus, cognitive decline is a major issue in PD. As in AD, patients with PD and MCI (PD-MCI) have a higher risk of developing dementia. Janvin et al. [9] reported that patients with PD-MCI had an increased risk of developing dementia than did cognitively intact PD patients (62% vs. 20%). Although few studies have examined the significance of SCD in patients with PD (PD-SCD), evidence suggests that SCD in PD patients is related with cognitive status. Previously, we reported that

* Corresponding author. Department of Neurology, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea. Tel.: +82 2 2228 1608; fax: +82 2 393 0705.
E-mail address: phisland@chol.net (P.H. Lee).

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patients with PD-SCD had more cortical atrophy and performed more poorly on neuropsychological tests than those without SCD, suggesting that SCD in PD is possibly related to PD-related pathological changes [10]. Another cross-sectional study also showed that self-rating and proxy-rating subjective memory functions were correlated with objective cognitive performance in patients with PD [11]. Importantly, our recent longitudinal study demonstrated that cognitively normal patients with PD and SCD exhibited more severe annual cognitive decline and converted to MCI status more frequently than those without SCD [12].

However, the similarity or difference of SCD between patients with and without PD has not been investigated. In this study, based on the hypothesis that different pathologies contribute distinctly to SCD, we investigated the patterns of cognitive profiles and cortical thickness in patients having SCD with (SCD-PD$^+$) and without PD (SCD-PD$^-$) to explore whether the neuroanatomical basis of SCD differs.

2. Materials and methods

2.1. Participants

Participants included 96 patients with SCD recruited consecutively from the movement disorders and dementia outpatient clinic at Yonsei University Severance Hospital. The presence of SCD was assessed by the question: "Do you feel that you have a declining memory?" PD was diagnosed following the clinical diagnostic criteria of the UK PD Society Brain Bank. Depending on the presence of PD, patients with SCD were classified into the SCD-PD$^+$ ($n = 49$) and SCD-PD$^-$ ($n = 47$) groups. In addition, 23 healthy age- and sex-matched volunteers were recruited as controls. The controls had neither an active neurologic disorder nor SCD.

The exclusion criteria included evidence of focal brain lesions or multiple lacunar infarctions in the basal ganglia based on magnetic resonance imaging (MRI). Possible medical comorbidities affecting cognition were excluded by laboratory testing, including thyroid function tests, vitamin B_{12} and folic acid levels, and the VDRL test. Patients with a history of drug use causing parkinsonian symptoms were also excluded.

We received approval from the Yonsei University Severance Hospital ethical standards committee on human experimentation for use of human subjects. Written informed consent was obtained from all subjects participating in this study.

2.2. Neuropsychological assessment

The neuropsychological performance was evaluated using a standardized neuropsychological test, the Seoul Neuropsychological Screening Battery (SNSB) [13]. The SNSB consists of the following cognitive subsets, as described previously: attention (forward digit span and color stroop test); language function (the Korean version of the Boston Naming Test [K-BNT]), visuospatial function (the Rey Complex Figure Test [RCFT]), verbal memory (20-min delayed recall using the Seoul Verbal Learning Test), visual memory (20-min delayed recall using the RCFT), and executive function (semantic and phonemic Controlled Oral Word Association Test [COWAT]). Abnormal cognitive function was defined as a score below the 16th percentile of the normal population. All patients showed normal performance in the neuropsychological test, and did not meet the MDS criteria for mild cognitive impairment in PD (PD-MCI) [14]. Additionally, all study subjects scored above the 16th percentile (1 standard deviation below mean) for their age- and education-appropriate norm on the Korean version of the Mini-Mental State Examination (K-MMSE). The participants showed no evidence of abnormal activities of daily living (ADL), judged both clinically and on an ADL scale.

2.3. Clinical assessment

Parkinsonian motor symptoms were assessed using the Unified Parkinson's Disease Rating Scale motor score (UPDRS III). A score for general white matter hyperintensities (WMH) was determined by grading the extent of the increased white matter signal intensity on fluid-attenuated inversion recovery images in the periventricular and subcortical white matter. It was graded was on a 10-point scale from 0 to 9, with a higher score indicating a more severe white matter grade [15]. An [^{18}F] FP-CIT PET scan was performed on all SCD-PD$^+$ subjects who had decreased dopamine transporter uptake in the posterior putamen. The self-rated Beck Depression Inventory (BDI) was used to assess depressive symptoms in patients with PD.

2.4. MRI acquisition

A Philips 3.0T scanner (Philips Achieva; Philips Medical System, Best, Netherlands) with a SENSE head-8 coil was used to obtain MR images. A high-resolution T1-weighted MRI volume dataset was obtained using a three-dimensional T1-TFE sequence configured with the following acquisition parameters: axial acquisition with a 224 × 224 matrix; 256 × 256 reconstructed matrix; 220 × 220-mm field of view; 0.86 × 0.86 × 1.0-mm voxels; echo time, 4.6 ms; repetition time, 9.6 ms; flip angle, 8°; and slice gap, 0 mm.

2.5. Image processing for cortical thickness

Images were processed using the standard Montreal Neurological Institute (MNI) anatomical pipeline. The native MR images were normalized into a standardized stereotaxic space using affine transformation and intensity nonuniformity artifacts in normalized images was corrected using the N3 algorithm [16]. Skull removal was performed to the images after correction using brain extraction tool (BET) and then classified into white matter (WM), gray matter (GM), cerebrospinal fluid (CSF) and background using an advanced neural net classifier. The cortical surfaces of the inner and outer cortex which consisted of 40,962 vertices were extracted automatically using the Constrained Laplacian-based Automated Segmentation with Proximities (CLASP) algorithm [17]. The cortical surfaces were inversely transformed to native space. Cortical thickness was defined using the t-link method, which measures the Euclidean distance between the linked vertices of the inner and outer surfaces [17,18]. The vertex-wise sphere-to-sphere warping nonlinear surface registration was performed to unbiased iterative surface template [19]. Using the surface registration, thickness information on native surfaces was transformed to a template after diffusion smoothing with 20-mm full-width half-maximum to increase the signal-to-noise ratio and improve the detection ability of population changes [18].

The statistical analysis of cortical thickness was performed in vertex-wise level using an analysis of covariance (ANCOVA) with intracranial volume, age, sex, and the side of parkinsonian motor dominance as covariates for comparisons among the groups. *Post hoc* analyses were performed to investigate the following contrasts: (1) controls vs. SCD-PD$^+$, (2) controls vs. SCD-PD$^-$, (3) SCD-PD$^+$ vs. SCD-PD$^-$. We performed false-discovery-rate (FDR) correction for comparison between SCD subjects and controls at a corrected probability value of $p < 0.05$. When comparing SCD-PD$^+$ and SCD-PD$^-$, a discriminative threshold was lowered at uncorrected $p < 0.001$.

2.6. Statistical analysis

The chi-square test was used for categorical variables, while independent *t*-test, one-way analysis of variance (ANOVA), and ANCOVA were adopted for continuous variables. For comparison of specific cognitive performance in the SNSB, age, sex, and years of education were used as covariates of multivariates analysis of covariance (MANCOVA), and *post-hoc* analyses were conducted following the Bonferroni method. Statistical analyses were performed using SPSS Statistics 20 (IBM SPSS, Armonk, NY, USA), and a $p < 0.05$ was considered to indicate statistical significance.

3. Results

3.1. Demographic characteristics

The demographic characteristics of the subjects are shown in Table 1. No significant differences were observed among the three

Table 1
Demographic characteristics of controls, patients having subjective cognitive decline with (SCD-PD$^+$) and without (SCD-PD$^-$) Parkinson's disease.

	SCD-PD$^+$	SCD-PD$^-$	Control	*p*-Value
Participants	49	47	23	
Age, y	63.2 ± 7.5	62.3 ± 8.5	66.4 ± 6.9	0.126[c]
Number of male	22	11	5	0.120[a]
Education duration, y	11.3 ± 4.2	11.8 ± 4.4	12.4 ± 4.3	0.576[c]
Memory complaints duration, y	2.6 ± 2.4	2.3 ± 2.1	N/A	0.630[b]
K-MMSE	28.7 ± 1.0	28.8 ± 1.0	28.6 ± 1.0	0.546[c]
CDR	0.26 ± 0.25	0.22 ± 0.25	0.26 ± 0.26	0.776[c]
WMH score	1.5 ± 1.5	1.2 ± 1.2	1.0 ± 1.0	0.355[c]
BDI	13.5 ± 9.4	15.2 ± 8.4	11.3 ± 8.7	0.213[c]
PD duration, y	2.5 ± 1.9	N/A	N/A	N/A
UPDRS III	20.7 ± 12.1	N/A	N/A	N/A
Levodopa dose, mg	357.0 ± 191.5	N/A	N/A	N/A

SCD-PD$^+$: subjective cognitive decline with Parkinson's disease; SCD-PD$^-$: subjective cognitive decline without Parkinson's disease; K-MMSE: the Korean version of the Mini-Mental State Examination; CDR: Clinical Dementia Rating scale; WMH: white matter hyperintensity; BDI: Beck depression inventory; UPDRS III: Unified Parkinson's Disease Rating Scale motor score; N/A: not applicable. Values are expressed as mean ± SD.

[a] Chi-square test.
[b] Independent *t* test.
[c] One-way ANOVA.

groups in terms of age, sex, years of education, duration of memory complaints, degree of WMH, K-MMSE scores, Clinical Dementia Rating scale (CDR) score, Sum of Boxes score of the CDR, or BDI scores. The mean duration of PD, UPDRS III score, and levodopa equivalent dose in patients with SCD-PD$^+$ were 2.5 years, 20.7, and 357.0 mg, respectively.

3.2. Neuropsychological findings

The detailed neuropsychological characteristics of the SCD-PD$^+$, SCD-PD$^-$, and control groups are compared in Table 2. A significant difference among groups was observed in confrontational naming (K-BNT score, $p = 0.007$), visual memory ($p = 0.009$), and semantic fluency ($p = 0.001$).

The *post-hoc* analysis revealed that patients with SCD-PD$^+$ performed poorly in the confrontational naming (K-BNT, 48.6 vs. 50.9, $p = 0.008$), visual memory (17.7 vs. 20.7, $p = 0.007$), semantic fluency scores (32.8 vs. 39.0, $p = 0.002$) compared to the controls. Compared to the SCD-PD$^-$ patients, those with SCD-PD$^+$ had lower scores in semantic fluency score (32.8 vs. 37.4, $p = 0.022$). There was no difference between the SCD-PD$^-$ patients and controls.

3.3. Cortical thickness

Cortical thickness analysis demonstrated that SCD-PD$^+$ patients had several areas with significant focal cortical thinning compared to controls. In the right hemisphere, cortical thinning in the superior temporal gyrus that extended to the transverse gyrus and insula, parahippocampal gyrus, angular gyrus that extended to middle occipital gyrus, parieto-occipital sulcus, and gyrus rectus were observed in SCD-PD$^+$ patients compared with controls. In the left hemisphere, pars opercularis, pars triangularis, supramarginal gyrus, and superior occipital gyrus showed cortical thinning in SCD-PD$^+$ patients compared with controls (Fig. 1A). There were no significant cortical thickness diff0erences between SCD-PD$^-$ patients and controls.

When comparing SCD-PD$^+$ and SCD-PD$^-$ patients directly with a lower threshold of uncorrected $p < 0.001$, the SCD-PD$^+$ patients exhibited cortical thinning in the medial part of the right superior frontal gyrus, right olfactory cortex, right fusiform gyrus, left parahippocampal gyrus, left calcarine sulcus, and bilateral cunei compared with SCD-PD$^-$ patients (Fig 1B). However, no area remained significant after FDR correction ($p < 0.05$).

4. Discussion

We demonstrated for the first time that the patterns of cortical thinning and cognitive profiles differed between SCD-PD$^+$ and SCD-PD patients. SCD-PD$^+$ patients had lower cognitive performance of frontal and temporal lobe-based domains and cortical thinning in fronto-temporo-parietal areas, whereas the cognitive performance and cortical thickness of SCD-PD$^-$ patients were comparable to those of controls. Furthermore, a direct comparison of SCD-PD$^+$ and SCD-PD$^-$ patients revealed an explicit difference in those patterns, showing that SCD-PD$^+$ patients had poorer cognitive performance of frontal executive function and cortical thinning in frontal-temporal areas than did SCD-PD$^-$ patients. These data suggest that SCD is more closely coupled to disease-related cortical thinning in patients with PD than in those without PD.

Comprehensive neuropsychological testing showed that SCD-PD$^+$ patients had poorer performance on the semantic fluency test than the controls as well as patients with SCD-PD$^-$. Ample evidence has suggested that decreased verbal fluency occur in the early stages of PD even without cognitive dysfunction and is a significant predictor of the dementia development in patients with PD [20,21]. In our previous report demonstrating that PD patients with SCD had lower semantic and phonemic fluency than patients without SCD [10], we suggested that SCD in patients with PD may represent an early manifestation of underlying PD-related pathological changes. Collectively, the present study revealed that semantic fluency performance of SCD-PD$^+$ patients is distinct from controls or SCD-PD$^-$ patients, which may further support the concept that the decline in semantic fluency in the SCD-PD$^+$ patients may be associated with the process of PD pathology. In addition, SCD-PD$^+$ patients had a lower visual memory score than controls. Poorer verbal or visual memory performance in non-demented PD patients has been reported previously [22,23]. A longitudinal study also reported that the decline of visuospatial memory was more rapid in PD than AD, and stated that visuospatial memory is a core feature of cognitive decline in PD [23]. In contrast, the cognitive performance of SCD-PD$^-$ patients was comparable to that of controls. Regarding the cognitive performance of SCD patients compared to healthy controls, the results are inconsistent; some studies reported that subjects with SCD had similar cognitive levels to the controls without SCD [3,24], whereas other studies suggested SCD to be a predictor for objective cognitive dysfunctions [5,7]. Accordingly, the neurocognitive profiles of the SCD-PD$^+$ and SCD-PD$^-$ patients indicate that SCD patients with PD are more closely reflective of objective cognitive dysfunctions compared to patients without PD, suggesting that the presence of an underlying PD pathology may act as an important factor for objective cognitive impairment in patients with SCD.

In cortical thickness analysis, patients with SCD-PD$^+$ patients exhibited more cortical thinning, involving mainly the frontal areas, as well as the temporal and parietal areas, when compared to controls. According to neuroimaging studies, performance of verbal fluency relies largely on the frontal lobes for the required mental lexicon search and maintenance of working memory to avoid repetitions [25], although the neural basis for lexical and semantic fluency seems to differ slightly; the former is associated with the dorsolateral portion of the frontal lobe and the latter with the ventral anterior portion of the frontal area along with the temporal lobe [26,27]. Particularly, a voxel-based morphometric analysis in PD patients demonstrated that the semantic fluency score was correlated significantly with gray matter volume in the bilateral inferior and middle frontal areas and temporal lobes [28]. Additionally, the lower visual memory score in SCD-PD$^+$ patients compared to controls is in accordance with cortical thinning of the right parahippocampal gyrus in SCD-PD$^+$ patients. When comparing cortical thickness between SCD-PD$^+$ and SCD-PD$^-$ patients, SCD-PD$^+$ patients exhibited cortical thinning in the orbitofrontal and prefrontal, parahippocampal, and retrosplenial areas. The retrosplenial areas are known to involve in memory and frontal

Table 2
Neuropsychological data in controls, patients having subjective cognitive decline with (SCD-PD$^+$) and without (SCD-PD$^-$) Parkinson's disease.

Test	SCD-PD$^+$	SCD-PD$^-$	Controls	p-Value[a]
Forward digit span	6.9 ± 1.1	7.0 ± 1.2	6.4 ± 1.2	0.124
Color stroop test	88.0 ± 18.9	96.0 ± 14.8	96.0 ± 21.0	0.166
K-BNT	48.6 ± 5.5[b]	50.3 ± 5.3	50.9 ± 5.1	0.007
RCFT copy	34.6 ± 1.5	35.2 ± 0.9	35.0 ± 1.3	0.252
Verbal memory (SVLT)	6.9 ± 1.9	7.5 ± 1.9	7.0 ± 1.6	0.356
Visual memory (RCFT)	17.7 ± 5.0[b]	18.9 ± 4.6	20.7 ± 7.0	0.009
Semantic fluency	32.8 ± 6.7[b,c]	37.4 ± 7.8	39.0 ± 7.6	0.001
Phonemic fluency	25.0 ± 8.2	28.5 ± 9.1	29.8 ± 10.4	0.106

K-BNT: Korea version of the Boston Naming Test; RCFT: Rey Complex Figure Test; SVLT: Seoul Verbal Learning Test.
Values are expressed as mean ± SD.
[a] MANCOVA using age, sex, and years of education as covariates.
[b] From cases with controls at $p < 0.01$.
[c] From cases with SCD-PD$^-$ at $p < 0.05$.

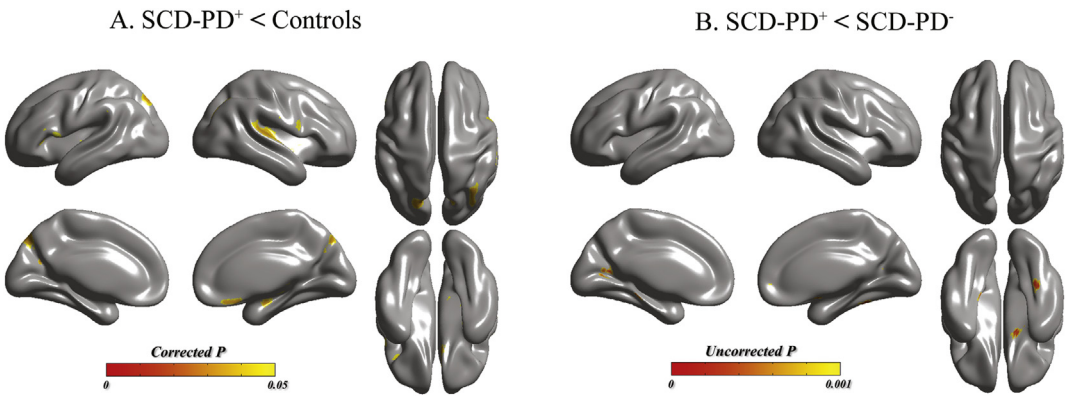

Fig. 1. Cortical thickness analyses in controls and patients having subjective cognitive decline with (SCD-PD$^+$) and without (SCD-PD$^-$) Parkinson's disease. Patients with SCD-PD$^+$ exhibited extensive cortical thinning in the frontal, temporal, and posterior cortical areas compared with controls (A, FDR correction, $p < 0.05$). On a direct comparison between SCD with PD and without PD, the SCD-PD$^+$ patients had cortical thinning in the frontal, parahippocampal, and posterior cortical areas compared with SCD-PD$^-$ patients (B, uncorrected $p < 0.001$).

lobe-based cognitive performance. Moreover, we demonstrated previously that posteromedial cortical areas could act as a pathological induction site for memory dysfunction in PD patients with MCI, which is a potential distinction from the atrophic pattern in MCI of the AD prototype [13]. Therefore, the areas of cortical thinning SCD-PD$^+$ patients seem to correspond to the cognitive subdomains that decline in SCD-PD$^+$ and the anatomical areas that may reflect the process of PD pathology. Unexpectedly, the cortical thickness in patients with SCD-PD$^-$ was comparable to the controls, as in previous studies using region-of-interest-based volumetric analysis showing that SCD patients had a smaller hippocampal volume than healthy controls without SCD [6]. Small sample size with difference in imaging analysis may lead to inconsistent neuroimaging data, and thus further assessment of cortical thickness analysis using a larger sample size is required. Accordingly, the present data indicate that the pathological burden leading to SCD may be greater in SCD-PD$^+$ patients with PD compared to SCD-PD$^-$ patients, suggesting that the presence of underlying PD pathology may be an important pathological determinant in the cerebral cortex responsible for objective cognitive impairments.

Several studies have shown that SCD is affected by different factors, such as psycho-affective factors, WMH, and lifestyle habits [29,30]. In the present study, we adjusted for the factors influencing the presence of SCD, and thus, the degree of WMH and depression did not differ significantly. In addition, the BDI score in our patients tended to be relatively high. However, according to a community-based study, the mean BDI score in our patients was comparable to the score in non-depressed Korean elderly population [31]. Moreover, our previous studies suggested that the BDI scores in patients with PD-SCD$^+$ were not significantly associated with cortical atrophy or future cognitive decline [10,12]. Discrepancy between SCD-PD$^+$ and SCD-PD$^-$ patients may be due to the difference in dopamine deficiency, leading potentially to variation in cognitive performance, as dopamine in PD patients plays an important role in frontal executive functions. However, inferring that dopamine status does not act as a determinant of SCD in PD patients [10], we hypothesize that the presence of PD pathology itself may be an important determinant of SCD. Another possible factor is chronic levodopa intake in patients with SCD-PD$^+$ that may have an impact on influence cortical thinning or cognitive performance, because chronic levodopa metabolism may induce neuronal degeneration via an augmented homocysteine and free radical synthesis [32].

SCD is a subjective symptom that is difficult to objectify or quantify and could lead to limitations in generalizing the significance of SCD. The definition of SCD is not uniform and there is no widely accepted diagnostic consensus, even within the AD field. Furthermore, questionnaires or scoring systems for assessment of SCD that have been introduced to detect underlying early AD pathology may not be suitable for use in PD patients, as the main subdomain in the early stage of PD-related cognitive dysfunction may be associated with fronto-striatal dysfunction [33]. Therefore, questionnaires implicating PD-specific cognitive dysfunction, including executive dysfunction, must be developed to evaluate whether SCD-PD$^+$ plays a longitudinally significant role in predicting future cognitive decline.

Addressing the strengths and limitations of this study, we used dopamine transporter imaging to determine the underlying PD pathology in SCD-PD$^+$ patients. Nevertheless, this study was not based on autopsy-proven data; therefore, we cannot exclude the influence of AD-like or other pathology rather than Lewy body pathology in our SCD-PD$^+$ group because mixed pathologies may have underlain the SCD as in PD-MCI. Similarly, it is possible that pathological heterogeneity might exist in the SCD-PD$^-$ group. Second, the one-question Yes-or-No survey used in this study might not have identified PD-specific cognitive complaints, which may result in decreased specificity and underestimation of its significance as a predictor of cognitive decline. Third, this study was of a cross-sectional design with a relatively small sample size. A longitudinal study with a larger sample size should be conducted.

Our findings show that cortical thinning and cognitive performance in patients with SCD may differ depending on the presence of PD, suggesting that SCD in patients with PD reflects disease-related cortical thinning and cognitive dysfunctions more closely than SCD in patients without PD.

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References

[1] Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 1999;56(3):303–8.
[2] Whitwell JL, Przybelski SA, Weigand SD, Knopman DS, Boeve BF, Petersen RC, et al. 3D maps from multiple MRI illustrate changing atrophy patterns as subjects progress from mild cognitive impairment to Alzheimer's disease. Brain 2007;130(Pt 7):1777–86.

[3] Antonell A, Fortea J, Rami L, Bosch B, Balasa M, Sanchez-Valle R, et al. Different profiles of Alzheimer's disease cerebrospinal fluid biomarkers in controls and subjects with subjective memory complaints. J Neural Transm 2011;118(2):259–62.
[4] Barnes LL, Schneider JA, Boyle PA, Bienias JL, Bennett DA. Memory complaints are related to Alzheimer disease pathology in older persons. Neurology 2006;67(9):1581–5.
[5] Geerlings MI, Jonker C, Bouter LM, Ader HJ, Schmand B. Association between memory complaints and incident Alzheimer's disease in elderly people with normal baseline cognition. Am J Psychiatr 1999;156(4):531–7.
[6] Striepens N, Scheef L, Wind A, Popp J, Spottke A, Cooper-Mahkorn D, et al. Volume loss of the medial temporal lobe structures in subjective memory impairment. Dement Geriatr Cogn Disord 2010;29(1):75–81.
[7] Wang L, van Belle G, Crane PK, Kukull WA, Bowen JD, McCormick WC, et al. Subjective memory deterioration and future dementia in people aged 65 and older. J Am Geriatr Soc 2004;52(12):2045–51.
[8] Aarsland D, Andersen K, Larsen JP, Lolk A, Kragh-Sorensen P. Prevalence and characteristics of dementia in Parkinson disease: an 8-year prospective study. Arch Neurol 2003;60(3):387–92.
[9] Janvin CC, Larsen JP, Aarsland D, Hugdahl K. Subtypes of mild cognitive impairment in Parkinson's disease: progression to dementia. Mov Disord 2006;21(9):1343–9.
[10] Hong JY, Lee JE, Sohn YH, Lee PH. Neurocognitive and atrophic patterns in Parkinson's disease based on subjective memory complaints. J Neurol 2012;259(8):1706–12.
[11] Sitek EJ, Soltan W, Wieczorek D, Robowski P, Slawek J. Self-awareness of memory function in Parkinson's disease in relation to mood and symptom severity. Aging Ment Health 2011;15(2):150–6.
[12] Hong JY, Sunwoo MK, Chung SJ, Ham JH, Lee JE, Sohn YH, et al. Subjective cognitive decline predicts future deterioration in cognitively normal patients with Parkinson's disease. Neurobiol Aging 2014;35(7):1739–43.
[13] Lee JE, Park HJ, Song SK, Sohn YH, Lee JD, Lee PH. Neuroanatomic basis of amnestic MCI differs in patients with and without Parkinson disease. Neurology 2010;75(22):2009–16.
[14] Litvan I, Goldman JG, Troster AI, Schmand BA, Weintraub D, Petersen RC, et al. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: movement disorder society task force guidelines. Mov Disord 2012;27(3):349–56.
[15] Yue NC, Arnold AM, Longstreth Jr WT, Elster AD, Jungreis CA, O'Leary DH, et al. Sulcal, ventricular, and white matter changes at MR imaging in the aging brain: data from the cardiovascular health study. Radiology 1997;202(1):33–9.
[16] Collins DL, Neelin P, Peters TM, Evans AC. Automatic 3D intersubject registration of MR volumetric data in standardized Talairach space. J Comput Assist Tomogr 1994;18(2):192–205.
[17] MacDonald D, Kabani N, Avis D, Evans AC. Automated 3-D extraction of inner and outer surfaces of cerebral cortex from MRI. NeuroImage 2000;12(3):340–56.
[18] Im K, Lee JM, Lee J, Shin YW, Kim IY, Kwon JS, et al. Gender difference analysis of cortical thickness in healthy young adults with surface-based methods. NeuroImage 2006;31(1):31–8.
[19] Lerch JP, Evans AC. Cortical thickness analysis examined through power analysis and a population simulation. NeuroImage 2005;24(1):163–73.
[20] Levy G, Jacobs DM, Tang MX, Cote LJ, Louis ED, Alfaro B, et al. Memory and executive function impairment predict dementia in Parkinson's disease. Mov Disord 2002;17(6):1221–6.
[21] Williams-Gray CH, Evans JR, Goris A, Foltynie T, Ban M, Robbins TW, et al. The distinct cognitive syndromes of Parkinson's disease: 5 year follow-up of the CamPaIGN cohort. Brain 2009;132(Pt 11):2958–69.
[22] Bronnick K, Alves G, Aarsland D, Tysnes OB, Larsen JP. Verbal memory in drug-naive, newly diagnosed Parkinson's disease. The retrieval deficit hypothesis revisited. Neuropsychology 2011;25(1):114–24.
[23] Johnson DK, Galvin JE. Longitudinal changes in cognition in Parkinson's disease with and without dementia. Dement Geriatr Cogn Disord 2011;31(2):98–108.
[24] O'Connor DW, Pollitt PA, Roth M, Brook PB, Reiss BB. Memory complaints and impairment in normal, depressed, and demented elderly persons identified in a community survey. Arch Gen Psychiatr 1990;47(3):224–7.
[25] Stuss DT, Alexander MP, Hamer L, Palumbo C, Dempster R, Binns M, et al. The effects of focal anterior and posterior brain lesions on verbal fluency. J Int Neuropsychol Soc 1998;4(3):265–78.
[26] Heim S, Eickhoff SB, Amunts K. Specialisation in Broca's region for semantic, phonological, and syntactic fluency? NeuroImage 2008;40(3):1362–8.
[27] Pihlajamaki M, Tanila H, Hanninen T, Kononen M, Laakso M, Partanen K, et al. Verbal fluency activates the left medial temporal lobe: a functional magnetic resonance imaging study. Ann Neurol 2000;47(4):470–6.
[28] Pereira JB, Junque C, Marti MJ, Ramirez-Ruiz B, Bartres-Faz D, Tolosa E. Structural brain correlates of verbal fluency in Parkinson's disease. Neuroreport 2009;20(8):741–4.
[29] Hanninen T, Reinikainen KJ, Helkala EL, Koivisto K, Mykkanen L, Laakso M, et al. Subjective memory complaints and personality traits in normal elderly subjects. J Am Geriatr Soc 1994;42(1):1–4.
[30] Minett TS, Dean JL, Firbank M, English P, O'Brien JT. Subjective memory complaints, white-matter lesions, depressive symptoms, and cognition in elderly patients. Am J Geriatr Psychiatry 2005;13(8):665–71.
[31] Jo SA, Park MH, Jo I, Ryu SH, Han C. Usefulness of Beck Depression Inventory (BDI) in the Korean elderly population. Int J Geriatr Psychiatry 2007;22(3):218–23.
[32] Muller T. Detoxification and antioxidative therapy for levodopa-induced neurodegeneration in Parkinson's disease. Expert Rev Neurother 2013;13(6):707–18.
[33] Kehagia AA, Barker RA, Robbins TW. Neuropsychological and clinical heterogeneity of cognitive impairment and dementia in patients with Parkinson's disease. Lancet Neurol 2010;9(12):1200–13.