Basal Ganglia Activation in Parkinson's Patients During a Motor Switching Task

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Introduction

Parkinson's disease is characterized pathologically by the degeneration of dopaminergic neurons in the substantia nigra. While several studies have examined the downstream cortical effects of the dysfunctional basal ganglia (BG) –thalamo-cortical loop resulting from this loss of nigral neurons, few have focused on the BG itself. Pre-existing evidence obtained with PET suggests an abnormality of basal ganglia function in Parkinson's disease (1)(2), but few Parkinson's studies to date have exploited the superior temporal and spatial resolution offered by fMRI. The present study compares BG functional activation in Parkinson's patients with that of age-matched controls using fMRI in conjunction with a motor activation paradigm known to elicit BG activation in healthy controls (3).

Methods

The paradigm consisted of 14 alternating epochs of rest and unilateral movement, each 30 seconds long. The movement consisted of finger-tapping alternating with toe-wiggling. Subjects were instructed to alternate between tapping their index finger against their thumb 4 times over two seconds (i.e. 2Hz frequency) and wiggling their big toe - also 4 times over 2 seconds. An external pacing tone played every 2 seconds notified the subject when to switch from toe-wiggle to finger tap and vice versa, and helped the subject pace movements at the desired 2 Hz frequency. The experiment was conducted twice for each subject, once for each side of the body. To minimize the effects of practice on task performance, half of the subjects conducted the left experiment first, the others the right one first. Participants included 6 mildly affected Parkinson's patients (age 61±12 years), off medication for ~12 hours, and 7 healthy controls (age 56±5 years). All subjects were right handed.

The study was conducted using a Siemens Sonata 1.5T scanner. One hundred and forty volumes were collected in each unilateral movement session using a single-shot, multislice, EPI sequence. Each volume consisted of twenty-four 4mm slices, with 1mm inter-slice spacing. The echo time and repetition time were 50 and 3000ms respectively. Other parameters used included a 22x22 cm FOV, a 128x128 matrix, a 90° flip angle and a bandwidth of 1628 Hz/Pixel. The first two images were discarded to allow for spin saturation effects. Subject motion was minimized by using head restraints placed about the subjects' ears.

The functional MRI data were pre-processed and analyzed using SPM99 software. Images were realigned to the first volume collected, normalized to a common stereotactic space and spatially smoothed with a 4mm FWHM isotropic Gaussian kernel. For the sample size of the present study, fixed effects analysis was more appropriate than a random effects analysis. Six motion (3 rotation and 3 translation) regressors characterizing each subject's movement during the scanning session were included as nuisance covariates. Analysis was restricted to the caudate nucleus, putamen and pallidum permitting small volume corrected p-values.

Results

Clear differences in basal ganglia activation were observed between the two subject groups. Control subjects activated the basal ganglia to a greater degree in both the left and right movement sessions – the right caudate body during left movements and the right caudate tail, right medial globus pallidus, and left putamen during right movements (Figure 1 (in colour), Table 1). In contrast, Parkinson's patients did not show any significantly greater basal ganglia activity than controls during either right or left movements. Subject motion was comparable across subjects. The average absolute displacement of any scan from the reference position in the x, y and z directions was: 0.18±0.21mm vs. 0.48±0.63mm, 1.24±0.70mm vs. 1.34±0.82mm, and 0.22±0.20mm vs. 0.72±0.86mm, for controls vs. patients respectively.

Discussion

In previous studies with Parkinson's patients, it was shown that the right caudate nucleus was active in controls but not in Parkinson's patients during a planning task (1) while the same was true for the contralateral putamen during movement selection (2). The present study confirms the previous findings of impaired activation within the basal ganglia of Parkinson's patients studied when off medication for 12 hours. The caudate nucleus and putamen activation which we observed may result from attention to the overlearned task and the inherent movement selection of the switching process (4). Given that task performance was similar in both subject groups we suggest that Parkinson's patients recruit alternate functional circuitry in preference to the dysfunctional basal ganglia-thalamo-cortical system.

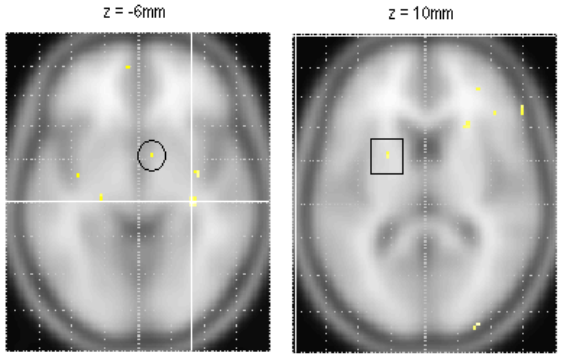

Figure 1. The R caudate tail (cross-hairs), R medial GP (circle) and the L Putamen (square) were significantly more active in Control subjects than in Parkinson's patients during right-sided movements (group comparison data shown).

Table 1. Basal Ganglia Clusters Displaying Significantly Greater Activation in Healthy Controls than in Parkinson's Patients (Small Volume Corrected, p = 0.05)

Task	Region	x	y	z	T-statistic
Left Movements					
	R Caudate Body	12	14	16	4.40
Right Movements					
	R Caudate Tail	32	-24	-4	6.37
	R Medial Globus Pallidus	8	2	-2	5.33
	L Putamen	-22	4	9	4.88

References

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