Asia Pacific Journal of Speech, Language and Hearing

ISSN: 1361-3286 (Print) (Online) Journal homepage: http://www.tandfonline.com/loi/yslh19

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To cite this article: Brooke-Mai Whelan, Bruce E. Murdoch, Deborah G. Theodoros, Peter Silburn & Jill Harding-Clark (2000) Towards a better understanding of the role of subcortical nuclei participation in language: the study of a case following bilateral pallidotomy, Asia Pacific Journal of Speech, Language and Hearing, 5:2, 93-111, DOI: 10.1179/136132800805576960

To link to this article: https://doi.org/10.1179/136132800805576960

Published online: 18 Jul 2013.

Towards a better understanding of the role of subcortical nuclei participation in language: the study of a case following bilateral pallidotomy

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Abstract
Pallidotomy is a neurosurgical procedure that involves the creation of discrete lesions within the globus pallidus, in an attempt to relieve the akinetic and hyperkinetic symptoms associated with Parkinson's disease (PD). Populations undergoing such procedures provide an unprecedented opportunity to test operative theoretical models of subcortical participation in language. This paper reports the effect of circumscribed lesions of the globus pallidus on linguistic functioning, in a 73-year-old female with PD who underwent a bilateral pallidotomy to control dyskinesias, dystonia and unpredictable 'on' and 'off' states. In order to monitor the effects of pallidotomy on language, a linguistic profile was compiled utilizing a battery of gross and high-level indices of language functioning in addition to an on-line measure of semantic processing, both before and after surgery. Baseline data were obtained one week prior to surgery and follow-up data were collected three months post-operatively. The results confirmed the presence of post-operative changes in language function subsequent to pallidotomy. Comparisons of pre- and post-operative language profiles revealed: (a) general language skills remained largely intact following pallidotomy; (b) post-operative fluctuations in performance on a number of measures of high-level linguistic functioning requiring complex divergent expressive language skills; (c) discrete lesions of the globus pallidus may impair performance on lexical decision tasks utilizing on-line measures of semantic processing, particularly for legal non-words (LNW) and words with few meanings (FM). These findings lend support to a hypothesized role for the globus pallidus in language, possibly via participation in a cortico-striato-pallido-thalamo-cortical loop.

Introduction

The existence of language disturbances subsequent to lesions of the globus pallidus has catalyzed the development of theoretical models of language processing incorporating this structure. Within the literature, two contemporary theories of subcortical participation in language endorse the globus pallidus to play a role in mediating linguistic processes (Crosson, 1985; Wallesch and Papagno, 1988). Crosson (1985) proposed the globus pallidus to participate in language via a cortico-striato-pallido-thalamo-cortical loop, functioning as a relay centre for messages passing from the striatum to the cortex. In essence, language formulated in the anterior language centre is relayed to the posterior language area, via the thalamus, for verification of semantic content. Once language segments have been verified for semantic accuracy, the temporoparietal cortex releases the caudate nucleus from inhibition. The caudate nucleus then serves to weaken inhibitory pallidal regulation of thalamic excitatory outputs to the anterior language centre, which, in turn, arouses the cortex to enable the generation of motor programmes for semantically verified language segments. Crosson (1985) hypothesized that lesions of the globus pallidus would result in disinhibition of the thalamus and, hence, hyperarousal of the anterior language centre. Uninhibited cortical activation was hypothesized to produce extraneous verbal output such as semantic paraphasias. Wallesch and Papagno's (1988) model also proposed the globus pallidus to participate in language processes via a cortico-striato-pallido-thalamo-cortical loop; however, the anticipated by-product of pallidal disruption was distinct from the previous model, given inherent differences in the mechanisms supporting this circuit. Wallesch and Papagno (1988) postulated that the subcortical components of the aforementioned loop constituted a 'frontal lobe system' with integrative and decision-making capabilities, rather than the regulatory function proposed in Crosson's (1985) model. Specifically, the basal ganglia system and thalamus were hypothesized to processes situational as well as goal-directed constraints and lexical information from the frontal cortex and posterior language area, and consequently to participate in the process of determining the most appropriate lexical item from a range of alternatives, for verbal production. The most appropriate lexical alternative is then released by the thalamus for processing by the frontal cortex and programming as speech. Cortical processing of selected lexical alternatives is made possible by inhibitory influences of the globus pallidus upon a thalamic gating mechanism. The most appropriate lexical alternative has an inhibitory effect on the thalamus, promoting closure of the thalamic gate, resulting in activation of the cortex and the production of the desired response (Murdoch, 1996). Cortical processing of subordinate alternatives is suppressed as a consequence of pallidal disinhibition of the thalamus, and the inhibition of cortical activity (Wallesch and Papagno, 1988). Lesions of the globus pallidus were hypothesised to result in characteristics of nonfluent language pathology (e.g. difficulty initiating speech) subsequent to disinhibition of the thalamus, opening of the thalamic gate and excitation of inhibitory cortical interneurons (Wallesch and Papagno, 1988).

The aforementioned theories of pallidal participation in language were largely derived from populations with language disturbances following vascular basal ganglia system lesions (Murdoch, 1996) and, to a much lesser extent, surgically induced pallidal lesions (Svennilson et al., 1960) using techniques that were associated with significant complications. An inability to strictly define vascular neuropathology and the use of rudimentary pallidotomy techniques that were supported by emergent neuroimaging technology have largely limited opportunities to further validate these operative models of subcortical participation in language, until now. An enhanced understanding of the pathophysiology underlying movement disorders, as well as advancements in neuroimaging, neurophysiological monitoring and neurosurgical techniques over the last 30 years, have instigated a revival of pallidotomy in the treatment of Parkinson's disease (Lozano and Lang, 1998), and an unprecedented opportunity to empirically test these language models.

A plethora of literature reports pallidotomy to be successful in ameliorating the motor symptoms associated with PD (Iacono et al., 1994; Iacono et al., 1995; Baron et al., 1996; Lang et al., 1997; Schuurman et al., 1997; Tasker et al., 1997; Kumar et al., 1998; Pfann et al., 1998; Samuel et al., 1998; Tan et al., 1998; Skalabrin et al., 1998; Kondziolka et al., 1999). In comparison, a paucity of information exists pertaining to the effects of this procedure on cognitive functioning, and among these reports, a number of studies have documented discordant post-operative cognitive profiles (Baron et al., 1996; Soukup et al., 1997). Furthermore, recent studies attempting to evaluate the effect of discrete, surgically induced pallidal lesions on cognitive functioning, including language skills, have been largely neuropsychologically based (Baron et al., 1996; Soukup et al., 1997; Troster et al., 1997; Scott et al., 1998; Lombardi et al., 2000). Reports have consistently described performance on tasks of attention, memory, concentration, visuospatial ability, executive functioning and in relation to language: confrontation naming, categorical and phonemic fluency. As is evident, in-depth linguistic analyses are lacking. Therefore, the aims of this research are to: (a) investigate the effect of surgically induced lesions of the globus pallidus on language function, utilizing a comprehensive linguistic assessment battery; (b) discuss post-operative language profiles in relation to operative theoretical models of subcortical participation in language; and (c) validate or nullify the hypothesis of a cortico-striato-pallido-thalamo-cortical loop subserving language, which promotes a functionally distinct role for the globus pallidus.

Method

Case study

L.M, a 73-year-old, right-handed female with idiopathic PD (12 years post-diagnosis) and goitre served as the subject for this case study. The subject reported that she had achieved 10 years of formal education, and that English was her first and only language. No previous history of head injury, cerebrovascular accident, cerebral tumour or abscess, coexisting neurological disease, substance abuse, psychiatric disorder, developmental language disorder or speech and/or language disturbance prior to the onset of PD was reported. LM underwent a bilateral ventromedial pallidotomy to alleviate dyskinesias, dystonia and unpredictable on/off states associated with PD.

Prior to this procedure, a neurological evaluation was conducted by a qualified neurologist. LM achieved a total score of 51/176 on the Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn and Elton, 1987). This score was achieved by summating component scores of sections 1-4 of the aforementioned scale, in the defined 'off' state (i.e. no medications overnight or one hour after waking). This rating was indicative of bilateral pathology with mild to moderate reduction in activities of daily living and mild to moderately reduced motor skills. In addition, LM achieved an overall rating of 3 on the Hoehn and Yahr Staging of Parkinson's Disease scale (HandY) (Hoehn and Yahr, 1967), indicative of a moderate to severe generalized dysfunction including a significant slowing of body movements and impaired balance on walking and standing. Pre-operative MRI noted no brain abnormalities. LM's drug regime prior to surgery consisted of the following: Parlodel 5 mg, Sinemet 100/25 mg, Sinemet 250/25 mg, Sinemet CR 200/50 mg, Inderal 40 mg and Thyroxine 100 mg. A mild dysarthria was evident at both the pre- and post- surgery assessment phases as perceived by a speech pathologist; however, this speech disturbance was not considered to adversely affect functional speech intelligibility on language measures requiring verbal responses.

An evaluation of cognitive functioning was also conducted by a neuropsychologist prior to surgery. An estimate of premorbid level of intellectual functioning placed LM within at least the average range of performance. Average to above-average performance was reported on assessments of cognitive functioning with the exception of angular judgement (mildly impaired ranked at the 22nd percentile) and facial recognition (moderately impaired ranked at <5th percentile) tasks. Executive functioning was reported as largely intact with no evidence of co-morbid dementing illness or indicators of anxiety or depression documented.

For measures of high-level language functioning where no age-appropriate normative data were available, the experimental subject's performance was compared with that of a group of seven non-neurologically impaired individuals. One standard deviation above or below the control group mean was established as the criterion for performance outside the range of normal. A conservative criterion was selected in order to account for any subtle changes in linguistic functioning post-pallidotomy. Control subjects were native speakers of English with no previous or existing history of head injury, cerebrovascular accident, cerebral tumour or abscess, substance abuse, psychiatric disorder, developmental language disorder or speech and/or language disturbance. The control subjects presented with perceptually normal speech as judged by a speech pathologist and scored within the range of normal cognitive functioning (i.e. score between 139.9-144.0) (Troster et al., 1989) on the Mattis Dementia Rating Scale (Mattis, 1988). The mean age of the control group was 63.86 years (range 50-78) and the mean level of formal education was 11.57 years (range 9-19).

Procedures

Language assessments

LM was administered a comprehensive battery of language assessments considered to be sensitive measures of both gross and high-level linguistic functioning in addition to on-line semantic processing. The assessments utilized were then subdivided into three separate test batteries for analysis purposes. LM was administered the test battery one month prior to bilateral pallidotomy and three months after surgery, within perceived 'on' periods (i.e. when optimally medicated). Testing was undertaken in a quiet, distraction-free environment according to standardized instructions and was conducted over two 2-hour sessions, in order to compensate for fatigue. The assessment battery incorporated tasks that were primarily dependent on oral language abilities; however, tasks dependent on written expression and reading comprehension skills were also included.

Battery 1 incorporated measures of gross language function including the Neurosensory Centre Comprehensive Examination of Aphasia (NCCEA) (Spreen and Benton, 1969) and the Boston Naming Test (Kaplan et al., 1983) including an analysis of error types derived from those methods utilized by LeDorze and Nespoulous (1989), Smith et al. (1989), LaBarge et al. (1992), and Chenery et al. (1996). Battery 2 contained measures of high-level linguistic functioning including the Test of Language Competence Expanded-Edition (TLC-E) (Wiig and Secord, 1989), The Word Test-Revised (TWT-R) (Huisingh et al., 1990), a subtest of the Test of Word Knowledge (TOWK) (Wiig and Secord, 1992), the Wiig-Semel Test of Linguistic Concepts (WSTLC) (Wiig and Semel, 1974), and the animal fluency subtest of the Western Aphasia Battery (WAB) (Kertesz, 1982). Battery 3 consisted of a lexical decision task incorporating legal non-words and real-word stimuli classified by number of meanings and meaning relatedness (Azuma and Van Orden, 1997).

Results

Post-operative neurological and neuropsychological profiles

A post-operative neurological evaluation, conducted by a neurologist, revealed a total score of 31/176 on the UPDRS. This score was indicative of mild improvements across a number of activities of daily living and general motor skills. Despite these overall improvements, a mild decline in LM's swallowing function and a moderate to severe decline in speech intelligibility and legibility of handwriting were reported. LM's overall HandY rating remained the same following pallidotomy. A post-operative MRI, taken one day following surgery, reported bilateral pallidotomy lesions measuring 1 cm in diameter in addition to possible small bilateral areas of associated haemorrhage and oedema extending into the posterior rim of the internal capsule (Figure 1). LM's post-operative drug regime included the following: Solprin 300 mg,

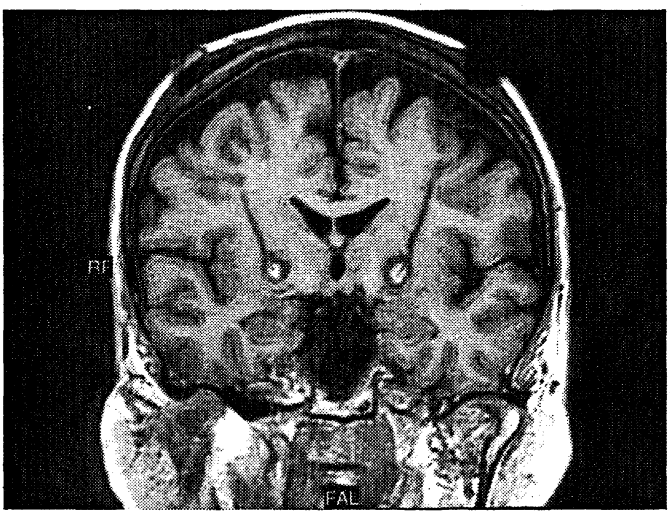

Figure 1: *LM's post-operative magnetic resonance image showing bilateral pallidotomy lesions measuring 1 cm in diameter and possible small bilateral areas of associated haemorrhage and oedema extending into the posterior rim of the internal capsule.*

Inderal 40 mg, Pravochol 40 mg, Probanthine 15 mg, Parlodel 2.5 mg, Sinemet 250/25 mg, Sinemet CR 200/50 mg, Madopar 200/50 mg.

Post-operative neuropsychological assessment conducted by a neuropsychologist indicated that executive functioning remained largely unaltered subsequent to pallidotomy; however, fluctuations in performance were observed across a number of measures of cognitive functioning. Mild declines on tasks of non-verbal reasoning and abstraction (50-75th percentile), focused attention (16th percentile), working memory and delayed recognition of verbal information were documented. In addition, a moderate decline in angular judgement skills (4th percentile) and a severe decline in the ability to retain verbal information were noted. Psychomotor speed was reportedly unchanged following pallidotomy but mild improvements in immediate attention span were documented. It was reported that post-operative declines in performance may have been partially attributable to demonstrated fatigue during follow-up assessment.

Language profile

Battery 1: Gross measures of language function

A general comparison of pre- and post-operative NCCEA language profiles revealed an overall decline in performance following pallidotomy (Table 1). With the exception of performance on phonemic fluency (PF) and sentence construction (SC) subtests, however, general pre- and post-operative language skills were largely intact (see Table 1), consistent with Spreen and Benton's (1969) classification of a non-aphasic performance to include scores ranked at or above the 40th percentile on a profile of normal adult performance (Form A).

LM's PF scores were ranked below the 2nd percentile on both pre- and post-operative language profiles, with a decline following pallidotomy that represented one of the subject's largest post-operative decrements in performance on this assessment. In contrast, a subtle improvement was evidenced in SC abilities post-operatively; however, both pre- and post-operative performances on this subtest fell below the range of normal. Pre-operative performance on this task was ranked at the 12th percentile (indicating a severe impairment), whilst post-operative ranking increased to the 26th percentile, suggesting only a mild deficit.

Despite a mild post-operative decline in performance on the BNT, both pre- and post-surgical scores achieved fell within the normal range (see Table 1). An analysis of error types produced revealed: semantic errors (71.43% pre-operatively; 87.5% post-operatively), no relationship errors (14.29% pre-operatively; 12.5% post-operatively), phonological errors (14.29% pre-operatively; 0% post-operatively).

Battery 2: Measures of high-level linguistic functioning

A general post-operative decline in performance on the TLC-E was observed; however, overall performance on this test was within the normal range, both prior to and following surgery (Table 2). Of note was that pre-operative scores greater than one standard deviation below the control group mean on the FL and RWP subtests increased following pallidotomy, to within the range of normal. LM demonstrated insignificant declines, relative to the control group, on additional subtests within this assessment following pallidotomy (see Table 2), contributing to the overall decline in performance observed.

Table 1: *Comparison of subject's pre- and post-pallidotomy performance on measures of gross language function with normal performance*

Language measure	Maximum score	Pre-pallidotomy results	Results 3 months post-pallidotomy	Normative data
NCCEA	(+)	551	546	(Spreen, Benton, 1969) Corrected Scores (Profile A)
VN	(16)	16	16	15–16
DU	(16)	16	16	16
TNR	(16)	16	16	16
TNL	(16)	16	15	15–16
SR	(27)	23	23	16–27
RPD	(18)	10	12	7–18
RVD	(18)	12	8	6–18
PF	(+)	*38	*34	>/=44
SC	(25)	*23	*24	25
IN	(16)	16	16	16
TT	(163)	162	163	161–163
ORN	(20)	20	20	20
ORS	(16)	16	16	16
RNM	(10)	10	10	10
RSM	(17)	17	17	17
VGN	(8)	8	8	8
WN	(28)	24	24	23–28
WD	(15)	14	14	13–15
WC	(13)	12	12	11–13
AN	(104)	102	102	99–104
BNT				(Worrall et al., 1995)
	(60)	57 (↑0.78)	53 (↑0.16)	M SD 52 6.4

Notes: NCCEA = Neurosensory Centre Comprehensive Examination of Aphasia total score; VN = Visual Naming; DU = Description of Use; TNR = Tactile Naming (right); TNL = Tactile Naming (left); SR = Sentence Repetition; RPD = Repetition of Digits; RVD = Reversal of Digits; PF = Phonemic Fluency; SC = Sentence Construction; IN = Identification by Name; TT = Token Test; ORN = Oral Reading (names); ORS = Oral Reading (sentences); RNM = Reading Names for Meaning; RSM = Reading Sentences for Meaning; VGN = Visual Graphic Naming; WN = Writing Names; WD = Writing to Dictation; WC = Writing (copying); AN = Articulation; BNT = Boston Naming Test; (+)= no restriction on maximum score; (↑) = number of standard deviations above control group mean; *= performance outside the range of normal.

LM also demonstrated a decrease in overall performance on the TWT-R from pre- to post-operative assessment phases. Prior to pallidotomy, LM achieved a total TWT-R score within the normal range (see Table 2); however, following pallidotomy LM's total score decreased more than one standard deviation below the

Table 2: *Comparison of subject's pre- and post-pallidotomy performance on measures of high-level linguistic functioning with normal performance*

Language measure	Maximum raw score	Pre-pallidotomy results	Results 3 months post-pallidotomy	Normal performance (*n* = 7) Mean raw score and standard deviation
		Raw score ↑↓ SD	Raw score ↑↓SD	M SD
TLC-E	*(221)*	*174 ↑0.06*	*167 ↓0.34*	*173 (17.8)*
AS	(39)	39 ↑0.99	33 ↑0.25	31 (8.1)
MI	(36)	33 ↑0.51	30 ↓0.26	31 (3.9)
RS	(78)	72 ↑0.47	66 ↓0.93	70 (4.3)
FL	(36)	**29* ↓1.07**	33 ↑0.36	32 (2.8)
RWP	(32)	**1* ↓1.36**	5 ↓0.68	9 (5.9)
TWT-R	*(90)*	*86 0.00*	***82* ↓1.21***	*86 (3.3)*
ASS	(15)	**12* ↓1.00**	13 0.00	13 (1.0)
SY	(15)	15 ↑0.91	14 0.00	14 (1.1)
SA	(15)	**14* ↓1.25**	**14* ↓1.25**	15 (0.8)
AN	(15)	15 0.00	15 0.00	15 (0.4)
DF	(15)	**15* ↑1.00**	**13* ↓1.00**	14 (1.0)
MD	(15)	15 0.00	**13* ↓2.50**	15 (0.8)
TOWK				
CAT	*(42)*	*40 0.00*	*41 ↑0.50*	*40 (2.0)*
WSTLC	*(50)*	***49* ↑1.25***	***50* ↑2.50***	*48 (0.8)*
CP	(10)	10 0.00	10 0.00	10 (0.4)
PS	(10)	**10* ↑1.00**	**10* ↑1.00**	9 (1.0)
TP	(10)	10 0.00	10 0.00	10 (0.4)
SP	(10)	9 0.00	**10* ↑2.00**	9 (0.5)
FL	(10)	10 0.00	10 0.00	10 (0.0)
				(Read, 1987)
SF (animals)	*(+)*	*20 ↑0.91*	*12 ↓0.91*	*16 (4.4)*

Notes: TLC-E = Test of Language Competence -Expanded total score; AS = Ambiguous Sentences; MI = Making Inference; RS = Recreating Sentences; FL = Figurative Language; RWP = Remembering Word Pairs; TWT-R = The Word Test-Revised total score; ASS = Associations; SY = Synonyms; SA = Semantic Absurdities; AN = Antonyms; DF = Definitions; MD = Multiple Definitions; TOWK = Test of Word Knowledge; CAT = Conjunctions and Transitions; WSTLC = Wiig-Semel Test of Linguistic Concepts; CP = Comparative; PS = Passive; TP = Temporal; SP = Spatial; FL = Familial; SF = Semantic Fluency; ↓↑ SD = number of standard deviations below or above control group mean; * = performance outside the range of normal.

control-group mean. This overall decline in performance was attributed to significant post-operative reductions in scores achieved on the definitions (DF) and multiple definitions (MD) subtests, from within the range of normal prior to surgery to below average following pallidotomy (see Table 2). Of additional note, performance on the semantic absurdities (SA) subtest was stable at more than one standard deviation below the control mean both pre- and post-operatively, and a post-operative improvement in performance on the associations (ASS) subtest was observed, to within the normal range (see Table 2).

LM demonstrated an overall superior performance to the control group on the WSTLC at both pre- and post-operative test phases, with a significant increase in total score observed following pallidotomy (see Table 2). The general post-operative improvement in performance observed was attributed to an above-average score achieved on the spatial relations subtest (see Table 2). Of additional note, pre- and post-operative scores achieved on the passive relationships subtest remained stable and above average across testing phases (see Table 2).

Pre- and post-operative scores on the Conjunctions and Transitions subtest of TOWK fell within the normal average (see Table 2). In addition, LM's semantic fluency (SF) scores were considered to be within the range of normal both prior to and following pallidotomy, despite a post-operative decline in performance (see Table 2).

Battery 3: Semantic processing

Pre-operative lexical decision data were not collected, therefore post-operative performance has been discussed in isolation, relative to normal performance.

Accuracy

LM achieved a total accuracy score greater than 11 standard deviations below the control group mean on the lexical decision task. In relation to stimulus type, the accuracy of LM's lexical decisions pertaining to words with many meanings (and high or low degrees of relatedness between meanings) (i.e. M/H and M/L, respectively) was consistent with the normal average, however, the accuracy of decisions pertaining to words with few meanings (and high or low degrees of relatedness between meanings) (i.e. F/H and F/L, respectively), fell well below the control group mean, where no variance in performance was demonstrated (Table 3). In addition, the accuracy of lexical decisions pertaining to legal non-words (LNW) fell more than nine standard deviations below the normal average.

Reaction time

In general, the mean lexical decision reaction times for the control group were faster for all stimulus items than those of the experimental control (see Table 4). Reaction times for each of the classified word types fell within one standard deviation of the normal average, with the exception of F/H words which were significantly higher than the normal average (see Table 4). Despite LM's overall slower performance and above-average reaction times to F/H words, similar response patterns were generally demonstrated for the same stimulus categories by both the experimental subject and the control group. Fastest responses were recorded for M/L words, followed by F/L words. Slowest responses were recorded for non-words. The only inconsistency observed was in relation to differential reaction rates for F/H and M/H words. The control group responded faster to F/H words than to M/H words; however, LM responded in a converse fashion (see Table 4).

Table 3: *Post-operative accuracy of lexical decisions in comparison with normal performance*

Stimulus type	Maximum raw score	Pre-pallidotomy performance	3 months post-pallidotomy: number of correct responses Raw score ↓↑SD	Normal performance (*n* = 7) Mean number of correct responses and standard deviations M SD
LDT	(80)	Not available	**60* ↓ 11.88**	79 (1.6)
F/H	(10)	Not available	**8* –**	10 (0.0)
M/H	(10)	Not available	10 0.00	10 (0.0)
F/L	(10)	Not available	**7* –**	10 (0.0)
M/L	(10)	Not available	10 0.00	10 (0.4)
LNW	(40)	Not available	**25* ↓ 9.33**	39 (1.5)

Notes: LDT = Lexical decision total correct; F/H = Few/ High total correct; M/H = Many/High total correct; F/L = Few/Low total correct; M/L = Many/Low total correct; LNW= legal non-words total correct; ↑↓ SD = number of standard deviations above or below group mean; - = no variance in control group performance; *=performance outside normal range.

Table 4: *Mean reaction times for lexical decision stimuli with multiple meanings and varying degrees of relatedness among meanings*

Stimulus type	Post-pallidotomy reaction time (msec) M ↑↓ SD	Normative performance (*n* = 7) Mean reaction time and standard deviation M SD
LDTRT	1317.74 ↑ 0.82	990.55 (396.64)
F/HRT	***1326.10 ↑ 1.64**	902.39 (257.93)
F/LRT	974.10 ↑ 0.33	880.09 (280.94)
M/HRT	1097.40 ↑ 0.63	908.49 (301.82)
M/LRT	926.10 ↑ 0.18	878.97 (265.42)
LNWRT	1554.55 ↑ 0.99	1088.62 (468.84)

Notes: LDTRT = Lexical Decision Total Reaction Time; F/HRT = Few/High Reaction Time; F/LRT = Few/Low Reaction Time; M/HRT = Many/High Reaction Time; M/LRT = Many/Low Reaction Time; LNWRT = Legal Non-Word Reaction Time; (msec) = milliseconds; ↑↓ SD = number of standard deviations above or below control group mean;*= below average performance.

Discussion

The results of this study support the hypothesis of a cortico-striato-pallido-thalamo-cortical loop subserving language function (Crosson, 1985; Wallesch and Papagno, 1988), and indeed confirm that the globus pallidus has a role to play in mediating linguistic processes. The results revealed that subsequent to pallidotomy, gross language skills remained relatively intact; however, fluctuations in performance across a number of high-level linguistic tasks were observed. When compared with a control group, the experimental subject also demonstrated reduced accuracy in conducting lexical decisions pertaining to legal non-words and words with few meanings following pallidotomy, in addition to overall longer mean reaction times for all stimuli. The post-operative changes in language profiles observed were attributed to disruption of the aforementioned cortico-subcortical-cortical loop, subsequent to the surgical generation of discrete lesions within the globus pallidus.

Battery 1: Gross language function

LM's performance on gross measures of language function was relatively intact following pallidotomy, with the exception of scores achieved on subtests PF and SC of the NCCEA. Of note, pre-operative scores achieved for each of these subtests were also below average, suggesting that pre-existing subcortical pathology may have negatively influenced performance on these tasks. Reduced scores on the SC task were attributed to the use of time restrictions in the administration of this subtest. Slow response initiation was observed during LM's pre-operative performance on this task and may have represented a form of linguistic akinesia. Indeed, Crosson (1992) hypothesized that a form of language akinesia may mirror manifestations of physical akinetic symptoms. This phenomenon was claimed to be the result of impaired language-release mechanisms, presenting as a deficit in initiating and maintaining the production of language (Crosson, 1985). Reduced post-operative performance was attributed to an inability to accurately and efficiently combine specified word forms into a syntactic structure. Despite the production of syntactically correct sentences post-operatively, the subject demonstrated a tendency to utilize word forms that were a close approximation to the target stimulus (e.g. drove versus drive; walked versus walk). This behaviour may be best interpreted in terms of Wallesch and Papagno's (1988) model, as an inability to efficiently integrate specified linguistic information and to apply and monitor the application of goal-directed rules in the production of verbal output. Lesions of the globus pallidus and the subsequent disruption of subcortical linguistic integration and rule application processes may manifest as sentences which contain linguistic units that deviate from the intended target, in terms of morphosyntactic structure, and remain uncorrected unless prompted. Despite the inclusion of a PF subtest within the NCCEA, this subtest has been routinely incorporated into cognitive assessment batteries that aim to evaluate high-level executive functions of the frontal lobe. As such, these results are discussed further below, relative to high-level linguistic abilities.

LM demonstrated a post-operative decline in confrontation-naming abilities, despite pre- and post-operative scores both falling within the range of normal. This decline in performance was associated with an increase in the number of semantic errors produced, supporting Crosson's (1985) theory that lesions of the globus pallidus would serve to disinhibit the thalamus, thereby increasing cortical activity to produce extraneous verbal output, such as semantic paraphasias. Significant changes in post-operative confrontation naming abilities have not been previously reported (Masterman et al., 1998; Scott et al., 1998), yet among these reports detailed error analyses of responses produced have not been conducted. As such, previous studies have failed to delineate any changes in lexical retrieval mechanisms subsequent to pallidotomy, which is an issue worthy of further consideration.

Battery 2: High-level linguistic functioning
The TWT-R, TLC-E and WSTLC, in addition to letter-cued fluency (PF), represented the measures of high-level linguistic functioning most sensitive to changes in complex language following pallidotomy. Average to above-average pre-operative performances on the MD and DF subtests of the TWT-R declined post-operatively to below the range of normal, indicating that lesions of the globus pallidus may impact upon the ability to formulate complex divergent language. Post-operatively, a number of LM's responses on the DF subtest were lacking essential semantic elements. For example, in defining the verb *scribble*, requiring the essential elements of write/colour/draw + without order/meaning, LM responded *used to take notes*. These results suggested a deficit in recognizing and describing key semantic attributes of a target word (Huisingh et al., 1990). Semantically inadequate definitions in terms of critical attributes, such as circumlocutory responses, support the hypothesis of Crosson (1985), that lesions of the globus pallidus will result in extraneous verbal output, as a consequence of thalamic disinhibition and hyperactivation of the anterior language area. In addition, post-operative errors produced on the MD task involved stimulus-bound responses (Huisingh et al., 1990) and definition references not indexed within the scoring criteria. Stimulus-bound responses (e.g. for the word *park*, LM provided the definitions *parking a car* and *to park yourself somewhere*) fulfilled only one definition reference criterion, *to leave temporarily*, as opposed to a minimum of at least two semantically distinct criteria (including *land* or *car gear*). Inflexibility in the production of definition references on this task may suggest a reduced capacity to accurately select or gate multiple competing definitions for expression following pallidotomy. As a result, the same definition reference is selected more than once for production. These results are in line with Wallesch and Papagno's (1988) model, suggesting that the basal ganglia system and thalamus integrate cortically generated situational and goal-directed constraints in addition to lexical information, and determine the most appropriate lexical alternative from a range of alternatives for production as speech. Lesions of the globus pallidus may disrupt thalamic gating mechanisms, resulting in disinhibited thalamic excitation of inhibitory cortical interneurons, preventing the processing of appropriate competing alternatives. It has been observed that lesions of the basal ganglia system typically impair performance on tasks where degrees of freedom, in relation to possible responses, are large (Wallesch and Papagno, 1988). On such tasks, syntax is preserved yet semantic content may be inadequate (Wallesch and Papagno, 1988), such as the replication of previously selected definition references on a multiple meanings task. The production of unindexed definition references (e.g. for the word *down*, one of LM's responses included *hair on your face*), also supports the

hypothesis of disturbed lexical selection mechanisms following pallidotomy, whereby subordinate alternatives are gated for verbal production.

LM's performance on verbal fluency subtests revealed post-operative declines on both phonemic and semantic fluency tasks. Pre-operative performance on the PF subtest was below normal, with LM demonstrating a further decline post-operatively. In contrast, LM's semantic fluency score was within the range of normal both pre- and post-operatively; however, a decline in performance was also evident following pallidotomy. These results suggested a post-operative impairment at the level of the phonological output lexicon and perhaps a reduction in semantic drive (Caplan, 1994). Murdoch (1996), in line with Wallesch and Papagno (1988), stated that lexical content in the production of responses on verbal fluency tasks would also involve many degrees of freedom, where a large number of appropriate responses generated by the cortex compete with each other for selection by the striatum and subsequent release to the anterior language centre via thalamic gating mechanisms. Consistent with the results achieved on the DF and MD subtests in the present study, where task responses were unrestricted, this postulate would explain the post-operative reduction in performance on both PF and SF tasks as an impaired or functionally reduced lexical selection mechanism, especially for words specified by a particular phonological form. Pallidotomy may serve to disrupt thalamic gating mechanisms resulting in the inefficient release of competing alternatives for frontal processing, and the inhibition of cortical activity. The results of the current study also suggest that a deficit in the ability to retrieve phonologically constrained word forms was evident prior to pallidotomy in this subject. Previous studies have reported variable results in relation to the performance of people with PD on PF tasks. A number of studies have reported reduced PF scores in people with PD (Beatty and Monson, 1989; Epker et al., 1999), while others report performances within the normal range (Beatty and Monson, 1989; Caltagirone et al., 1989; Raskin et al., 1992; Auriacombe et al., 1993; Lewis et al., 1998). The variation in results reported may be attributed to the possible existence of heterogeneous cognitive profiles across subject groups and the premise that as cognition declines in PD, linguistic deficits may manifest across a wide range of language tasks (Lewis et al., 1998). Indeed, Beatty and Monson's (1989) study identified PD subgroups relative to performance on the BNT. PD subjects with impaired naming abilities performed below normal on a PF task relative to controls; however, PD subjects with normal naming abilities performed within the range of normal on the same task. In addition, a number of distinct criterion levels were utilized to classify normal performance across studies, perhaps contributing to the variable results reported. Furthermore, surgically induced lesioning of the globus pallidus contributed to an exacerbation of the aforementioned lexical selection deficit for phonologically constrained word forms, and also a decline in performance on a task of category cued fluency. In relation to other studies, reductions in PF and SF scores following pallidotomy have been reported. Declines in PF have been reported following unilateral pallidotomy of the left hemisphere (Trepanier et al., 1998; Lombardi et al., 2000) in addition to bilateral pallidotomy (Scott et al., 1998), but not subsequent to unilateral pallidal lesions within the right hemisphere (Lombardi et al., 2000). Declines in semantic fluency scores have also been reported following unilateral (Masterman et al., 1998; Scott et al., 1998) and bilateral (Scott et al., 1998) posteroventral pallidotomy, with no identifiable interhemispheric effects (Lombardi et al., 2000). Of note, however, more anteromedially placed lesions were documented to produce declines in performance in the production of words that were related categorically, and posterolaterally positioned lesions to affect an increase in performance on this task (Lombardi et al., 2000).

In contrast, post-operative improvements in performance were observed on the FL and RWP subtests of the TLC-E, the ASS subtest of the TWT-R and on the SP component of the WSTLC. An increase in the total score achieved for RWP may have been closely related to the mild post-operative improvement in immediate attention span reported in the post-surgical neuropsychological evaluation, rather than an enhancement in linguistic functioning. The increase in scores achieved on the FL subtest of the TLC-E and the ASS subtest of the TWT-R, however, was highly inconsistent with the results achieved on other complex expressive language tasks within the present study. LM was expected to perform below the control group mean on these tasks, consistent with her performance on other tasks where the degrees of freedom for lexical content pertaining to potential responses were great. The FL and ASS subtests involved complex divergent expressive language tasks, requiring the interpretation of metaphorical speech and the explanation of differences between category members in terms of critical semantic features, where degrees of freedom in relation to possible responses were unrestricted. LM, however, achieved normal post-operative scores on these tasks, her performance improving from below the range of normal prior to pallidotomy to within normal following surgery (see Table 2). In addition, required responses on the WSTLC (yes/no) involved a restricted number of degrees of freedom and, consequently, reduced competition for selection between potential lexical alternatives. As such, performance was not expected to change significantly on this task between pre- and post-operative test phases. Despite this prediction, however, LM demonstrated an increase in total score achieved on the WSTLC following surgery.

LM's performance on the SA subtest of the TWT-R and the PS subtest of the WSTLC remained stable across pre- and post- operative test phases. Pre- and post-operative scores on the SA subtest that were stable yet reduced, relative to normal controls, lent support to both Crosson's (1985) and Wallesch and Papagno's (1988) models of subcortical participation in language. Despite recognizing semantic incongruities within absurd statements, LM demonstrated an inability to consistently repair incongruities by evaluating and contrasting the critical semantic features of discordant words (Huisingh et al., 1990). Explanatory and negated responses lacking critical semantic features were observed inconsistently. These extraneous responses may have been the result of an impaired response-release mechanism for semantically verified language (Crosson, 1985) or a defective lexical selection mechanism that resulted in the thalamic gating of semantically subordinate or rudimentary responses for frontal processing, on tasks where potential responses entailed large degrees of freedom (Wallesch and Papagno, 1988). Reports of PD performance on semantic absurdity tasks have not been previously reported in studies of high-level linguistic functioning in this population (Lewis et al., 1998). Despite an inability to draw comparisons from previous research, the results achieved in the current study may represent the existence of dysfunctional cortico-subcortical-cortical circuitry in populations with pre-existing subcortical neuropathology that remains similarly impaired following pallidotomy. In addition, stable yet enhanced performance on the PS subtest was also acceptable in relation to contemporary models of subcortical participation in language. Required responses for this task involved limited degrees of freedom and, as such, were not hypothesized to change significantly subsequent to pallidotomy.

The variation in post-operative performance observed across high-level language tasks indicates that disruption to the hypothesized cortico-striato-pallido-thalamo-cortical loop alters the way in which complex language is understood and formulated, lending support to models of subcortical participation in language (Crosson, 1985; Wallesch and Papagno, 1988). Despite the documented changes in high-level linguistic performance following pallidotomy, the inconsistencies observed complicate the delineation of the mechanism underlying these post-operative alterations in function. Scott et al. (1998) also reported significant individual variation in post-pallidotomy cognitive gains and deficits, despite minimal post-operative alterations in cognitive functioning within a group of 20 pallidotomy patients. Post-operative fluctuations in performance within the current study may have been indicative of normal variability between assessment phases, possible improvements in motivation and attention subsequent to pallidotomy (Scott et al., 1998), cyclical alterations in medication levels throughout assessment sessions, which served to influence cognitive functioning (Gotham et al., 1988; Saint-Cyr et al., 1993) or may in fact negate the hypothesis of a specific linguistic function for the globus pallidus. In the event of the globus pallidus undertaking a specialized linguistic function, similar levels of impairment were predicted following pallidotomy for task responses that potentially involved large degrees of freedom, such as complex divergent expressive language tasks. The post-operative inconsistencies in performance (i.e. decrements and improvements) observed on comparable linguistic tasks in this study may be more accurately interpreted as the result of disruption to, or the disorganization of, the regulation of language processes along reciprocal cortical-subcortical loops (Crosson, 1985; Wallesch and Papagno, 1988). The precise mechanism underlying the subcortical-cortical integration and regulation of lexical information, however, remains largely misunderstood, further complicating the interpretation of results. The capacity for lexical alternatives to also be gated via thalamo-frontal and fronto-thalamic circuits which bypass the basal ganglia system, in addition to the assumption of functional plasticity within a disordered neural network (Wallesch and Papagno, 1988), may explain in part some of the post-operative inconsistencies in performance observed in a subject with long-standing basal ganglia pathology. In order to further validate these findings future research requires the compilation of linguistic profiles for larger subject numbers.

Despite the above limitations, defective or reduced lexical selection mechanisms were identified in this single case, following pallidotomy. These results directed the current study to investigate further the patency of the lexical-semantic system subsequent to lesions of the globus pallidus, utilizing a measure of on-line semantic processing.

Battery 3: Semantic processing

Deficits in lexical access have been identified in patients with PD who demonstrate normal performances on the BNT (Beatty and Monson, 1989). On-line measures of semantic processing such as lexical decision tasks may better serve to evaluate lexical access integrity in people with subcortical pathology. Cognitive deterioration in PD has been associated with mental inflexibility, involving a deficit in shifting mental set or shift aptitude (Levin et al., 1992). In essence, PD patients typically demonstrate impairments on tasks that require the switching of attention from one perceptual dimension to another (Gauntlett-Gilbert et al., 1999). It was hypothesized, therefore, that people with PD, particularly those with surgically induced lesions of the subcortical region, would demonstrate difficulty conducting lexical decisions pertaining to stimuli occupying distinct perceptual dimensions, such as non-words and words with a variable number of meanings and degrees of relatedness between meanings. Pre-operative lexical decision data were unavailable for this case, therefore the status of lexical access on this task prior to surgery has not been discussed. Post-operative performance, however, revealed reduced accuracy for lexical decisions pertaining to LNW and FM words in relation to a control group. In addition, LM demonstrated slower reaction times for all stimuli relative to the controls, and within stimuli classifications demonstrated considerably faster reaction times for words with many meanings (MM) in comparison with FM words, relative to the control group. Relatedness effects were not demonstrated by the experimental or control subjects. Despite considerable differences in performance between the control group and experimental subject on a number of parameters within this task, an inability to compare post-pallidotomy results with pre-surgical baseline data limits the findings of this study. Previous research has reported deficient lexical access strategies in non-surgical PD patents, which manifest as slower reaction times and reduced accuracy of lexical decisions for words in neutral conditions (McDonald et al., 1996). The potential for pre-surgical lexical access deficits attributed to chronic basal ganglia pathology, therefore, must also be considered in the current case, with pallidotomy perhaps contributing to an exacerbation of these deficits.

Azuma and Van Orden (1997) proposed that word recognition in lexical decision tasks occurs when the orthographic, phonological and semantic representations of a word cohere, or these features are strongly correlated. Non-words were hypothesized never to achieve absolute coherence and, as such, are not recognized as real words (Lewenstein and Nowak, 1989). In the present study, LM identified a number of LNW as real words, suggesting defective coherence mechanisms. Azuma and Van Orden (1997) postulated that LNW are not capable of activating semantic representations and, as such, lexical decisions may be exclusively directed by spelling familiarity or phonology (Besner et al., 1984). LM demonstrated artificial coherence within the present study, suggesting an inability to base lexical decisions pertaining to LNW exclusively on orthographic or phonological forms. Consequently, inaccurate semantic representations may have been activated resulting in the classification of LNW as real words. In addition, LM inconsistently classified FM words as non-words, further supporting the hypothesis of defective coherence mechanisms. According to spreading activation theory, words with many meanings have a probability advantage for nodal activation (Rubenstein et al., 1970) and hence, typically produce faster reaction times when compared with FM words (Rubenstein et al., 1970). Relative to the control group, LM demonstrated considerably faster reaction times for MM words in comparison with FM words. The reduced accuracy of lexical decisions pertaining to FM words and slower mean reaction times recorded to process these stimuli again suggested inefficient coherence mechanisms in this subject. It was postulated that lexical entries for a number of FM words failed to reach a recognition threshold via the correlation of orthographic, phonological and semantic representations and, as such, were classified as non-words. In relation to the models of subcortical participation in language previously discussed, these results further support evidence of a lexical-semantic deficit following pallidotomy, in relation to both the formulation of complex expressive language and the semantic processing of orthographic word forms. The effect of pallidotomy on semantic processing cannot be exclusively defined, however, until future research compares pre- and post-surgical data on this task, within a larger subject group.

Conclusion

Based on the results of this single case study, it may be concluded that fluctuations in cognitive functioning following pallidotomy extend into the domain of high-level linguistics and semantic processing. The results of this study revealed evidence of deficient lexical selection mechanisms on complex divergent expressive language tasks subsequent to pallidotomy, in addition to inefficient lexical access in the semantic processing of orthographic word forms. These post-operative linguistic impairments lend support to a hypothesized role for the globus pallidus in language, which is in all probability performed via participation in a cortico-striato-pallido-thalamo-cortical loop (Crosson, 1985; Wallesch and Papagno, 1988). Despite these endeavours, however, the results of the present study will remain unsubstantiated until comprehensive pre- and post-operative linguistic profiles are compiled for larger subject numbers.

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