Degeneration of motor cortical areas in Parkinson's Disease: A follow up fMRI study

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Introduction: In Parkinson's disease (PD), the striatal dopamine depletion in the substantia nigra and basal ganglia disrupts the cortico-striatal balance leading to motor deficit[1]. Dopamine is considered to be essential for focusing the neural activity in the cortex[2]. Using BOLD imaging we studied motor activity (fist clenching) in PD patients and the L-dopa effectiveness over a period of one year.

Materials and Methods: Fourteen right handed PD patients (group I) and seventeen healthy age and gender matched controls (table 1), were recruited from the movement disorder clinic of our institute. Standard diagnostic and exclusion criteria were followed. The follow-up study was carried out after approximately 12 months, in nine patients (group II) (as remaining were lost to follow-up), which is a sub-group of Group I. Both the scans were carried out at 1.5 T (Magnetom Avanto, Siemens, Erlangen, Germany). Each scan had two sessions, 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 with the following parameters: number of slices: 31, slice thickness: 4.0 mm; TR: 4000 ms, TE: 44 ms, FOV: 230mm and resolution: 128 x 128. We used a block design with four cycles, with fist clenching exercise during active state and a period of rest during the baseline state. Pre- and post-processing was carried out using SPM2. The MNI Bold activation pattern was converted to Talairach co-ordinates using Ginger ALE software and then overlaid onto the Talairach and Tornoux atlas. One way ANOVA ($p<0.001$, cluster threshold 10) was used for group analysis.

Table 1. The clinical profile of Parkinson's patients and controls

Group	Subjects	Age (years)	Duration	Daily dopa intake (mg)	Stage H & Y	MMSE	UPDRS III
PD-Gp. I	14(10M/4F)	55.5±13.3	4.6±3.4	531.5±335.1	1.5± 0.5	28.3± 1.89	16.7±7.1
PD-Gp-II (on recruitment)	7M/2F	62.11± 4.19	5.56 ± 3.54	606.17 ± 343.16	1.72 ± 0.67	24.33 ± 9.38	20.67±10.32
PD-Gp-II (on follow-up)				645.83 ± 363.12	2.11 ± 0.70		28.56 ± 13.48
Controls	10M/7F	48.3±6.89	-	-	-	29.0 ± 1.0	-

MMSE: Mini-mental State Examination; UPDRS: Unified Parkinson's Disease Rating Scale; H&Y: Hoehn & Yahr staging sytem for PD

Results: The activation in medial frontal gyrus, superior temporal gyrus, cerebellum, thalamus putamen and postcentral gyrus were enhanced in the follow-up study as compared to the initial BOLD motor activation (on recruitment) in group II. The BOLD activation pattern is given in table 2. Precentral gyrus did not show any difference in activation with respect to disease progression. We compared the activation of these patients with results of 14 PD patients (group I) wherein we observed hyper-activated inferior parietal cortex, SMA and PMC and ipsilateral cerebellum.

Discussion: Activation of primary motor cortex, supplementary motor cortex and inferior parietal cortex (BA 40) for fist clenching in our study are in accordance with the earlier studies[3]. We observed hyperactivity in primary motor cortex in patients in the 'off' state, which normalizes to some extent on dopaminergic administration. During the 'off-state' ipsilateral cerebellum has been positively correlated to the severity of the limb rigidity in PD patients[4,5]. In the "off state" patients involved IFG, insula and cerebellum, to achieve a motor performance at par with that of controls to compensate for dopaminergic hypoactivity[6]. Enhanced activation in SMA 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[7]. Increased cortical activity has been attributed to the dopaminergic nigro-striatal loss along with meso-cortical dopamine reduction[8]. The PD patients have been shown to employ cerebellar- thalamic pathway to compensate for the basal ganglia motor loop[7]. Basic movement parameters are believed to be controlled by sensory motor cortex[9]. The rostral part of supplementary motor area is reported to be responsible for automated movements and planning of movements[10].

Conclusion: The enhanced activation of primary motor cortex could be normalized to an extent by dopaminergic replacement. The study suggests hyperactivation in SMA, medial frontal gyrus, thalamus, putamen and postcentral gyrus. The cerebellar involvement was enhanced probably as a compensatory mechanism or increased involuntary motion. With the progress of the disease in PD, BOLD activation involves areas other than sensorimotor areas due to dyskinesia.

Table 2. Cluster counts for BOLD activation pattern in PD follow-up study (group II).

			Clusters				
			Controls	PD 'Off' state		PD 'On' state	
Brain Region	side	BA		Initial	Fup	Initial	Fup
IPL	L	40	40	600	11	714	-
Putamen	L		-	18	-	34	20
Insula	L	13	-	24	-	-	-
MeFG	L	6	28	-	15	25	312
PrCG	L	4	10	68	12	-	12
CBL	R		51	780	862	679	1198
PoCG	L	2,3,5	54	-	820	10	456
Thalamus	L		-	-	30	40	33
STG			-	-	-	16	10

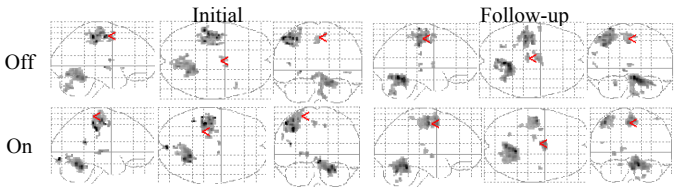

Fig 1. The brain activation pattern for the PD, in response to dopaminergic administration for a period of one year.

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