Introduction

While unilateral movements typically result in highly asymmetric activations in fMRI, an increase in symmetry of motor activation has been reported in drug-naive Parkinson's disease (PD) [1]. The finding of reduced lateralization is in line with the reduced inhibition – increased facilitation hypothesis of basal ganglia-thalamo-cortical compensation. We used fMRI to study motor activations and cortical motor network connectivity in long-term PD patients – ‘ON’ and ‘OFF’ of their usual dopamine medication, as well as in healthy controls (HC). Our hypotheses were as follows: (1) Decreased lateralization of motor activation persists in long-term PD, particularly during movements of the body side dominantly affected by the disease. (2) Administration of levodopa restores laterality measures, bringing them closer to levels observed in HC. (3) Altered network interactions – as observed through DCM – in PD patients mirror lateralization changes, with dopamine administration partially reinstating ‘normal’ connectivity, both in terms of connectivity strengths and connectivity lateralization.

Results

Behavior – percent correct and force

Lateralization of motor activation (AveLI)

Possible contralateral–ipsilateral activation scenarios

Connectivity strength (DCM) and connectivity laterality (connLI)

Characterization of between-group differences (PEB)

Methods

Participants: 10 PD (5F), 18 age-matched HC (9F).
All participants right-handed, PD patients left-dominant symptom side, tested ‘OFF’ and ‘ON’ dopaminergic medication

Data acquisition: Siemens Prisma 3T MRI 1.5 mm MPMs, 2 mm fMRI (TR = 3.328 s)
Experimental design: Externally paced (visually cued) 0.5 Hz frequency movements of right hand, left hand, right foot, left foot. Block design with 5 blocks per limb, 8 mvts per block.

Data analysis
- Activation laterality quantification (AveLI)
- Estimation of effective connectivity through dynamic causal modeling (DCM)
- Quantification of connectivity laterality (connLI)

- Parametric empirical Bayes (PEB) (7.8) used to compare parameter estimates between each of the group pairs
- Characterization of between-group differences – increased/decreased excitation/inhibition

Conclusions

- Increase in symmetry of motor activation persists in long-term PD, regardless of medication status
- Decrease in laterality corresponds to decrease in contralateral activation and/or increased ipsilateral activation
- Connectivity laterality, as estimated through DCM analysis, is significantly different across groups, with particularly pronounced differences in inhibitory interhemispheric and homologous connectivity
- PEB analysis revealed qualitatively more between-group differences in input-specific modulation on the more affected PD side and included many interhemispheric connections
- Connectivity changes can mainly be characterized as reduced inhibition – reduced facilitation

References