Published in final edited form as:

Mov Disord. 2011 February 15; 26(3): 436–441. doi:10.1002/mds.23453.

Focal Cortical and Subcortical Atrophy in Early Parkinson's Disease

Sule Tinaz, MD, PhD[1,*], **Maureen G. Courtney, MA**[1], **Chantal E. Stern**, and **D Phil**[1,2]

[1]Center for Memory and Brain, Boston University, Boston, Massachusetts, USA

[2]Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, Massachusetts, USA

Abstract

Neurodegeneration in clinically manifest Parkinson's disease affects the substantia nigra pars compacta, and gradually spreads to the limbic cortices and the neocortex. We used MRI imaging coupled with automated surface reconstruction and segmentation methods to examine cortical thickness and subcortical volumes in nondemented, early-stage Parkinson's disease patients compared to matched healthy control participants. These methods, which have been previously used to document cortical thickness changes in patients with Alzheimer's disease and Huntington's disease but not Parkinson's disease, use MR signal intensity information and the geometric constraints of the cortical and subcortical structures for an accurate tissue classification. Parkinson's disease patients were matched to the control group in psychomotor processing speed and executive functioning, but showed higher anxiety state scores. Our results demonstrated focal cortical thinning in the Parkinson's disease group in the orbitofrontal cortex, ventrolateral prefrontal cortex, and occipito-parietal areas. Subcortically, striatal volume loss was noted. These results demonstrate that both cortical and subcortical structural changes occur at relatively early stages of the disease, and are discussed in terms of the emotional dysregulation that occurs early on in patients with Parkinson's disease.

Keywords

MRI; orbitofrontal cortex; emotional dysregulation; cognition

In this study, our goal was to use structural MRI methods to investigate changes in cortical thickness and subcortical volumes in the early stages of Parkinson's disease (PD). Lewy bodies (LB) are the pathological hallmark of PD. From the onset of the pathology, LB inclusions are associated with damage to many extranigral regions,[1] and the involvement of the substantia nigra, pars compacta is associated with the classical clinical manifestation of the disease.[2] It has been proposed that the pathological process gradually spreads from the

*Correspondence to: Dr. Sule Tinaz, Center for Memory and Brain, Boston University, 2 Cummington Street, Room 109, Boston, MA 02215; aysesule.tinaz@nih.gov.

Relevant conflicts of interest/financial disclosures: Nothing to report. Full financial disclosures and author roles may be found in the online version of this article.

subcortical structures to the limbic cortices, and eventually to the neocortex[1] leading to structural abnormalities.

Findings of in vivo structural neuroimaging studies in demented PD patients are consistent with these neuropathological changes. Studies have reported gray matter volume loss in medial temporal,[3,4] frontal,[3–5] and in occipital, temporal, and parietal areas[5] in PD patients with dementia compared to controls. Subcortically, significant volume loss has been shown in the basal ganglia and thalamus in demented PD patients.[4,5]

Structural changes in nondemented PD patients have also been reported, but are more variable. In the midstages of the disease (Hoehn and Yahr score 2–3), atrophy has been observed in the putamen,[6] caudate,[7] and hippocampus,[4] and in cortical areas including the temporal,[4] parietal,[8] and frontal lobes[4,5,9] in nondemented PD patients compared to controls.

In this study, our aim was to quantitatively investigate changes in cortical thickness and subcortical volumes at relatively early stages of PD using MRI-based automated surface reconstruction and segmentation procedures.

Using these methods, diffuse and focal thinning of the cortical ribbon has been reported in normal aging[10] and in neurodegenerative diseases including Huntington's disease,[11,12] multiple sclerosis,[13] schizophrenia, [14] and Alzheimer's disease.[15,16]

These automated surface reconstruction methods rely on intensity information and the geometric constraints imposed by the planar structure of the gray-white matter borders and gray matter-CSF boundaries, and allow for precise tissue classification. These methods differ from more widely used MRI segmentation methods that use only the MR signal intensity information to classify different tissue types (i.e., voxel-based morphometry) and are prone to misclassifications due to partial volume errors, magnetic susceptibility artifacts, and magnetic field inhomogeneities.

The PD participants in this study met the clinical criteria for mild to moderate bilateral PD with no signs of dementia. Based on the Braak and Braak classification of the pathoanatomical disease progression in PD,[1] we predicted that significant focal thinning would occur predominantly in limbic cortices in the PD group compared with the controls. We also hypothesized that there would be significant focal thinning in heteromodal association areas including the frontal and parietal cortices. Subcortically, we predicted relative volume loss in the basal ganglia, predominantly in the putamen, in the PD group.

Methods

Subjects

Fifteen volunteers with idiopathic PD (46.7–67.3 years of age, mean 59.73 years (SD: 6.64), 16 years of education (SD: 2.8; 5 males) and 15 matched healthy control volunteers (43.3–71.8 years of age, mean 59.87 years (SD: 7.5), 16.13 years of education (SD: 1.6; 5 males) participated with informed consent and approval of Massachusetts General Hospital and Boston University.

Diagnoses were made by staff neurologists in the outpatient clinic of the Parkinson's Disease Center in the Department of Neurology, Boston Medical Center, and participants were recruited through the Vision & Cognition Laboratory at Boston University and through the Harvard Cooperative Program on Aging.

Exclusion criteria for all participants included neurological disease or medical disorders that impair the central nervous system functioning, head trauma with more than a few minutes loss of consciousness, learning disability, psychiatric conditions including schizophrenia, bipolar disorder, personality disorder, history of substance dependence or intravenous drug use, and specific safety considerations for MRI. Participants were not excluded for anxiety and depression since these conditions are often comorbid with PD.

All PD patients had unilateral symptom onset (left in 9, and right in 6 PD participants). The average duration of disease was 6 years (SD: 2.8). All patients were responsive to either levodopa-carbidopa or dopamine receptor agonists. Most patients were on a combination of levodopa-carbidopa, dopamine receptor agonists, catechol-O-methyl-transferase inhibitors, monoamine oxidase B inhibitors, amantadine, and anticholinergics (2 patients on 1 med, 6 on 2 meds, 3 on 3 meds, and 4 on 4 meds). Eight patients were also on antidepressant medication, five on antianxiety medication as needed, and four on wakefulness-promoting drugs.

Before scanning, patients underwent a neurological assessment including Hoehn and Yahr staging[17] and the Unified Parkinson's Disease Rating Scale (UPDRS).[18] The assessment was performed when patients were on dopaminergic medication, within 2 ± 1.5 hours after the last dose. The mean total UPDRS score was 46.73 points (SD: 11.34). The mean score on the motor examination part was 31.53 (SD: 5.84). The mean Hoehn and Yahr score was 2.17 (SD: 0.3) (11 subjects had a score of 2; 3 subjects had 2.5; and 1 subject had 3).

Behavioral Tests

Dementia was assessed by the Mini Mental State Examination (MMSE)[19] (cut-off 25 points) and the Dementia Rating Scale (DRS) (cut-off 135 points).[20] Participants were tested and matched on standard clinical neuropsychological tests: American National Adult Reading Test for premorbid intellectual functioning [21]; Digit Symbol and Symbol Search subtests of Wechsler Adult Intelligence Scale–III[22] for psychomotor speed; FAS fluency and category generation (Animals) tests,[23] Trail Making A and B tests,[24] and Digit Span forward and backward[22] for complex attention and executive functioning. Emotional status was evaluated using the Beck Depression Inventory-II (BDI-II) [25] and Spielberger State Trait Anxiety Inventory (STAI).[26]

Tests were administered at the time of scanning. PD and control groups were compared using independent-sample *t*-tests for each behavioral measure. All analyses were performed using SPSS 11.0.2 statistical analysis software for Macintosh.

Imaging

High-resolution T1-weighted MPRAGE scans were obtained on a 1.5 Tesla Siemens Avanto scanner (Imaging parameters: Voxel size = 1.3 × 1.3 × 1 mm, slice thickness = 1.33 mm,

repetition time = 2730 ms, echo time = 3.31 ms, inversion time = 1000 ms, Flip angle = 7°, field of view (FoV) = 256 × 256 mm, matrix= 192 × 256). These parameters were empirically optimized for high gray matter-white matter and gray matter-CSF contrast. Two scans were collected, motion corrected, averaged, and intensity normalized to create a single high-signal, high-contrast volume for each subject. Extracerebral voxels were removed. The white matter segmentation was based on the MR signal intensity information and the geometric constraints of the gray-white interface. The gray-white and the gray-pial interfaces were then tessellated.[27,28] Topological defects on surfaces were corrected.[29] Thickness was defined as the shortest distance between the gray-white and pial surfaces measured in millimeters. Each participant's reconstructed surface was inflated to enable visualization across the entire cortex (i.e., sulci and gyri), and the thickness measures were mapped onto these inflated surfaces.[30] Each participant's reconstructed brain was then registered to an average spherical surface representation that optimally aligned sulcal and gyral features across participants.[31] The maps were then smoothed using a 7 mm Gaussian blurring kernel to decrease the variance due to noise.[28] Group comparisons were made based on the thickness measurements. These methods have been validated by direct comparison with the measurements made on postmortem brains using standard neuropathological techniques.[11]

Region of Interest Analysis

Regions of Interest (ROI) were created using an automated parcellation technique based on manually labeled anatomical data.[32] Thickness was measured in millimeters and averaged across the ROI. Based on our a priori hypothesis, we focused our ROI analysis on the frontal, parietal and middle temporal areas, and the temporal pole, all of which are heteromodal association or limbic cortices. Groups were compared using independent-sample *t*-tests.

Subcortical Volumetry

The labels were created using an automated subcortical labeling algorithm based on a probabilistic atlas obtained from a manually labeled training set.[14] Then, an automated segmentation procedure assigned a label to each voxel in a dataset based on signal intensity information and the spatial relationship of the subcortical labels in the training set. Basal ganglia, thalamus, hippocampus, and amygdala volumes of both groups were compared using independent-sample *t*-tests.

Results

Imaging

Cortical

We found significant focal, but not global, cortical thinning in the PD group compared to the control group on the global maps in the following areas: In the left hemisphere, inferior frontal gyrus, pars triangularis, middle and inferior occipital gyrus, lingual and fusiform gyri, and cuneus/calcarine sulcus; in the right hemisphere, inferior frontal gyrus, pars orbitalis extending to the triangular part and orbital gyrus (Fig. 1). The ROI analysis

confirmed thinning in the left triangular (t = 2.8, P = 0.009) and right orbital (t = 2.15, P = 0.041) parts of the inferior frontal gyri, and demonstrated additional thinning in the PD group along the banks of the left parietal sulcus intermedius primus (Jensen) (t = 2.1, P = 0.043). Post hoc ROI analysis of the occipital areas revealed focal thinning along the banks of the left posterior collateral transverse sulcus (t = 3.1, P = 0.005) (Table 1). No significant thinning was observed in the remaining ROIs.

Subcortical—Direct comparison of the subcortical volumes between the groups did not reveal significant differences. The intracranial and whole brain segmentation volumes were also not significantly different (Fig. 1). We also calculated the ratio of each subcortical volume to the whole brain volume and found significant atrophy bilaterally in the putamen (Left: t = 2.3, P = 0.03; Right: t = 2.4, P = 0.02) and a trend towards atrophy in the right nucleus accumbens (t = 1.8, P = 0.08) in the PD group relative to the control group (Table 2).

Behavioral

None of the participants were demented as assessed by the MMSE and DRS tests. The independent-sample t-tests after Bonferroni correction for multiple comparisons revealed significant differences between the PD and control groups only on the anxiety-state scores (t = −3.3, P = 0.03). We also detected a subtle difference between the groups on the depression BDI-II scores (t = −2.2, P = 0.035, uncorrected) (Table 3).

Correlation Between Imaging and Behavioral Data

Our primary aim was to examine the structural brain changes in PD. A secondary interest was to relate the structural changes to behavioral data. To this end, we performed correlation analyses between the ROIs and behavioral data.

To avoid the problem of overfitting the correlation curve, we grouped the behavioral tests under three categories: psychomotor speed (digit-symbol and symbol search scores), executive function (digit span total, trails A-B, and FAS scores), and emotional status (STAI-S and STAI-T scores), and computed all individual raw scores to Z-scores based on published normative data. The Z-scores were then averaged for the tests in each category to compute one composite score per participant. Finally, all composite scores were included in the stepwise regression models simultaneously. ROIs were entered as dependent and the composite scores as independent variables.[33]

We did not find a significant correlation between the behavioral tests and the imaging data.

Discussion

Consistent with our a priori hypothesis, we observed significant focal cortical thinning in the PD group relative to controls in the ventral prefrontal and parietal cortices. We also found significant focal cortical thinning in unimodal visual association areas in our PD group.

Subcortically, we found that the bilateral putamen volume/whole brain volume ratio was significantly reduced, which is consistent with the results of a volumetric study.[6] Our

findings of limbic and heteromodal cortical thinning are consistent with neuropathological studies that have documented the sequential evolution of the Lewy body/neurite pathology across the cortex.[1]

The finding of focal cortical thinning in the unimodal visual association areas was not predicted. Previously, atrophy has been reported in the fusiform and lingual gyri in PD patients with dementia, but not in subjects without dementia.[5] The nature of the occipital pathology at relatively early stages of PD is currently unclear. However, evidence from imaging and neuropsychological literature suggests that an occipito-parietal pathology and selective visuospatial impairment exists in nondemented PD patients.[34,35]

Cognition, Emotion, and Parkinson's Disease

Neocortical information is the dominant source of feed-forward input to the limbic areas, and the limbic areas in turn provide massive feedback to the neocortical regions. This reciprocal connectivity pattern plays an important role in regulating behavior.[36] In addition to the disruption in the cortical-subcortical circuits, we propose that focal cortical thinning in PD disrupts the bidirectional information flow between limbic and neocortical regions, and the earliest consequences are observed in the form of emotional processing deficits, as reflected in increased anxiety scores in our PD patients.

Our results demonstrate that cortical and subcortical structural changes occur in PD patients before clinically detectable cognitive changes can be measured. Our PD cohort was not demented, and was well matched to the control group in cognitive performance. Behaviorally, the only significant difference between our PD and control groups was in measurement of anxiety state. The majority of our PD patients were on antidepressant or antianxiety medications, and mood disorders including anxiety, depression, and lack of motivation are frequently observed in PD patients.[37]

There is also evidence that an impaired functioning in the orbitofrontal cortex (OFC) may also play a role in depression. A PET study showed relative hypometabolism in the caudate and OFC in PD patients with depression compared to those without depression and to healthy controls.[38] We think that the significant OFC thinning in the PD group may partly be the underlying cause of the mood disorders observed in this group. OFC has robust connections with the amygdala and is directly involved in emotional processing. It receives rich sensory information and is involved in global processing of the external environment. [36] Through its connections with the ventral striatum, including the nucleus accumbens, OFC also plays an important role in goal-directed behaviors. Taken together, this connectivity pattern renders the OFC capable of integrating the external environment with the internal emotional status of the organism, capturing the emotional significance of events, and thereby placing them in the appropriate context for action.[36,39] We suggest that structural changes in the OFC may result in dysregulation of these integrative processes, and may consequently diminish the motivation for action in PD. In addition, the right nucleus accumbens showed a trend towards significance in our data, suggesting that it may also contribute to emotional dysregulation in PD by interrupting the integrity of the OFC-ventral striatal limbic loop.

We did not find a correlation between behavioral and imaging data, which may be due to the fact that it was necessary to collapse the behavioral scores as *Z*-scores due to statistical limitations, and the cognitive domains assessed in the tests overlapped with each other. Future studies could avoid these limitations by using a smaller number of behavioral tests that target a single cognitive domain. In addition, the relatively small PD cohort studied should also be taken into consideration when interpreting the data.

In conclusion, the highly precise automated imaging and analysis methods used in this study showed focal thinning in limbic and neocortical areas, and volume loss in the striatum in nondemented, early-stage PD patients. We suggest that emotional processing deficits might be a manifestation of these structural changes and seem to precede cognitive impairment. Therefore, detecting early signs and symptoms and developing biological markers for the preclinical diagnosis and progression of PD seem particularly important. MRI morphometry could be a potential biomarker in that regard.[15,16]

Acknowledgments

We also thank: Alice Cronin-Golomb, PhD, the head of the Vision and Cognition Laboratory at Boston University for assistance with participant recruitment and neuropsychological testing; Marie-Helene Saint-Hilaire, M.D., the staff neurologist at Boston University Medical Center, for assistance with participant recruitment; Haline E. Schendan, Ph.D. for discussions about the study; Stephen Maher for help with data acquisition, Jenni Pacheco for providing technical support for data analysis, and Sigurros Davidsdottir for help with participant recruitment and neuropsychological testing.

The study was supported by NIMH award R21 MH066213, and the Athinoula A. Martinos Center for Biomedical Imaging award (NCRR P41 RR14075).

References

1. Braak H, Braak E. Pathoanatomy of Parkinson’s disease. J Neurol. 2000; 247 (Suppl 2):3–10. [PubMed: 10701890]
2. Galvin JE, Lee VM, Trojanowski JQ. Synucleinopathies: clinical and pathological implications. Arch Neurol. 2001; 58:186–190. [PubMed: 11176955]
3. Double KL, Halliday GM, McRitchie DA, Reid WG, Hely MA, Morris JG. Regional brain atrophy in idiopathic Parkinson’s disease and diffuse Lewy body disease. Dementia. 1996; 7:304–313. [PubMed: 8915036]
4. Summerfield C, Junque C, Tolosa E, et al. Structural brain changes in Parkinson disease with dementia: a voxel-based morphometry study. Arch Neurol. 2005; 62:281–285. [PubMed: 15710857]
5. Burton EJ, McKeith IG, Burn DJ, Williams ED, O’Brien JT. Cerebral atrophy in Parkinson’s disease with and without dementia: a comparison with Alzheimer’s disease, dementia with Lewy bodies and controls. Brain. 2004; 127:791–800. [PubMed: 14749292]
6. Geng DY, Li YX, Zee CS. Magnetic resonance imaging-based volumetric analysis of basal ganglia nuclei and substantia nigra in patients with Parkinson’s disease. Neurosurgery. 2006; 58:256–262. [PubMed: 16462479]
7. Brenneis C, Seppi K, Schocke MF, Benke T, Wenning GK, Poewe W. Voxel-based morphometry detects cortical atrophy in the Parkinson variant of multiple system atrophy. Mov Disord. 2003; 18:1132–1138. [PubMed: 14534916]
8. Cordato NJ, Duggins AJ, Halliday GM, Morris JG, Pantelis C. Clinical deficits correlate with regional cerebral atrophy in progressive supranuclear palsy. Brain. 2005; 128:1259–1266. [PubMed: 15843423]
9. Nagano-Saito A, Washimi Y, Arahata Y, et al. Cerebral atrophy and its relation to cognitive impairment in Parkinson disease. Neurology. 2005; 64:224–229. [PubMed: 15668417]

10. Salat DH, Buckner RL, Snyder AZ, et al. Thinning of the cerebral cortex in aging. Cereb Cortex. 2004; 14:721–730. [PubMed: 15054051]
11. Rosas HD, Liu AK, Hersch S, et al. Regional and progressive thinning of the cortical ribbon in Huntington's disease. Neurology. 2002; 58:695–701. [PubMed: 11889230]
12. Rosas HD, Salat DH, Lee SY, et al. Cerebral cortex and the clinical expression of Huntington's disease: complexity and heterogeneity. Brain. 2008; 131 (Part 4):1057–1068. [PubMed: 18337273]
13. Sailer M, Fischl B, Salat D, et al. Focal thinning of the cerebral cortex in multiple sclerosis. Brain. 2003; 126:1734–1744. [PubMed: 12805100]
14. Kuperberg GR, Broome MR, McGuire PK, et al. Regionally localized thinning of the cerebral cortex in schizophrenia. Arch Gen Psychiatry. 2003; 60:878–888. [PubMed: 12963669]
15. Fischl B, Salat DH, Busa E, et al. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. Neuron. 2002; 33:341–355. [PubMed: 11832223]
16. Dickerson BC, Bakkour A, Salat DH, et al. The cortical signature of Alzheimer's disease: regionally specific cortical thinning relates to symptom severity in very mild to mild AD dementia and is detectable in asymptomatic amyloid-positive individuals. Cereb Cortex. 2009; 19:497–510. [PubMed: 18632739]
17. Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology. 1967; 17:427–442. [PubMed: 6067254]
18. Fahn, S.; Elton, R. Unified Parkinson's disease rating scale. In: Fahn, S.; Marsden, CD.; Calne, D.; Goldstein, M., editors. Recent developments in Parkinson's disease. New Jersey: MacMillan Health Care Information; 1978. p. 153-163.
19. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12:189–198. [PubMed: 1202204]
20. Mattis, S. Dementia rating scale. Odessa, FL: Psychological Assessment Resources; 1988.
21. Grober E, Sliwinski M. Development and validation of a model for estimating premorbid verbal intelligence in the elderly. J Clin Exp Neuropsychol. 1991; 13:933–949. [PubMed: 1779032]
22. Wechsler, D. Wechsler adult intelligence scale-III. San Antonio, TX: The Psychological Corporation; 1997.
23. Spreen, O.; Benton, AL. Neurosensory center comprehensive examination for aphasia. Victoria, BC: Univestiy of Victoria Neuropsychology Laboratory; 1977.
24. Reitan, RM.; Wolfson, D. The Halstead-Reitan neuropsychological test battery: theory and clinical interpretation. Tucson, AZ: Neuropsychology Press; 1993.
25. Beck, AT. Beck depression inventory-II. San Antonio, TX: The Psychological Corporation; 1997.
26. Spielberger, CD.; Gorusch, RL.; Lushene, R. Spielberger state trait anxiety inventory I and II. Palo Alto, CA: Consulting Psychologists Press; 1983.
27. Dale AM, Fischl B, Sereno MI. Cortical surface-based analysis. I. Segmentation and surface reconstruction. Neuroimage. 1999; 9:179–194. [PubMed: 9931268]
28. Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proc Natl Acad Sci USA. 2000; 97:11050–11055. [PubMed: 10984517]
29. Fischl B, Liu A, Dale AM. Automated manifold surgery: constructing geometrically accurate and topologically correct models of the human cerebral cortex. IEEE Trans Med Imaging. 2001; 20:70–80. [PubMed: 11293693]
30. Fischl B, Sereno MI, Dale AM. Cortical surface-based analysis. II. Inflation, flattening, and a surface-based coordinate system. Neuroimage. 1999; 9:195–207. [PubMed: 9931269]
31. Fischl B, Sereno MI, Tootell RB, Dale AM. High-resolution intersubject averaging and a coordinate system for the cortical surface. Hum Brain Mapp. 1999; 8:272–284. [PubMed: 10619420]
32. Fischl B, van der Kouwe A, Destrieux C, et al. Automatically parcellating the human cerebral cortex. Cereb Cortex. 2004; 14:11–22. [PubMed: 14654453]

33. Castelo JM, Courtney MG, Melrose RJ, Stern CE. Putamen hypertrophy in nondemented patients with human immunodeficiency virus infection and cognitive compromise. Arch Neurol. 2007; 64:1275–1280. [PubMed: 17846265]

34. Cronin-Golomb A, Braun AE. Visuospatial dysfunction and problem solving in Parkinson's disease. Neuropsychology. 1997; 11:44–52. [PubMed: 9055268]

35. Abe Y, Kachi T, Kato T, et al. Occipital hypoperfusion in Parkinson's disease without dementia: correlation to impaired cortical visual processing. J Neurol Neurosurg Psychiatry. 2003; 74:419–422. [PubMed: 12640053]

36. Barbas, H.; Ghashghaei, HT.; Rempel-Clower, NL.; Xiao, D. Anatomic basis of functional specialization in prefrontal cortices in primates. In: Grafman, J., editor. Handbook of neuropsychology. Amsterdam; New York: Elsevier; 2002. p. 1-27.

37. Brandstadter D, Oertel WH. Depression in Parkinson's disease. Adv Neurol. 2003; 91:371–381. [PubMed: 12442696]

38. Mayberg HS, Starkstein SE, Sadzot B, et al. Selective hypometabolism in the inferior frontal lobe in depressed patients with Parkinson's disease. Ann Neurol. 1990; 28:57–64. [PubMed: 2375634]

39. Bechara A, Damasio H, Tranel D, Damasio AR. Deciding advantageously before knowing the advantageous strategy. Science. 1997; 275:1293–1295. [PubMed: 9036851]

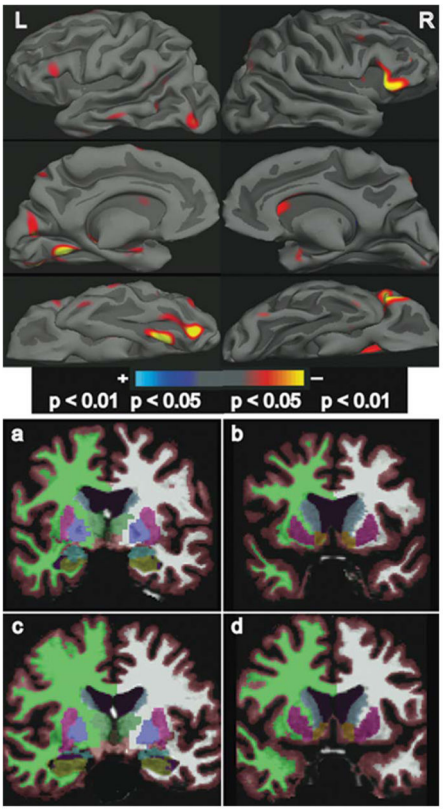

FIG. 1.

Top. Global cortical thickness difference maps show the cortical thinning in the PD group compared to the controls. Results are presented on a partially inflated cortical surface of a representative subject (red: $P < 0.05$, yellow: $P < 0.01$). Bottom. Subcortical segmentation results are displayed on the coronal slices of individual subject brains. a,b: Control. c,d: PD.

TABLE 1

Cortical thickness measurements

Region	PD mean ± SD (mm) (range)	Control mean ± SD (mm) (range)
Global		
Whole Brain Mean Global Thickness	1.99 ± 0.11 (1.23–2.74)	2.02 ± 0.09 (1.25–2.78)
Right Hemisphere Mean Global Thickness	1.99 ± 0.11 (1.23–2.74)	2.02 ± 0.09 (1.25–2.78)
Left Hemisphere Mean Global Thickness	1.98 ± 0.11 (1.23–2.74)	2.02 ± 0.09 (1.25–2.78)
Regions of Interest		
Left Inferior Frontal Gyrus, pars triangularis	2.18 ± 0.16[a] (1.68–2.69)	2.34 ± 0.14 (1.81–2.86)
Right Inferior Frontal Gyrus, pars orbitalis	2.17 ± 0.22[b] (1.66–2.69)	2.33 ± 0.19 (1.76–2.9)
Left Sulcus Intermedius Primus (Jensen)	1.62 ± 0.21[b] (1.17–2.07)	1.82 ± 0.3 (1.34–2.3)
Left Transverse Collateral Sulcus, posterior (post hoc)	1.38 ± 0.14[a] (1.04–1.71)	1.56 ± 0.19 (1.15–1.97)

[a] $P < 0.01$.

[b] $P < 0.05$.

TABLE 2

Subcortical volume measurements

Region	PD mean ± SD (mm^3)	Control mean ± SD (mm^3)
Intracranial volume	1.700.140 ± 165.891	1.681.105 ± 138.930
Whole Brain	1.076.685 ± 93.026	1.052.349 ± 105.202
Left hippocampus	3423 ± 298	3509 ± 353
Right hippocampus	3524 ± 309	3419 ± 405
Left amygdala	1718 ± 200	1687 ± 195
Right amygdala	1557 ± 257	1539 ± 210
Left thalamus	6502 ± 580	6302 ± 819
Right thalamus	6190 ± 642	6088 ± 932
Left caudate	3266 ± 303	3376 ± 467
Right caudate	3313 ± 382	3447 ± 631
Left putamen	4.620 ± 510	4.905 ± 379
Right putamen	4.272 ± 500	4.591 ± 399
Left pallidum	2027 ± 341	2047 ± 287
Right pallidum	2410 ± 352	2382 ± 356
Left accumbens	593 ± 119	608 ± 93
Right accumbens	516 ± 98	554 ± 85

Left putamen/whole brain volume PD < Control, $P = 0.03$.

Right putamen/whole brain volume PD < Control, $P = 0.02$.

Right nucleus accumbens/whole brain volume PD < Control, $P = 0.08$.

TABLE 3

Neuropsychological data

	Control (n = 15)	PD (n = 15)
MMSE	29.5 ± 0.9 (n = 13)	29.15 ± 1.5 (n = 13)
DRS	143.3 ± 0.9 (n = 12)	142.8 ± 2.4 (n = 13)
ANART	121.1 ± 6.6	121.3 ± 4
Digit Span total score	20.73 ± 4.2	21.2 ± 4.1
FAS	50.73 ± 13.1	47.13 ± 10.8
Animals	22.2 ± 6.3	21.1 ± 4.2
Digit Symbol	71.53 ± 16.5	61.2 ± 14.5 (n = 14)
Symbol Search[a]	32.3 ± 7.5	27.3 ± 5.8
Trails A (sec.)[a]	29.13 ± 7.7	39.8 ± 18.2
Trails B (sec.)	77.5 ± 52.5	77.5 ± 23
BDI-II[b]	4.13 ± 6.4	9.2 ± 6.2
STAI-S[c]	25.1 ± 4.7	33.3 ± 8.4
STAI-T	30.4 ± 10.1	36.2 ± 10.2

Neuropsychological data (mean ± SD) for Parkinson's disease (PD) and control subjects (n = 15, unless noted otherwise).

[a] $P = 0.05$.

[b] $P = 0.035$.

[c] $P = 0.003$ (P values not corrected for multiple comparisons).

MMSE, Mini Mental State Examination; DRS, Dementia Rating Scale; ANART, American National Adult Reading Test; Digit span total score, Sum of forward and backward scores; FAS, Letter fluency; Animals, Category fluency; BDI, Beck Depression Inventory; STAI, Spielberger State and Trait Anxiety Inventory; S, State; T, Trait.