Motor dysfunction in Parkinson's disease and Multiple System Atrophy and the effect of dopamine drug

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Introduction: In Parkinson's disease (PD) and Multiple system atrophy (MSA), the striatal dopamine depletion in the substantia nigra and basal ganglia disrupt the cortico-striatal balance leading to motor dysfunction (Whone et al. 2003). Dopamine drugs restore the deficit to some extent (Swagushi, 2001). Using BOLD imaging we studied motor activity (fist clenching) in PD and MSA, with reference to the L-dopa effectiveness in a follow-up study (after a period of approximately twelve months).

Materials and Methods: Nine right handed MSA-P, 13 Parkinson's disease patients 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. Both the scans were carried out at 1.5T (Magnetom Avanto, Siemens). The MRI scan was conducted in the practically "off" state (i.e. after 12 hours of last dopa administration) and 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, etl:127, FOV: 230mm and resolution: 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 were carried out using SPM2. The MNI coordinates of BOLD clusters were converted to Talairach coordinates 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 (years)	Daily dopa intake (mg)	Stage	MMSE	UPDRS III
PD (n=13)	10M/ 3F	58.75 ± 13.98	5.33 ± 3.66	525.0 ± 191.70	1.58 ± 0.47 (H & Y)	28.25 ± 1.76	17.92 ± 10.17
MSA (n=9)	5M/ 4F	62.20 ± 6.70	3.67 ± 1.80	365.63 ± 156.38	2.70 ± 1.06 (UMSARS)	27.60 ± 3.06	24.70 ± 11.96
Cont. (n=17)	10M/ 7F	48.3 ± 6.89	-	-	-	29.0 ± 1.0	-

Table 2. BOLD activation pattern for the Fist clenching task in Controls PD,MSA and PSP subjects in "Off" and "On" states using SPM2 One way ANOVA(Voxel threshold 10, p<=.001)

	Cont-rols	"Off-State"				"On-State"			
		PD	PD Fup	MSA	MSA Fup	PD	PD Fup	MSA	MSA Fup
Precentral Gyrus (L)	40	233	72	3320	13	594	124		834
Postcentral Gyrus (L)	11	1517	4277		706	97		19	52
Middle frontal gyrus (L)		10		176		27	860	20	28
Middle frontal gyrus (R)		562	26	70	351	317			143
Thalamus (L)		28	86			33		151	111
Thalamus (R)		46					40	23	21

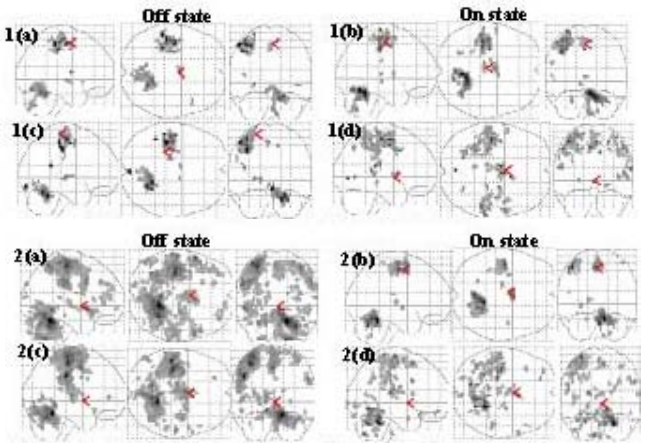

Figure 1.The glass brain view of the BOLD activation pattern ($p \leq 0.001$ and cluster threshold 10) for the fist clenching task for Parkinson's disease in "off-state" (1a) and "on-state" (1b) ; Multiple system atrophy in "off-state" (2a) and "on-state" (2b). The activation on follow up after 12 months for Parkinson's disease in "off-state" (1c) and "on-state" (1d) ; Multiple system atrophy in "off-state" (2c) and "on-state" (2d).

Results: We observed an increased activation in the precentral gyrus during the initial 'off' state, which reduced during the follow-up 'off' state, while the activation was enhanced in the post central gyrus during the followup study in the' off' state. The supplementary motor area (SMA; middle frontal gyrus), and left cerebral thalamus had enhanced activation during the followup study during the "on-state" as compared to the baseline 'on' state.

Discussion: Activation of primary motor cortex (BA 4), supplementary motor cortex (BA 6) and inferior parietal cortex (BA 40) in our study are in accordance with the earlier studies (Haslinger et al. 2001) (Table2). Increased cortical activity has been attributed to the dopaminergic nigro-striatal loss along with meso-cortical dopamine reduction (Cools et al., 2002). This might also indicate that in the MSA patients the loss of dopaminergic neurons occurs at a rapid rate, that after 12 months, the effect of dopaminergic drug is less pronounced. The abnormal activation of primary motor cortex suggests neurodegeneration in the precentral gyrus, SMA, medial frontal gyrus, thalamus, putamen and postcentral gyrus, more pronounced in MSA.

References:

Cerasa et al. 2006. Brain Research Bulletin 71:259–269

Haslinger et al.2001 Brain. 124: 558-570

Swagushi et al.2001. Parkinsonism Relat Disord. 7: 9–19.

Whone et al.2003 Ann Neurol : 53:206–213.