Effect of dopaminergic drugs on motor and speech tasks in PD: an fMRI study

M. SAXENA[1], S. SENTHIL KUMARAN[2], S. SINGH[1], V. NARANG[3], and M. BEHARI[1]

[1]NEUROLOGY, ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI, DELHI, India, [2]DEPARTMENT OF N.M.R., ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI, DELHI, India, [3]SCHOOL OF LANGUAGES, JAWAHARLAL NEHRU UNIVERSITY, NEW DELHI, India

Introduction: Parkinson's disease (PD) is a chronic and progressive neuro-degenerative disorder of the central nervous system that often impairs the subject's motor skills, speech and high level cognitive dysfunction. It is characterized by tremor, bradykinesia, rigidity and postural disturbance, occurring mainly due to deficiency of dopamine. L-dopa remains to be the most effective therapy although it has some side effects including inhibition of its endogenous production. The present functional MRI study is undertaken to investigate the dopaminergic challenge on articulation of speech and motor coordination and also to evaluate the drug response in PD patients.

Materials and methods: Six subjects of 59.57 $\pm$ 15.4 years, (5 male and 1 female) suffering from PD for 6 $\pm$ 4 years were recruited from the neurology clinic of our institute. The patients were investigated using standard Unified Parkinson's disease rating scale (UPDRS) and functional MRI both in the 'off' (no dopaminergic drugs or any other medication for at least 12 hrs before the fMRI scan) and 'on' (2 hours after dopa was administered). The studies were carried out on 1.5 T MR Scanner (Avanto, Siemens, Erlangen, Germany) using head and cervical coils. Single-shot EPI (no. of slices: 31, slice thickness: 4mm; TR: 4020 ms, TE: 44 ms, FOV: 210 mm, resolution: 128x128) was used for the BOLD sessions. BOLD studies consisted of two tasks: motor task and task involving articulation of speech. The motor task was finger tapping of Lumina response switch (LP-400) with uniform frequency during active phase and rest during baseline phase. Total of four cycles of active and baseline phases of 10 measurements each, preceded by one phase of baseline, totaling 90 measurements were acquired. The speech paradigm design consisted of visual presentation of 20 two-letter Hindi words each for the six categories of articulatory phonemes (velar, palatals, retroflexals, dentals, bilabials and nasals) during the active state, with each category presented for 10 measurements and the baseline consisted of single letter Hindi alphabets interleaved between the above six categories. The patients were instructed to read aloud the two letter words and staying silent when single letter words were presented. The stimuli were presented onto an LCD screen and a mirror arrangement on the head coil. Anatomical T1 and T2 weighted images were acquired to rule out morphological deficits. Pre and post-processing was done on an offline sever using SPM2 (http://www.fil.ion.ucl.ac.uk/spm/software/spm2/) running in MATLAB environment. One way ANOVA was used for group analysis, with $p<0.001$, cluster threshold 5.

Results: The average UPDRS part III score was 21 $\pm$ 15. Hoehn & Yahr Stage was 1.64 $\pm$ 0.98; the mean L-dopa equivalent was equal to 110 $\pm$ 13 mg per day. The speech part of UPDRS part III was estimated to be 1.85 $\pm$ 0.6. For the motor task in the off-stage, activation was observed more in the left supplementary motor area (BA 6) as compared to the primary motor area (BA 4). In addition, left sensorimotor cortex and right cerebellum were activated. No activation was seen in the right hemispheric M1. In the 'on' stage for the motor task, enhanced activation in the BA6 was observed, other than activation in the primary motor and cerebellar cortex. For the speech task, the study revealed increased activation in BA6 more in the right hemisphere and very less activation in the middle temporal gyrus (BA21) in the 'off' stage. After 2 hours of dopa administration, we observed greater activation in primary motor cortex (BA 4, 43), right frontal gyrus and supplementary motor area (BA 6).

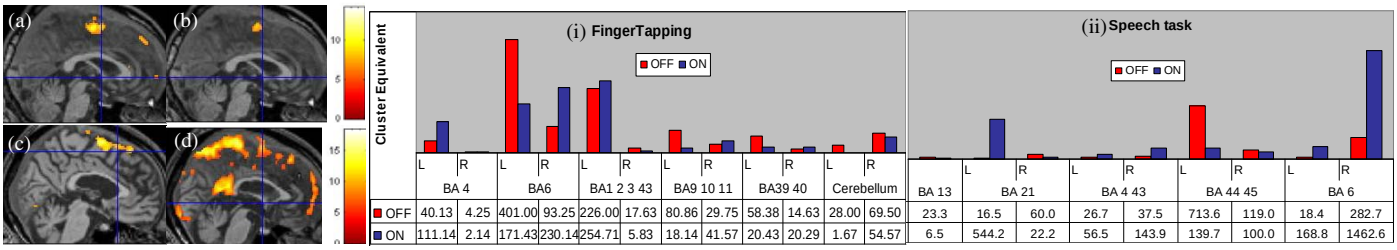

Fig. 1. Bold activation during 'off'(a,c) and 'on' (b,d) stage for motor (a,b) and speech (c,d) tasks in a subject.

	BA 4		BA6		BA1 2 3 43		BA9 10 11		BA39 40		Cerebellum	
	L	R	L	R	L	R	L	R	L	R	L	R
OFF	40.13	4.25	401.00	93.25	226.00	17.63	80.86	29.75	58.38	14.63	28.00	69.50
ON	111.14	2.14	171.43	230.14	254.71	5.83	18.14	41.57	20.43	20.29	1.67	54.57

	BA 13	BA 21		BA 4 43		BA 44 45		BA 6	
		L	R	L	R	L	R	L	R
OFF	23.3	16.5	60.0	26.7	37.5	713.6	119.0	18.4	282.7
ON	6.5	544.2	22.2	56.5	143.9	139.7	100.0	168.8	1462.6

Table 1. Cluster count in various Brodmann areas for (i) finger tapping and (ii) speech tasks in 'off' (red) and 'on' (blue) stages. L denotes Left hemisphere, R-right hemisphere

Discussion: The results observed for the motor task correlate with earlier studies in PD patients (1, 2). Reduced activity in BA 4 as compared to controls may be due to the tremors in the baseline, which has negated the active task to a greater extent and also due to the fact that the subjects were not able to tap at sufficiently high frequency (3). For the speech task, activation of BA 21 corresponds to lexical and semantic processing and insula (BA13) for articulatory planning. BOLD activation in inferior frontal gyrus (BA 44, 45) and supplementary motor area (BA 6) are ascribed motor sequencing and initiation of planning (3). Interestingly, the involvement of basal ganglia, substantia nigra and cerebellum are not observed in our study (4, 5). In spite of dopamine deficient substantia nigra, PD patients compensate for normal speech by involving left supplementary motor area and other areas (5). The results with L-dopa indicate that BA 21 and BA 6 are having positive drug effects and BA 44, 45 and BA 13 have negative dopaminergic effects in PD subjects.

References:

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