SHORT REPORT

Neuropsychological sequelae of bilateral posteroventral pallidotomy

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Objectives: To document the impact of bilateral posteroventral pallidotomy on cognitive status.
Methods: 17 patients with Parkinson's disease were evaluated with a neuropsychological battery before and six months after bilateral pallidotomy. A comparison group (n = 8) was also assessed at six month intervals. Outcome variables were tests of memory, language, visuospatial function, attention, executive skills, and depression.
Results: Despite a large number of variables studied, a significant postsurgical change was found only in performance of the tower of London task, a measure of planning abilities. The effect size of this change was larger than that of the comparison group, and a reliable change index score established that 5 of 13 surgical patients had statistically reliable reductions in planning performance.
Conclusions: Patients with a young age of onset and long duration of Parkinson's disease who underwent bilateral pallidotomy had a relatively circumscribed reduction in neuropsychological functioning, being limited to motor planning efficiency. These data suggest that the cognitive role of the posteroventral globus pallidus is limited, at least in people with Parkinson's disease.

Stereotactic posteroventral pallidotomy (PVP), where lesions are made in the internal globus pallidus to reduce thalamic inhibition,[1] is frequently used in Parkinson's disease (PD) to relieve motor symptoms and medication side effects. Bilateral surgery (lesions or more recently neurostimulation) is generally deemed appropriate for those with severe bilateral disabilities. The procedure is associated with amelioration of dyskinesia,[2–5] rigidity,[2–6] and bradykinesia.[2–7] A less consistent finding is reduction in tremor.[8–9]

The impact of PVP on cognitive status is poorly documented and the literature is limited almost entirely to examining unilateral lesions. A recent review[10] noted a number of methodological shortcomings in this body of literature and not surprisingly neuropsychological findings to date are mixed. The pattern of conflicting findings also characterises the small amount of bilateral surgery cognitive research.[8–11] There have been no studies of long term changes after bilateral PVP, and in the studies reported control groups are rare and groups are small (4, 8, and 10 participants, respectively).

Impaired planning is implicated in PD,[12] in the globus pallidus[13] by regional cerebral blood flow studies, and in circuits involving these nuclei.[14] However, there has been no formal examination of changes to planning ability after PVP. Studies examining the effect of PVP on mood are rare, although two studies have described a reduction in depression.[15 16]

The paucity of investigations into neuropsychological functioning and mood following bilateral PVP have provided the impetus for the current study. Practice effects and progressive natural decline of PD were controlled by using a six month follow up period and a non-surgical PD comparison group.

METHOD

This study was approved by the Macquarie University Human Ethics Committee and informed consent was obtained from each participant.

Participants

All participants met diagnostic criteria for PD.[3] Surgical participants (n = 17) were those undergoing bilateral pallidotomy in a single hospital during two time periods (1995–1996 and 1999–2000; time 1). Postsurgical examinations (time 2) were done between 6 and 12 months later. A comparison group (n = 8) of volunteers was recruited from community PD support groups.

Exclusion criteria

People with a history of head injury, cerebrovascular disease, alcohol abuse, tumours, onset of PD at > 70 years, significant atrophy on preoperative magnetic resonance (MR) scans, or minor motor manifestations of PD were excluded from the study. A conservative cut off of a score of 21[17] in the mini-mental state examination[18] was used to exclude patients whose performance was indicative of dementia. Parietal dysfunction was assessed to exclude patients with cortical dysfunction. Apraxia was measured with the praxis subtest of the western aphasia battery,[19] and constructional apraxia and neglect were measured with figural copies (cross, coils, and cube; total 27) and clock drawing.[20 21]

Neuropsychological outcome variables

Verbal and visual functioning were assessed by the Rey auditory verbal learning test (RAVLT)[22] and the Benton visual retention test (multiple choice version),[23] respectively. For the RAVLT, total learning was the number of words recalled over five consecutive learning trials; delayed recall was measured after 20 minutes; and new recognition was derived to consider recognition and false positives.[24]

Category fluency was assessed with the animals test.[25] Speed of verbal generativity was measured with the controlled oral word association task (FAS).[26] A version of the Boston naming test (items 30–60)[27] was used to test confrontation naming.

Visuoconstruction was tested with the block design of the Wechsler adult intelligence scale-revised (WAIS-R).[28]

Working memory and attention were assessed using the digit span and mental control subtests of the WAIS-R and Wechsler memory scale-revised, respectively.[28 29]

Abbreviations: MR, magnetic resonance; PD, Parkinson's disease; PVP, posteroventral pallidotomy; RAVLT, Rey auditory verbal learning test; TOLT, tower of London task; WAIS-R, Wechsler adult intelligence scale-revised

Table 1 Results of neuropsychological testing in surgical and non-surgical groups

	Surgical group			Non-surgical group	
	Time 1	Time 2	Wilcoxon two-tailed test	Time 1	Time 2
RAVLT total learning	40.2 (10.1)	39.7 (9.3)	0.3815	42.9 (6.5)	45.7 (3.7)
RAVLT delayed recall	6.6 (3.4)	6 (3.9)	0.0828	7.9 (2.5)	8.3 (2.5)
RAVLT new recognition	0.86 (0.09)	0.86 (0.13)	0.8585	0.92 (0.1)	0.91 (0.1)
Benton visual retention test multiple choice	9.3 (2.6)	9.1 (2.9)	0.6623	11.1 (2.4)	12.3 (1.8)
Animals	16.8 (4.2)	15.5 (5.1)	0.2052	17.3 (5.5)	16.6 (2.9)
Controlled oral word association task	40.4 (15)	40 (14)	0.5753	36.5 (7.6)	35.7 (14.5)
Boston naming test 31 item	20.9 (6.1)	21.9 (5.4)	0.0201	27.5 (2.4)	29 (1.1)
WAIS-R block design	20.1 (12.5)	19.9 (11.7)	0.8136	24.4 (8.3)	27 (10.9)
WAIS-R digit span	14.2 (3.9)	15.1 (3.2)	0.1982	17.1 (3.9)	18.2 (2.3)
WMS-R mental control	5.3 (1.1)	5.4 (.8)	0.7055	5.6 (0.7)	5.8 (0.4)
Raven's coloured progressive matrices	26.6 (5.5)	26.9 (5.5)	0.9496	32.4 (2.4)	33.7 (0.82)
WAIS-R similarities	16.4 (5.6)	16.4 (4.7)	0.6791	22.4 (2)	22.5 (2.3)
Tower of London total moves trials 8–12	36.1 (8.5)	46 (14.3)	0.0087*	30.9 (3)	34.5 (7.4)
Geriatric depression scale	11.5 (6.2)	9.4 (6.4)	0.1188	8.9 (7.6)	5 (3.9)

*p<0.01. RAVLT: Rey auditory verbal learning task; WAIS-R, Wechsler adult intelligence scale-revised; WMS-R, Wechsler memory scale-revised

Raven's coloured progressive matrices[30 31] were used to assess non-verbal reasoning and the similarities subtest of the WAIS-R was used to measure verbal abstract reasoning. A short version of the tower of London task (TOLT) (practice and trials 8–12)[32] was used to measure planning and problem solving, where the number of attempts for each trial was summed (TOLT) as the outcome measure.

The 30 item geriatric depression scale[33–34] was used to measure the impact of PVP on mood.

Neurosurgical procedure

The surgical procedure for making bilateral 4–6 mm lesions in the posteroventral portion of the internal globus pallidus has been described elsewhere.[2] In brief, preoperative T1 weighted MR and localised computed tomography images are fused and registered to stereotactically defined MR images. The probe passage is represented graphically with respect to a Cosman Robert Wales head frame and computed tomographic and MR images. The lesion site is confirmed during surgery with physiological macrostimulation and after surgery using a postoperative MR. The lesions are confined to the internal pallidum and are comet shaped with the apex sited in the ansa lenticularis directly above the optic tract lateral to the internal capsule.

RESULTS

No participants scored less than 21 on the mini-mental state examination, and praxis and parietal functioning were intact. There were 17 participants in the surgical group (eight men and nine women) and eight in the non-surgical group (six men and two women). Follow up data are limited to 16 and 6 in the two groups, respectively, as one surgical and two non-surgical participants dropped out of the study.

Group characteristics

The comparison group was older than the surgical group (mean (SD) 67.6 (8.9) and 60.4 (6.6) years), had a later age of onset (59.1 (6.4) and 46.8 (8.9) years), and had had the disease for a shorter time (8.5 (4.2) and 13.7 (5.4) years). The majority of the surgical group was at Hoehn and Yahr (HY)[35] stages 2.5–4, and most members of the non-surgical group were at Hoehn and Yahr stage 2.

In a preliminary analysis, Pearson correlations, box plots, and histograms showed that the groups differed on covariates (age, age at onset, duration), that the relation between the covariates and outcomes differed for the groups, and that outcomes were not normally distributed. A within group comparison of the surgical group alone (time 1 versus time 2) was therefore used, and only those tests showing significant change were examined in the non-surgical group (time 1 versus time 2).

Matched pairs non-parametric Wilcoxon tests were applied and only one variable changed significantly from time 1 to time 2. Scores on the TOLT increased, suggesting reduced planning ability (table 1). A large difference in effect size[36] was found for the TOLT, as 0.39 and 0.97 for the non-surgical and surgical group, respectively. The reliable change index[37 38] was computed and a confidence interval for the TOLT was established[37]. A correction factor was added to 90% confidence intervals based on an estimated mean practice effect, which was the mean difference score for the comparison group (2.83). The 90% confidence interval was calculated at ±16.19. Five of the 13 surgical patients who completed the task on two occasions had difference scores outside the confidence interval. None of the comparison group had scores outside this interval.

DISCUSSION

This study isolated the impact of bilateral PVP to a six months' postsurgical decline in planning. It is unlikely that this was due to aging or disease progression, as the effect size (0.97) was greater than in a PD comparison group (0.39).

These results are comparable with those from a study that found that executive deficits were not apparent in a non-surgical PD group[39] and are consistent with reports of no cognitive change after PVP,[3–40] where planning was not assessed. The findings conflict with reports of a post-PVP language change,[9] which may be attributable to confounding factors such as practice or to transient sequelae.

The results fit with recent assertions that the basal ganglia and globus pallidus have a non-motor role[13–41] and with neuroimaging studies implicating the prefrontal, anterior cingulate, premotor cortex,[42–44] and globus pallidus[13] in specific planning processes. However, a striking feature of this study was that it documented limited cognitive decline after bilateral lesions using the technique described[2] and suggests that the posterior globus pallidus has a relatively limited role in cognitive function, at least in PD, isolated to motor planning efficiency.

The fact that speed of processing, language, memory, visuospatial skills, and abstract reasoning remained intact after surgery supports recent assertions that there are multiple segregated thalamocortical circuits with distinct cognitive and motor circuits.[18–47] However, the conjoint occurrence of postsurgical motor changes[2–49] and the planning changes determined here are not predicted by theories localising cognitive circuits to the anterior and intermediate globus

pallidus and motor circuits to the posterior globus pallidus.[1–46] Alternatively, within the globus pallidus, distinct elements of cognitive circuitry are anatomically dissociable, and motor planning circuits projecting to the prefrontal cortex may not be dissociable from premotor motor circuits.

Clinical research such as this has limitations including small sample sizes and difficulty matching groups, which reflect difficulties studying a relatively rare treatment with a particular selection bias. It is of course possible that a larger sample size would have detected performance decrements in other systems. As PVP is favoured for patients with medication tolerance associated with a long duration of PD, relative to other cohorts the surgical group had a long duration of disease (13 years, range 5–23). Despite this risk factor for cognitive impairment,[7] PVP was tolerated well. Future studies should incorporate matched waiting list controls to permit management of response biases such as long duration of disease or early onset. The conclusions from the present study about the processes reduced by PVP and the role of the posterior globus pallidus in PD would be strengthened by future research using functional scanning and variants of the TOLT.[13–44]

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