

Behavioral and personality features in patients with lateralized Parkinson's disease

S. Piacentini^a, R. Versaci^a, L. Romito^a, F. Ferré^a and A. Albanese^{a,b}

^aFondazione IRCCS Istituto Neurologico “Carlo Besta”, Milano; and ^bIstituto di Neurologia, Università Cattolica del Sacro Cuore, Milano, Italy

Keywords:

conversion disorder, drug effects, functional laterality, impulsive behavior, mood disorders, Parkinson's disease

Received 8 May 2010

Accepted 28 October 2010

Background: Dopamine neurotransmission plays a key role in several brain activities, including motor, cognitive, and behavioral functions. Parkinson's disease (PD) typically begins with asymmetrical motor features related to asymmetrical dopamine denervation. This study was designed to examine whether distinct cognitive, behavioral, and personality features are related to this asymmetry.

Methods: Fifty-six patients with mild PD and lateralized motor features were grouped according to dominant side of motor features and evaluated using a neuropsychological assessment focused on attention and executive functions, impulse control disorders, and personality inventory.

Results: There were no differences in neuropsychological functions between patients with right and left lateralized PD, but differences occurred in personality features. Patients with motor impairment predominant on the left-hand side had prevalence of hypomania and conversion profile.

Conclusions: This study suggests that side dominance of dopaminergic denervation may be related to personality features in patients with PD that could influence behavioral aspects.

Introduction

Parkinson's disease (PD) typically begins with unilateral motor signs, and the original motor asymmetry is preserved throughout the natural course of the disease [1,2]. Asymmetry of PD motor signs matches a reciprocal asymmetry of dopamine reduction in the basal ganglia, and the degree of motor impairment correlates with the severity of contralateral dopamine depletion [1,3]. Dopamine neuromodulation is intrinsic to processes of movement and motor learning, cognition, reward processing, food intake, nociception, and endocrine and autonomic regulation. Studies on the lateralization of cognitive functions in patients with PD yielded conflicting results: some reported that neuropsychological deficits are consistent with the lateralization of motor symptoms [4–10], whilst others failed to find a correlation [11–15]. A limitation of several of these studies is that they prevalently investigated global lateralized brain functions in patients with variable

disease severity. Few studies have correlated PD motor asymmetry with behavioral and personality traits, such as mood disorders or impulsive–compulsive behaviors [16–19], which are influenced by dopamine replacement treatments. Risk factors for impulse control disorders in PD are still poorly defined, and we hypothesized that side dominance of dopaminergic depletion may influence the generation of behavioral abnormalities.

Patients and methods

Fifty-six men with a diagnosis of PD according to the UK Parkinson Disease Brain Bank criteria [20] were studied. Their motor condition and medication regimen were stabilized. The patients were grouped according to the lateralization of motor features: group R had right-hand-side motor onset and impairment at the time of evaluation (dominant left hemisphere dopaminergic depletion), and group L had left-hand-side motor onset and motor impairment (dominant right hemisphere depletion). Patients with unclear motor asymmetry were excluded. Other exclusion criteria were Hoehn–Yahr score > III, insufficient asymmetry, relevant axial impairment [sum of Unified Parkinson's Disease Rating Scale (UPDRS) items 18, 19, 27, 28, 29, 30 > 5], occurrence of motor

Correspondence: Sylvie Piacentini, Fondazione IRCCS Istituto Neurologico Carlo Besta, Via G. Celoria, 11, 20133 Milano, Italy (tel.: +39 02 2394 2704; fax: +39 02 2394 2539; e-mail: piacentini@istituto-besta.it).

fluctuations or dyskinesias, ongoing psychiatric problems, prior brain surgery, dementia (score < 85.5/100 on the adjusted Milan Overall Assessment of Dementia (MODA) [21]), non-right handedness (score ≤ 9 as assessed by Handedness Inventory [22]), and invalid MMPI-2 entry criteria. The two groups were matched for disease duration, UPDRS motor score, and Hoehn–Yahr stage (Table 1). Ethical approval was obtained from the Internal review Board of the Besta Institute, which is registered with the Office for Human Research Protection (IORG0006168). The patients signed an informed consent before entering the study.

Patients received a complete neurological examination, including a diagnostic workout whenever necessary. Motor lateralization was measured with the UPDRS motor score, by considering items 20 (rest tremor), 21 (action tremor), 22 (rigidity), 23 (finger taps), 24 (hand grips), 25 (hand pronation/supination), and 26 (leg agility) (Table 1). The patients were evaluated in the best ON condition under their current antiparkinsonian regimen. Levodopa-equivalent daily dose (LEDD) was calculated in mg [23]. Quality of life was assessed with the Italian version of PDQ-39 [24] and SF-36 questionnaires [25].

Neuropsychological assessment included tests for executive functions (fluency – FAS and Ruff Figural Fluency Test, cognitive flexibility – Nelson's modified

sorting card test, Hayling and Brixton test); tests for attention (dual task [26], Stroop task, digit cancellation test [27], digit span, visual pattern test [28]); and global assessment (MODA, emotion hexagon test [29]). Behavioral aspects were assessed by the following tests for impulse control disorders: South Oaks Gambling Screen, Internet addiction scale [30], sexual addiction screening test [31], and compulsive shopping evaluation scale [32].

Personality assessment was performed using the MMPI-2 [33]. The following MMPI-2 entry criteria were used to include patients in the study: (i) less than 30 omitted items, (ii) variable response inconsistency T-scores less than 80, (iii) true response inconsistency raw scores between 6 and 12, (iv) F raw scores less than 30, and (v) both lie and correction T-scores less than 80 [34]. The MMPI-2 clinical scales were explored. Code-types, clinical scales highest in the MMPI-2 profile, were annotated. To determine the code-types, raw scores of the scales were converted to T-scores having a mean of 50 and a standard deviation of 10. Scores greater than 65 are considered high scores and are significantly different from standardized group [35].

Statistical analysis was performed using the SPSS-PC package, version 12.01. Raw scores of patients' characteristics, motor features, quality of life, cognitive, and behavioral and personality measures in L and R groups

Table 1 Demographic, clinical, and quality-of-life measures in patients with lateralized Parkinson's disease (PD). Averages ($\pm$ SD) are indicated

	Total	Group R	Group L	P value
Patients (number)	56	28	28	
Age (years $\pm$ SD)	54.7 ($\pm$ 9.6)	55.9 ($\pm$ 10.6)	53.5 ($\pm$ 8.5)	0.35
Education (years $\pm$ SD)	12.3 ($\pm$ 3.7)	11.5 ($\pm$ 4.2)	13.0 ($\pm$ 3.1)	0.14
Disease duration (years $\pm$ SD)	4.1 ($\pm$ 2.5)	3.9 ($\pm$ 1.8)	4.3 ($\pm$ 3.0)	0.56
Hoehn–Yahr stage (range)	0–2.5	0–2.5	0–2.5	0.39
Total LEDD (mg)	331.8 ($\pm$ 254.5)	359.3 ($\pm$ 248.1)	304.3 ($\pm$ 262.2)	0.42
UPDRS motor score				
UPDRS total score ($\pm$ SD)	21.4 ($\pm$ 8.0)	21.2 ($\pm$ 8.1)	21.6 ($\pm$ 8.0)	0.84
UPDRS left ^a ($\pm$ SD)	7.5 ($\pm$ 5.0)	3.8 ($\pm$ 2.0)	11.3 ($\pm$ 3.5)	0.00
UPDRS right ^b ($\pm$ SD)	7.3 ($\pm$ 4.7)	10.9 ($\pm$ 3.4)	3.8 ($\pm$ 2.7)	0.00
UPDRS tremor ^c ($\pm$ SD)	3.6 ($\pm$ 2.5)	3.7 ($\pm$ 2.4)	3.6 ($\pm$ 2.5)	0.90
UPDRS bradykinesia ^d ($\pm$ SD)	9.5 ($\pm$ 4.0)	9.1 ($\pm$ 4.1)	9.9 ($\pm$ 4.0)	0.82
UPDRS rigidity ^e ($\pm$ SD)	4.2 ($\pm$ 2.2)	4.3 ($\pm$ 2.0)	4.1 ($\pm$ 2.4)	0.46
UPDRS axial impairment ^f ($\pm$ SD)	2.7 ($\pm$ 2.0)	2.7 ($\pm$ 1.9)	2.8 ($\pm$ 2.2)	0.86
Quality of life				
PDQ-39 score ($\pm$ SD) (range 0–156) ^g	29.2 ($\pm$ 15.8)	28.0 ($\pm$ 14.1)	30.3 ($\pm$ 17.4)	0.64
SF-36 score ($\pm$ SD) (range 0–149) ^h	106.6 ($\pm$ 6.9)	105.8 ($\pm$ 8.0)	107.4 ($\pm$ 5.8)	0.47

LEDD, Levodopa-equivalent daily dose.

^a, Sum of items 20–26 for the left-hand side.

^b, Sum of items 20–26 for the right-hand side.

^c, Sum of items 20–21.

^d, Sum of items 23–26 and 31.

^e, Sum of items 22.

^f, Sum of items 27–30.

^g, Lower scores denote better outcome.

^h, Higher scores denote better outcome.

Boldface indicates significant differences ($P < 0.001$; t -test).

Test	Total	Group R	Group L	<i>P</i> value
<i>Executive functions</i>				
FAS	35.0 ($\pm$ 9.7)	36.2 ($\pm$ 10.7)	33.9 ($\pm$ 8.7)	0.38
RFFT Number figures	70.3 ($\pm$ 21.9)	67.2 ($\pm$ 19.6)	73.4 ($\pm$ 24.1)	0.30
MSCT N° perseveration	2.2 ($\pm$ 3.3)	2.3 ($\pm$ 3.5)	2.1 ($\pm$ 3.1)	0.87
Hayling test	14.7 ($\pm$ 4.7)	14.7 ($\pm$ 5.7)	14.8 ($\pm$ 3.6)	0.96
Brixton test	20.4 ($\pm$ 6.6)	20.6 ($\pm$ 7.0)	20.1 ($\pm$ 6.4)	0.75
<i>Attention</i>				
Dual task test	89.4 ($\pm$ 11.8)	88.5 ($\pm$ 10.0)	90.4 ($\pm$ 13.4)	0.57
Stroop test time effect	17.6 ($\pm$ 6.3)	17.6 ($\pm$ 6.2)	17.7 ($\pm$ 6.5)	0.97
Digit Cancellation Test	53.3 ($\pm$ 5.0)	52.7 ($\pm$ 5.2)	53.9 ($\pm$ 4.7)	0.37
Digit span	5.2 ($\pm$ 1.1)	5.3 ($\pm$ 1.2)	5.1 ($\pm$ 1.0)	0.72
Visual pattern test	5.3 ($\pm$ 1.6)	5.4 ($\pm$ 1.7)	5.1 ($\pm$ 1.5)	0.57
<i>Global assessment</i>				
MODA	95.8 ($\pm$ 2.4)	95.8 ($\pm$ 2.2)	95.9 ($\pm$ 2.7)	0.96
Emotion hexagon test	102.6 ($\pm$ 15.0)	102.8 ($\pm$ 13.7)	102.4 ($\pm$ 16.4)	0.92
<i>Behavioral tests</i>				
SOGS	0.9 ($\pm$ 2.3)	0.6 ($\pm$ 1.5)	1.2 ($\pm$ 2.4)	0.34
IAS	30.1 ($\pm$ 10.6)	28.5 ($\pm$ 8.9)	31.5 ($\pm$ 11.8)	0.38
SAST	2.8 ($\pm$ 3.2)	2.2 ($\pm$ 2.2)	3.3 ($\pm$ 3.8)	0.22
CSES	0.4 ($\pm$ 0.8)	0.4 ($\pm$ 0.9)	0.3 ($\pm$ 0.7)	0.63

MODA, Milan Overall Assessment of Dementia; FAS, Verbal fluency; RFFT, Ruff Figural Fluency Test; MCST, Nelson's Modified Card Sorting Test; SOGS, South Oaks Gambling Screen; IAS, Internet addiction scale; SAST, Sexual addiction screening test; CSES, Compulsive shopping evaluation scale.

Table 2 Neuropsychological and behavioral tests in patients with lateralized Parkinson's disease (PD). The raw scores (standard deviation) of the experimental groups are indicated. There are no significant between-group differences

MMPI-2 scale	Total	Group R	Group L	<i>P</i> value
<i>Clinical scales (codetype)</i>				
<i>Mood Disorders</i>				
Depression (2)	58.8 ($\pm$ 9.1)	58.5 ($\pm$ 11.4)	59.1 ($\pm$ 6.1)	0.84
Hypomania (9)	46.8 ($\pm$ 11.3)	43.4 ($\pm$ 7.8)	49.9 ($\pm$ 16.3)	0.04
<i>Somatoform disorders</i>				
Hypochondriasis (1)	62.4 ($\pm$ 11.4)	61.1 ($\pm$ 10.5)	63.6 ($\pm$ 13.0)	0.47
Hysteria (3)	55.3 ($\pm$ 12.6)	53.7 ($\pm$ 9.2)	56.9 ($\pm$ 15.3)	0.39
<i>Other disorders</i>				
Psychopathic deviate (4)	47.8 ($\pm$ 8.7)	47.2 ($\pm$ 8.1)	48.3 ($\pm$ 9.5)	0.68
Paranoia (6)	49.5 ($\pm$ 8.8)	48.9 ($\pm$ 7.4)	50.2 ($\pm$ 10.1)	0.62
Psychasthenia (7)	51.2 ($\pm$ 10.7)	49.9 ($\pm$ 11.8)	52.6 ($\pm$ 9.6)	0.39
Schizophrenia (8)	53.4 ($\pm$ 9.5)	53.2 ($\pm$ 8.9)	53.6 ($\pm$ 10.2)	0.88
Social introversion (0)	57.2 ($\pm$ 8.0)	57.3 ($\pm$ 8.6)	57.1 ($\pm$ 7.5)	0.94

Boldface indicates significant differences ($P < 0.05$; *t*-test)

Table 3 MMPI-2 analysis of patients with lateralized Parkinson's disease (PD). The raw scores (standard deviation) of the experimental groups are indicated

were compared using independent two-sample *t*-test (Tables 1–3). We performed linear regression analyses between the left- and right-sided aggregated UPDRS scores and the cognitive tests.

For codetype analysis, scores were dichotomized (over or under 65) and analyzed with Fisher's exact test (Table 4). The significance level was set to a probability of 5%.

Results

Fifty-six patients were recruited in the study, 28 in each group. There were no between-group differences for

age, education, disease duration, Hoehn–Yahr stage, LEDD, UPDRS, and quality-of-life measures (Table 1). Groups R and L differed only for items related to side dominance of motor features.

On the neuropsychological battery, groups R and L performed similarly, with no between-group differences (Table 2). Further, we did not find any correlation between the left- and right-sided aggregated UPDRS scores and the cognitive scores.

Behavioral tests showed no significant differences on impulse control disorder scales (Table 2). However, four patients in group L and only one in group R scored pathologically in one or more tests for impulse control

Table 4 MMPI-2 codetypes. The number (and percentage) of patients with high score (T-score > 65) is indicated

		Total	Group R	Group L	P value
1-point codetypes	Depression (2)	26 (46.4%)	14 (50%)	12 (42.9%)	0.40
	Hypochondriasis (1)	29 (51.8%)	16 (57.1%)	13 (46.4%)	0.30
2-point codetypes	1-3/3-1	11 (19.6%)	2 (7.1%)	9 (32.1%)	0.02
	2-7/7-2	3 (5.4%)	3 (10.7%)	0 (0%)	0.12

Boldface indicates significant differences ($P < 0.05$ Fisher's exact test).

disorder behaviors (South Oaks Gambling Screen, the Internet addiction, and the sexual addiction screening tests). No patients had compulsive shopping.

Assessment of personality traits (Table 2) with the MMPI-2 showed a significant difference between group R and group L in the hypomania scale ($p = 0.04$). Furthermore, six patients in group L (21.4%) and only one patient in group R scored pathologically on the MMPI-2 Hypomania scale.

One-point codetype (one clinical scale ≥ 65) analysis showed that both groups were characterized by a high number of patients with high scores (≥ 65) on hypochondriasis (51.8%) and depression (46.4%) scales with a comparable distribution in groups R and L.

Considering two-point codetypes (two clinical scales ≥ 65), types 1-3/3-1 and 2-7/7-2 were the only ones to emerge. They were unevenly distributed between groups; profile 1-3/3-1 was the most prevalent overall. The frequency of 1-3 codetype was prevalent in the L group ($p = 0.02$) and occurred significantly almost only in group L (32.1%).

Discussion

The present study shows that cognitively intact patients with right- or left-dominant motor PD do not differ on cognitive tasks, but on personality features. Compared to group R, patients with belonging to group L have higher incidence of hypomania. In addition, group L patients have a prevalence of 2 codetype personality profiles characterized by more elevated hypochondriasis and hysteria scales (as shown by codetypes 1-3).

Unbalance between dopaminergic neurotransmission in the right and left hemispheres, with a relative right hypofunction, is a likely explanation of our findings on hypomania based on previous observations of patients who received deep brain stimulation or suffered from unilateral brain lesions. In a patient with manic episodes related to deep brain stimulation, the manic episodes recurred when settings were changed in the right contact (patient 1 [36]). In another case, a unilateral infarct of the right substantia nigra was reported to produce mania in combination with PD motor symptoms [37]. Finally, an association between right hemi-

sphere lesions or decreased right frontal arousal and mania has also been reported [38,39]. In keeping with these observations, increased activation of the left basal ganglia has been reported in bipolar patients who are in a elevated or euthymic state [40,41], and functional neuroimaging studies have found that mania is often associated with less activation of the right hemisphere compared to the left, whereas the opposite occurs in depressed patients [42–44].

Impulse control disorders occurred predominantly in group L patients, in keeping with the observation that the severity of impulse dyscontrol, such as gambling, correlates with reduced activation of the right ventral striatum [45]. Their number fits in nicely with the reported prevalence of impulse control disorder in patients with PD under dopaminergic replacement therapy [46].

The 1-3 codetype prevalence indicates that group L patients' personality is characterized by the tendency to report more somatic complaints, to increase physical symptoms under stress and lack of psychological insight [35], the so-called conversion profile (or conversion V pattern). In keeping with our data, a recent study has found significantly higher presence of somatic complaints in patients with PD with onset in the right hemisphere compared to patients with prevalent left hemisphere denervation [47]. This is also consistent with an observed improvement in the MMPI hypochondria scale following unilateral post-eroventral pallidotomy [48,49].

All five patients with impulse control disorders had a 1-3 personality profile. Three of them were pathological on hypomania scale (all in Group L).

Our data on cognition confirm a number of earlier studies reporting no association between laterality of motor impairment and executive functions [12,13,15] and challenge other studies suggesting that patients with left hemisphere involvement have a reduced performance in verbal fluency [7,9,10], digit span [7], and Wisconsin Card Sorting Test [8,10]. The strict inclusion criteria of this protocol probably accounts for the observed normal cognitive features. Some earlier studies included patients with different degrees of disease severity [7–9], whereas others also included patients

with dementia [10]. In keeping with our observation, previous studies that matched patient groups for disease severity and overall intellectual impairment failed to find cognitive differences in lateralization [12,13,15].

The selection of patients with mild PD features allowed to avoid the inclusion of subjects with cortical Lewy body pathology and to emphasize differences related to dopaminergic innervation of the basal ganglia. Furthermore, dopaminergic medication did not differ between groups and was kept at low doses. Early disease stage does not mean lack of dopaminergic innervation, as shown by prominent DAT scan denervation observed in our patients and confirmed by recent imaging studies showing that prominent dopaminergic denervation occurs early in PD and is followed by a slowing down in more advanced disease stages [3].

The behavioral and personality differences observed in this highly selected PD population are subtle but may be amplified by the prescription of dopaminergic medication or the implant of chronic high-frequency stimulators. Although the population considered in this study is numerically limited, the accurate selection of patients allows us to draw intergroup comparisons. The observation that patients with a dominant right hemisphere depletion have a higher risk of conversion personality profile and hypomania poses interesting questions on their potentially higher risk to develop dopamine dysregulation symptoms.

There are some clear limitations of the current study. First, it has to be considered a preliminary observation, because our multiple univariate comparisons inflate the risk of making a type I error, increasing the probability of false positive results; nevertheless, our data suggest interesting correlated aspects of personality and behavior, leading us to believe that this association would hold in a larger study. Second, although there were no correlations with UPDRS left- and right-aggregated scores, the presence of bilateral symptoms could still have somehow contributed to negative findings. Third, all the evaluations were performed on dopaminergic treatment, and this could have softened the effect of lateralization. Fourth, measures used for personality and behavioral aspects were all self-reported and therefore limited by their subjectivity. The patients were able to correctly fill the inventory (patients with dementia were excluded), and we were able to check the compliance (e.g., MMPI-2 provides different validity indicators), but the results of self-reported tests for impulse control disorders could have been underestimated for denial.

Future studies will investigate the incidence and the features of right- or left-dominant PD patients who suffer from dopamine dysregulation syndrome or bear deep brain stimulation implants. Epidemiological

studies should assess in large population samples whether the features of dopamine dysregulation syndrome or impulse control disorders vary according to the dominant side of dopamine denervation and personality aspects.

Acknowledgements

We thank Ludovico Minati, MSc, for his critical comments on the manuscript. The source of funding is the Italian Ministry of Health.

References

1. Djaldetti R, Ziv I, Melamed E. The mystery of motor asymmetry in Parkinson's disease. *Lancet Neurol* 2006; **5**: 796–802.
2. Lee CS, Schulzer M, Mak E, Hammerstad JP, Calne S, Calne DB. Patterns of asymmetry do not change over the course of idiopathic parkinsonism: implications for pathogenesis. *Neurology* 1995; **1**: 435–439.
3. Pirker W, Holler I, Gerschlagner W, Asenbaum S, Zetting G, Brucke T. Measuring the rate of progression of Parkinson's disease over a 5-year period with beta-CIT SPECT. *Mov Disord* 2003; **18**: 1266–1272.
4. Blonder LX, Gur RE, Gur RC, Saykin AJ, Hurtig HI. Neuropsychological functioning in hemiparkinsonism. *Brain Cogn* 1989; **9**: 244–257.
5. Chouza C, Romero S, Laguardia G, *et al.* Hemi-parkinsonism: clinical, neuropsychological, and tomographical studies. *Adv Neurol* 1984; **40**: 415–425.
6. Huber SJ, Miller H, Bohaska L, Christy JA, Bornstein RA. Asymmetrical cognitive differences associated with hemiparkinsonism. *Arch Clin Neuropsychol* 1992; **7**: 471–480.
7. Spicer KB, Roberts RJ, LeWitt PA. Neuropsychological performance in lateralized parkinsonism. *Arch Neurol* 1988; **45**: 429–432.
8. Starkstein S, Leiguarda R, Gershanik O, Berthier M. Neuropsychological disturbances in hemiparkinson's disease. *Neurology* 1987; **37**: 1762–1764.
9. Taylor AE, Saint-Cyr JA, Lang AE. Frontal lobe dysfunction in Parkinson's disease. The cortical focus of neostriatal outflow. *Brain* 1986; **5**: 845–883.
10. Tomer R, Levin BE, Weiner WJ. Side of onset of motor symptoms influences cognition in Parkinson's disease. *Ann Neurol* 1993; **34**: 579–584.
11. Blonder LX, Gur RE, Gur RC. The effects of right and left hemiparkinsonism on prosody. *Brain Lang* 1989; **36**: 193–207.
12. Finali G, Piccirilli M, Rizzuto S. Neuropsychological characteristics of parkinsonian patients with lateralized motor impairment. *J Neural Transm Park Dis Dement Sect* 1995; **3**: 165–176.
13. Huber SJ, Freidenberg DL, Shuttleworth EC, Paulson GW, Clapp LE. Neuropsychological similarities in lateralized parkinsonism. *Cortex* 1989; **25**: 461–470.
14. Riklan M, Stellar S, Reynolds C. The relationship of memory and cognition in Parkinson's disease to lateralization of motor symptoms. *J Neurol Neurosurg Psychiatry* 1990; **53**: 359–360.
15. St Clair J, Borod JC, Sliwinski M, Cote LJ, Stern Y. Cognitive and affective functioning in Parkinson's disease

- patients with lateralized motor signs. *J Clin Exp Neuropsychol* 1998; **20**: 320–327.
16. Barber J, Tomer R, Sroka H, Myslobodsky MS. Does unilateral dopamine deficit contribute to depression? *Psychiatry Res* 1985; **15**: 17–24.
 17. Fleminger S. Left-sided Parkinson's disease is associated with greater anxiety and depression. *Psychol Med* 1991; **21**: 629–638.
 18. Tomer R, Levin BE, Weiner W. Obsessive-compulsive symptoms and motor asymmetries in Parkinson's Disease. *Neuropsychiatry Neuropsychol Behav Neurol* 1993; **6**: 26–30.
 19. Tomer R, Aharon-Peretz J. Novelty seeking and harm avoidance in Parkinson's disease: effects of asymmetric dopamine deficiency. *J Neurol Neurosurg Psychiatry* 2004; **75**: 972–975.
 20. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry* 1992; **55**: 181–184.
 21. Brazzelli M, Capitani E, Della Sala S, Spinnler H, Zuffi M. A neuropsychological instrument adding to the description of patients with suspected cortical dementia: the Milan overall dementia assessment. *J Neurol Neurosurg Psychiatry* 1994; **57**: 1510–1517.
 22. Briggs GG, Nebes RD. Patterns of hand preference in a student population. *Cortex* 1975; **11**: 230–238.
 23. Moro E, Esselink RJ, Xie J, Hommel M, Benabid AL, Pollak P. The impact on Parkinson's disease of electrical parameter settings in STN stimulation. *Neurology* 2002; **5**: 706–713.
 24. Peto V, Jenkinson C, Fitzpatrick R. PDQ-39: a review of the development, validation and application of a Parkinson's disease quality of life questionnaire and its associated measures. *J Neurol* 1998; **245**(Suppl 1): S10–S14.
 25. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; **30**: 473–483.
 26. Baddeley A, Della SS, Papagno C, Spinnler H. Dual-task performance in dysexecutive and nondysexecutive patients with a frontal lesion. *Neuropsychology* 1997; **11**: 187–194.
 27. Della Sala S, Laiacina M, Spinnler H, Ubezio C. A cancellation test: its reliability in assessing attentional deficits in Alzheimer's disease. *Psychol Med* 1992; **22**: 885–901.
 28. Della Sala S, Gray C, Baddeley A, Wilson L. *Visual Patterns Test (VPT)*. Oxford, United Kingdom: Pearson Assessment, 1997.
 29. Young A, Perrett D, Calder A, Sprengelmeyer R, Ekman P. *Facial Expression of Emotion: Stimuli and Tests (FEEST)*. Thurston, Suffolk: Thames Valley Test Company, 2002.
 30. Young KS. Internet addiction: the emergence of a new clinical disorder. *Cyberpsychol Behav* 1998; **1**: 237–244.
 31. Carnes P. Sexual addiction screening test. *Tenn Nurse* 1991; **54**: 29.
 32. Guerreschi C. *Il gioco d'azzardo patologico*. Rome: Kap-pa, 2003.
 33. Butcher JN, Dahlstrom WG, Graham JR, Tellegen A, Kaemmer B. *Minnesota Multiphasic Personality Inventory-2 (MMPI-2): Manual for Administration and Scoring*. Minneapolis, MN: University of Minnesota Press, 1989.
 34. Butcher JN, Graham JR, Ben-Porath YS. Methodological problems and issues in MMPI, MMPI-2, and MMPI-A research. *Psychol Assess* 1995; **7**: 320–329.
 35. Graham JR. *MMPI-2 Assessing personality and Psychopathology*, 4th edn. New York: Oxford University Press, 2006.
 36. Kulisevsky J, Berthier ML, Gironell A, Pascual-Sedano B, Molet J, Pares P. Mania following deep brain stimulation for Parkinson's disease. *Neurology* 2002; **12**: 59.
 37. Kulisevsky J, Avila A, Berthier ML. Bipolar affective disorder and unilateral parkinsonism after a brainstem infarction. *Mov Disord* 1995; **10**: 799–802.
 38. Braun CM, Daigneault R, Gaudelet S, Guimond A. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition symptoms of mania: which one(s) result(s) more often from right than left hemisphere lesions? *Compr Psychiatry* 2008; **49**: 441–459.
 39. Garcia-Toro M, Montes JM, Talavera JA. Functional cerebral asymmetry in affective disorders: new facts contributed by transcranial magnetic stimulation. *J Affect Disord* 2001; **3**: 103–109.
 40. Caligiuri MP, Brown GG, Meloy MJ, et al. A functional magnetic resonance imaging study of cortical asymmetry in bipolar disorder. *Bipolar Disord* 2004; **6**: 183–196.
 41. Caligiuri MP, Brown GG, Meloy MJ, Ebersson S, Niculescu AB, Lohr JB. Striatopallidal regulation of affect in bipolar disorder. *J Affect Disord* 2006; **3**: 235–242.
 42. Kennedy SH, Javanmard M, Vaccarino FJ. A review of functional neuroimaging in mood disorders: positron emission tomography and depression. *Can J Psychiatry* 1997; **42**: 467–475.
 43. Koek RJ, Yerevanian BI, Tachiki KH, Smith JC, Alcock J, Kopelowicz A. Hemispheric asymmetry in depression and mania. A longitudinal QEEG study in bipolar disorder. *J Affect Disord* 1999; **53**: 109–122.
 44. Nobler MS, Sackeim HA, Prohovnik I, et al. Regional cerebral blood flow in mood disorders, III. Treatment and clinical response. *Arch Gen Psychiatry* 1994; **51**: 884–897.
 45. Reuter J, Raedler T, Rose M, Hand I, Glascher J, Buchel C. Pathological gambling is linked to reduced activation of the mesolimbic reward system. *Nat Neurosci* 2005; **8**: 147–148.
 46. Weintraub D, Koester J, Potenza MN, et al. Impulse control disorders in Parkinson disease: a cross-sectional study of 3090 patients. *Arch Neurol* 2010; **67**: 589–595.
 47. MacNamara P, Stavitsky K, Harris E, Szent-Imrey O, Durso R. Mood, side of motor symptom onset and pain complaints in Parkinson's disease. *Int J Geriatr Psychiatry* 2010; **25**: 519–524.
 48. Fukuda M, Kameyama S, Yoshino M, Tanaka R, Narabayashi H. Neuropsychological outcome following pallidotomy and thalamotomy for Parkinson's disease. *Stereotact Funct Neurosurg* 2000; **74**: 11–20.
 49. Narabayashi H, Miyashita N, Hattori Y, Saito K, Endo K. Posteroventral pallidotomy: its effect on motor symptoms and scores of MMPI test in patients with Parkinson's disease. *Parkinsonism Relat Disord* 1997; **3**: 7–20.