Accounting for Movement Increases Sensitivity in Detecting Brain Activity in Parkinson’s Disease

Stefan Holiga1, Harald E Möller1, Tomáš Sieger2-3, Matthias L Schroeter1-4, Robert Jech2, and Karsten Mueller1

1Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany; 2Department of Neurology and Center of Clinical Neuroscience, Charles University in Prague, Czech Republic; 3Department of Cybernetics, Faculty of Electrical Engineering, Czech Technical University in Prague, Czech Republic; 4Clinic for Cognitive Neurology, Leipzig, Germany

Introduction: Parkinson’s disease (PD) is a progressive neurological disorder manifested by motor impairment, which may impede the ability to accurately perform motor tasks during functional magnetic resonance imaging (fMRI). In motor experiments with PD patients researchers often neglect that due to motor deficits, performance is likely to deviate from an idealized paradigm. Both temporal and amplitude deviations of movement performance affect the blood oxygenation level-dependent (BOLD) response (1, 2). Such deviations are of particular importance in areas with only tenuous BOLD signal changes of ~1%, such as the basal ganglia (BG), which are predominantly affected in PD. Finally, movement performance variability within and between sessions need to be addressed in experiments with PD patients.

Without explicit quantitative knowledge of movement performance, statistical tests relying on the generic BOLD model may be degraded by inappropriate estimates of partial regression coefficients, β, and potentially result in biased and invalid interpretations. We hypothesized that assessment and consideration of individual movements increases the sensitivity of BOLD fMRI to detect brain activity of PD patients during a motor task.

Methods: Twelve right-handed male patients with advanced PD (Hoehn-Yahr stages II-III, 45-64 years of age) were measured in two conditions, (a) after overnight withdrawal of levodopa (OFF) and (b) one hour after administration of 250 mg of levodopa / 25 mg carbidepina (ON). Both hands were investigated separately. A block-based motor paradigm consisting of resting and finger tapping epochs was conceived. A T2*-weighted gradient-echo echo-planar imaging (EPI) sequence (flip angle 90°; repetition time, TR = 1 s; echo time, TE = 54 ms) was used for BOLD fMRI at 1.5T. Patients’ motor outcome was recorded using MRI-compatible sensory rating scales, with a set of 14 sensors measuring the flexion and abduction of fingers. Two types of fixed-effects models were generated (Figure 1): (i) The standard model incorporated a constant term and a predictor containing a condition-specific, constant-amplitude boxcar function characterized by onsets and durations of task-related epochs, as conventional to calculated percent signal change for each approach in a region of interest (ROI), which was formed as the intersection of parametric maps resulting from standard and all kinematic group-level approaches. Analysis of variance with repeated measures with factors ‘Hand’ and ‘Modeling approach’ for ON medication condition was calculated for quantitative assessment of the results.

Results & Discussion: Strikingly, all variations of kinematic modeling outperformed standard modeling and resulted in an extensive sensitivity increase (Figure 2). They provided a larger spatial extent of activity and higher family-wise error (FWE) corrected cluster p-values. In contrast, the right subcortical cluster obtained with standard modeling did not remain significant after FWE multiple test correction. All kinematic approaches provided significantly higher (p<0.05) amplitudes of activity (Figure 3). In addition, all kinematic approaches except ‘mean’ showed a significant interaction (p<0.05) between factors ‘Hand’ and ‘Modeling approach’. Interestingly, a significant difference (p<0.05) between amplitude-sensitive and amplitude-invariant versions of eigenvariate kinematic approach was discovered. Our results provide a clear evidence of increasing sensitivity in detecting brain activity in PD patients compared to generic fMRI statistics, when quantitatively accounting for their movement.


Figure 1. Comparison of session-specific predictors in fixed-effects model (left, blue: standard approach; right, orange: kinematic, mean amplitude-sensitive approach).

Figure 2. Group-level response to levodopa treatment in PD patients as random effect parametric maps (p<0.001; uncorrected).

Figure 3. Average effect size in basal ganglia functional ROI.