Strength and Onset of Basal Ganglia Activation in Parkinson’s Disease Patients and Healthy Subjects During Different Movement Conditions

C. Windischberger[1,2], R. Cunnington[3], B. Hoheisel[1,4], L. Deecke[5], E. Moser[1,6]

[1]MR Center of Excellence, Medical University of Vienna, Vienna, Austria, [2]Department of Psychiatry, Medical University of Vienna, Vienna, Austria, [3]Howard Florey Institute, University of Melbourne, Melbourne, Australia, [4]Institute for Clinical, Biological and Differential Psychology, University of Vienna, Vienna, Austria, [5]Department of Neurology, Medical University of Vienna, Vienna, Austria, [6]Center for Biomedical Engineering and Physics, Medical University of Vienna, Vienna, Austria

Introduction:

According to the model of Alexander [1] the basal ganglia are part of functionally segregated loops connecting various cortical areas and the thalamus. Motor dysfunctions found in Parkinson's disease (PD) patients have been linked to the loss of neurons in the nigrostriatal pathways causing dopamine depletion in the striatum as the primary input site to the basal ganglia resulting in excessive inhibition of thalamic projections to the cortex. The SMA therefore shows impaired activation in PD [2], while lateral premotor areas, which receive less basal ganglia input, are found to be relatively overactive [3,4]. In addition, PD patients show particular motor deficits when movements must be internally-generated, but show improved performance when external cues are available to guide movement [5]. It remains unclear what reorganisational/compensatory changes or altered movement strategies occur in PD patients and to what extent the basal ganglia are involved. In this study we have addressed this issue by examining activation in various basal ganglia and thalamic regions in PD patients and healthy controls, both in terms of activation strength and onset.

Materials and Methods:

We studied 14 medicated PD patients (UPDRS 1-2) and 9 age-matched healthy control subjects using three paradigms. Participants were required to perform finger movements according to (1) a predictable cue, (2) an unpredictable cue and (3) self-initiated. Cues were presented acoustically via headphones. Data acquisition employed single-shot EPI (14 slices along ac-pc, TE/TR=40/1000ms, MA=96x64, thickness=5mm) at 3 Tesla and each of the three runs consisted of 12 right-hand finger movement trials, with three brief button presses in each trial. An ISI of 33s was chosen to allow the haemodynamic response to fully return to baseline. After slice-timing and motion correction data sets were normalized to MNI-space and spatially smoothed (FWHM=6mm) using SPM2. Finger movements were modeled with the canonical haemodynamic response function (HRF) and its temporal derivative. Parameter estimates for the temporal derivative were used to calculate the temporal delay between the assumed HRF and the actual signal change. ROIs for Caudate (Caud), Putamen (Put), Pallidum (Pall), Thalamus (Th), supplementary motor area (SMA) and primary motor cortex (M1) was based on the aal-template as included in MRIcro. All ROIs except SMA were defined separately for the left and right hemisphere. All voxels that showed activation above a t-value of 2 were selected for further analysis. For these voxels, mean parameter estimates and delays (via the temporal derivative) were calculated separately for all ROIs. All delays were related to the activation delay in the left M1 ROI to minimize effects of individual haemodynamic response delays. Statistical testing was done across paradigms and study groups.

Results:

Compared to controls PD patients showed significantly increased activation in the right ($p<0.03$) and left Put ($p<0.02$) for the predictable-cue condition. For the unpredictable cue condition no significant differences with respect to activation strength were found, however, activation onset in the right Th ($p<0.02$) and SMA ($p<0.05$) was earlier in PD patients. The only significant difference for self-initiated movements was found in the left Caud with activation occurring significantly later in PD patients than in controls ($p<0.02$).

Comparing predictable and unpredictable movements PD patients showed increased activation for the predictable cue in the left Put ($p<0.004$) and SMA ($p<0.04$) while in controls no differences were found. Also, when comparing the predictable cue condition to the self-initiated movements activation levels in PD patients were higher in left Put ($p<0.003$) and left Pall ($p<0.02$), which was not replicated in the control group.

Discussion:

Our results show increased activation in the Putamen of medicated PD patients during unpredictable and self-initiated finger movements compared to movements performed according to a predictable cue, not observed in the control group. These results reflect the neuronal basis for the well-known clinical observation that PD patients motor performance substantially decreases when external guidance is absent. It seems that there exists decreased excitatory input (from M1 and other cortical areas and the Substantia nigra via D1-receptors) and/or increased inhibitory input to the Putamen (from the Substantia nigra via D2-receptors). Differences in activation onset times between conditions further indicate altered movement strategies in PD patients compared to the healthy control group.

References:

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