

Differential brain activation pattern for a simple motor task in Parkinsonism: An fMRI Study

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Introduction: The striatal dopamine depletion in the substantia nigra and basal ganglia disrupts the cortico-striatal balance leading to motor deficit in Parkinsonism namely, Parkinson's disease (PD), multiple system atrophy (MSA) and progressive supranuclear palsy (PSP). Using functional magnetic resonance imaging (fMRI) we have studied motor activity (fist clenching) in patients with idiopathic Parkinsonism and also have studied the dopa drug effectiveness in the three groups.

Materials and Methods: Thirty two right handed patients (table 1), and 8 healthy controls were recruited from the movement disorder clinic of our institute. Standard diagnostic and exclusion criteria were followed. Two fMRI scans were carried out at 1.5 T (Magnetom Avanto, Siemens, Erlangen, Germany); one in the practically "off" state (i.e. after 12 hours of last dopa administration) and the other after 2 hours of dopa administration in the "on" state. Single-shot echo planar imaging was used for the functional MRI studies to study the blood oxygen level dependent (BOLD) effects in the whole brain (number of slices: 31, slice thickness: 4.0 mm; TR: 4000 ms, TE: 44 ms, FOV: 230mm, matrix: 128 x 128). We used a block design with four cycles, with fist clenching exercise during active state and rest during the baseline state. Pre- and post-processing was carried out using SPM2 (Wellcome Department of Cognitive Neurology, London, UK). The Bold activation pattern was overlaid onto the 'mni' template using the Talairach and Tornoux co-ordinates. One way ANOVA ($p < 0.001$, cluster threshold 5) was used for group analysis, while paired t-test was carried out for comparing the results during "on" and "off" states.

Results: The clinical evaluation data are presented in table 1. In PD, we observed that primary and supplementary cortex (BA 4,6) and occipital lobe were more activated in the "off- state" as compared to the "on-state" (Table 1). The subjects of MSA showed lesser activation of primary motor area (BA 4) in the "off-state" (as compared to PD) that reduced on dopaminergic therapy. In PSP, the activation of left primary motor cortex was enhanced significantly (table 2) whereas we observed no difference in the activation of left supplementary motor cortex with respect to dopaminergic therapy. Similar activation of occipital area (BA18,19) was observed during both the states (off and on) in MSA and PSP (table 2). The controls showed very limited supplementary motor area activation.

Discussion: Activation of primary motor cortex, supplementary motor cortex and superior parietal cortex (BA 7) in our study are in accordance with the earlier studies (Haslinger et al.2001). We observed hyperactivity in primary motor cortex in patients, which normalizes to some extent on dopaminergic administration (Haslinger et al.2001). The patients in the "off state" involve three specific neural networks, i.e., the medial premotor pathway, IFG-insula and cerebellum, to achieve a motor performance at par with that of controls and to compensate for hypoactivity of the dopaminergic system (Cerasa et al. 2006). Enhanced activation in SMA post-therapy and activation pattern in controls suggest the importance of the pallido-thalamo-SMA connections, as the SMA receives its major inputs from the basal ganglia. However, cerebellar- thalamic pathway may be more active in PSP patients as compared to PD and MSA, to compensate for the degeneration in basal ganglia (Ivry et al.1996).

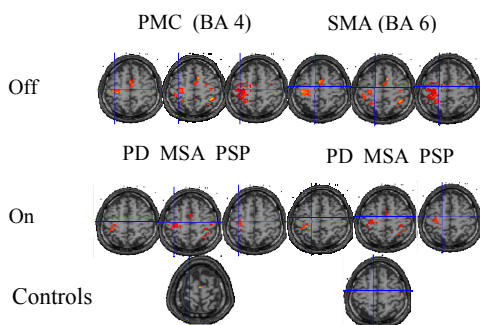
The patients tend to use the lateral premotor cortex to compensate for the hypofunction in the striato-frontal cortex even for a simple task (Haslinger et al. 2001). It has been shown that patients recruit more of the prefrontal cortex in comparison to controls and also more regions in posterior cortical areas such as the posterior parietal cortex and prestriate cortex (Monchi et al 2007). The rostral part of supplementary motor area is reported to be responsible for automated movements and planning of movements (Roland et al.1980). This study confirms the dopaminergic aided reversal of premotor/ motor/parietal cortical hyperfunction in Parkinsonism. Also distinct pattern of activation among the three types of Parkinsonism might be of help in differential diagnosis.

Table 1. The clinical profile of Parkinsonian patients (PD, MSA, PSP) and controls and the respective brain activation pattern for the primary and supplementary motor area and cerebellum.

Group	Subjects	Age (yrs)	Disease Duration	Daily dopa intake (mg)	Stage of the disease	MMSE	UPDRS III	BOLD cluster count					
								BA 4		BA 6		Cerebellum	
								Off	On	Off	On	Off	On
PD	18 (11M/7F)	59.8±14.3	6.53±3.5	712.5±303.5	H & Y 1.7±0.61	27.2± 2.67	20.5±10.8	106	30	10	4	.	.
MSA	9 (7M/2F)	61.7±7.02	6.2±8.9	401.5±181.9	UMSARS 2.6±0.96	28.3 ± 1.8	22.0±8.8	32	26	0	0	.	.
PSP	5 (4M/1F)	64.6±8.1	2.96±0.9	215.6±141.2	PSP rating 3.0±1.0	25.5 ± 3.2	27.3±4.0	19	50	60	77	35	24
Controls	8 (5M/3F)	48.6±5.2	-	-	-	29.0 ± 1.0	-	0		10		0	

MMSE: Mini-mental State Examination; UPDRS: Unified Parkinson's Disease Rating Scale; UMSARS: Unified Multiple System Atrophy Rating Scale; H&Y: Hoehn & Yahr staging system for PD; BA4: Primary motor cortex; BA6: Supplementary motor area.

Figure 1. BOLD activation pattern in PD, MSA and PSP subjects in the primary motor cortex (BA 4) and supplementary motor area (BA 6) in response to dopaminergic administration.



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