

# An analysis of working memory in Parkinson's disease with reference to deficiency of Dopamine: an fMRI study

M. SAXENA<sup>1</sup>, S. SENTHIL KUMARAN<sup>2</sup>, S. SINGH<sup>1</sup>, and M. BEHARI<sup>1</sup>

<sup>1</sup>NEUROLOGY, ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI, DELHI, India, <sup>2</sup>DEPARTMENT OF N.M.R., ALL INDIA INSTITUTE OF MEDICAL SCIENCES, NEW DELHI, DELHI, India

**Introduction:** Parkinson's disease (PD) is a chronic and progressive neuro-degenerative disorder of the central nervous system that is often associated with dementia. Grey matter loss has been observed in frontal cortex in PD (1). We studied whether working memory loss, if any, in such patients is due to dopamine deficiency or cerebral atrophy (2).

**Materials and methods:** Six patients of  $59.57 \pm 15.44$  years (5 male and 1 female), suffering from PD for  $6 \pm 4$  years were recruited from the clinics 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: 44ms, FOV: 210mm, matrix resolution: 128x128) was used for the BOLD sessions. As shown in figure 1, the stimulus consisted images of known objects (objects that the subjects have across in daily life) and unknown images (landscapes and sceneries, which the subjects have never seen or visited). The baseline for the known objects was circular spots of the colors matching with those of known items. For the natural scenes the baseline used was of cloud images. The stimuli were presented onto an LCD screen positioned towards the posterior side of using a mirror arrangement on the head coil. The design consisted of a study phase during which the patients observe carefully 26 pictures were presented for 2000ms each on a LCD screen using a mirror arrangement on the head coil. During the recollection phase (15 minutes later) when EPI was acquired, 96 images (28 from household items, 28 from fruits and vegetables, 20 from landscapes and 20 from water bodies) were presented, which also consisted study phase pictures shown earlier. The subjects were instructed to give a response by pressing the assigned key on the Lumina LP400 response pad as to whether they had seen that image earlier or not. Each image remained on the monitor for 2000 ms and a response time of 2000 ms was provided for the subjects to respond. The responses were registered using Superlab software. 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 (with  $p < 0.001$ , cluster threshold 5) was used for group analysis while paired t-test was applied between the on and off state in the second level analysis.

**Results:** The patients exhibited MMSE  $23 \pm 10.44$ ; Hoehn & Yahr Stage  $1.64 \pm 0.98$ ; having dopa dependence of  $110 \pm 13$  mg per day. During the 'off' state, BOLD activation was observed in the right middle frontal gyrus (BA 46, 9), right thalamus, inferior frontal gyrus (BA 45, 46, 47), left superior frontal gyrus (BA 6) and bilateral medial frontal gyrus. Bilateral occipital and fusiform gyri (BA 17, 18, 19) and parahippocampal gyrus (BA 30, 36, 37) were significantly activated on the group analysis. During the 'on' state, bilateral activation was observed in middle frontal gyrus, inferior frontal gyrus, and medial frontal gyrus. Also right hemispheric superior frontal gyrus (BA 6, 8) and inferior parietal lobule (BA 39, 40) activation were observed. Group analysis results during the 'on' stage show that activation was confined to left insula (BA 13) and right hippocampal gyrus (BA 36, 37). Based on the feedback records of Lumina response pad, 75% ( $\pm 12\%$ ) were correct for the target objects (which were shown prior to study) in the 'off' stage and 78% ( $\pm 11\%$ ) during the 'on' stage and the response times were 1160ms and 1190 ms during 'off' and 'on' stages respectively.

**Discussion:** In the present study, areas associated with memory retrieval and visual processing were active during 'off' and 'on' stages. Activation of parahippocampal gyrus, during both the stages, could be attributed to its role in scene processing and episodic memory (3). The fronto-striatal network was observed to be active during individual analysis during the 'on' stage, but was not observed in the group analysis. This could be due to partial brain volume loss in the medial temporal lobe in some of the subjects (1). Similar feedback responses or reaction times during 'on' and 'off' states show that memory was unaffected with drug administration in these subjects. Frontal gyrus activation is observed only during the 'on' stage, which indicates that L-dopa increases the attentional capabilities of the PD subjects, but may not have any significant role in working memory.

## References:

1. Burton *et al.* (2004). Brain, **127**: 791-800.
2. Lewis *et al.* (2003). The Journal of Neuroscience, **23**: 6351– 656.
3. Bar M, Aminoff E, Schacter DL (2008). J Neurosci. **28**: 8539-44.

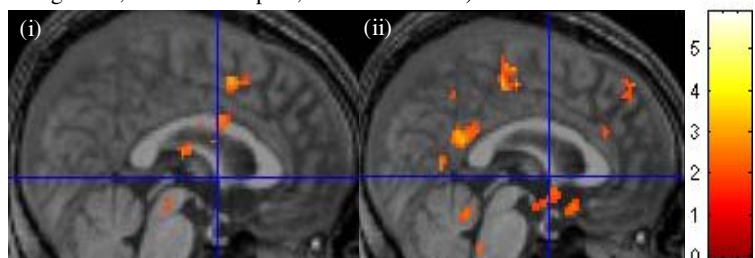
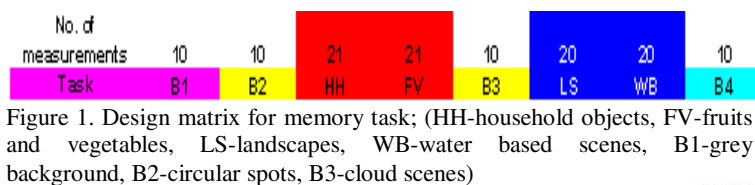


Figure 2. The BOLD activation pattern in a sagittal section in PD patients (group analysis) with reference to L-Dopa therapy during (i) Off state and (ii) On state.