



Brain connectivity change with deep brain stimulation and levodopa treatment in Parkinson's disease



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Introduction

- Levodopa and later, deep brain stimulation (DBS) have become the mainstays of therapy for motor symptoms associated with Parkinson's disease (PD).
- Although these therapeutic options lead to similar clinical outcomes, the neural mechanisms underlying their efficacy are different.
- Investigating the differential effects of DBS and levodopa on functional brain architecture and associated motor improvement is of paramount interest.
- Here, we addressed a direct comparison between the effect of levodopa medication and DBS of the subthalamic nucleus (STN) on functional brain connectivity in the same group of PD patients examined before and after electrode implantation.

Methods

- Clinical assessment and resting-state functional magnetic resonance imaging (fMRI) were performed before and after implanting electrodes for DBS in the STN.
- 13 PD patients: equivalent akinetic/rigid type, Hoehn-Yahr stages II-III, 11 males, age 52.8±6.9 y, first signs of PD with a mean age of 44.8±8.9 y, disease duration 12.6±2.7 y, levodopa treatment duration 9.5±3.1 y
- All measurements were acquired in a within-subject design with and without levodopa treatment, and with and without DBS.
- Imaging was performed using a 1.5-T MAGNETOM Symphony scanner (Siemens, Germany) and T2*-weighted gradient-echo echo-planar imaging (EPI) (repetition time, TR=3 s; echo time, TE=51 ms, 200 repetitions).
- For investigating brain connectivity changes, eigenvector centrality (EC) was computed using the Lipsia software package (Lohmann et al, 2010).
- EC maps for all patients and all experimental conditions were merged into a group analysis using the general linear model with a flexible factorial design.
- To detect brain regions which contribute to EC differences, correlation analyses were performed using seed-regions in the left and right motor cortex.
- Voxels exhibiting severe magnetic susceptibility artifacts were excluded from the search space. Calculations were restricted to the motor system based on the WFUPickAtlas (Jech et al, 2013).

Figures

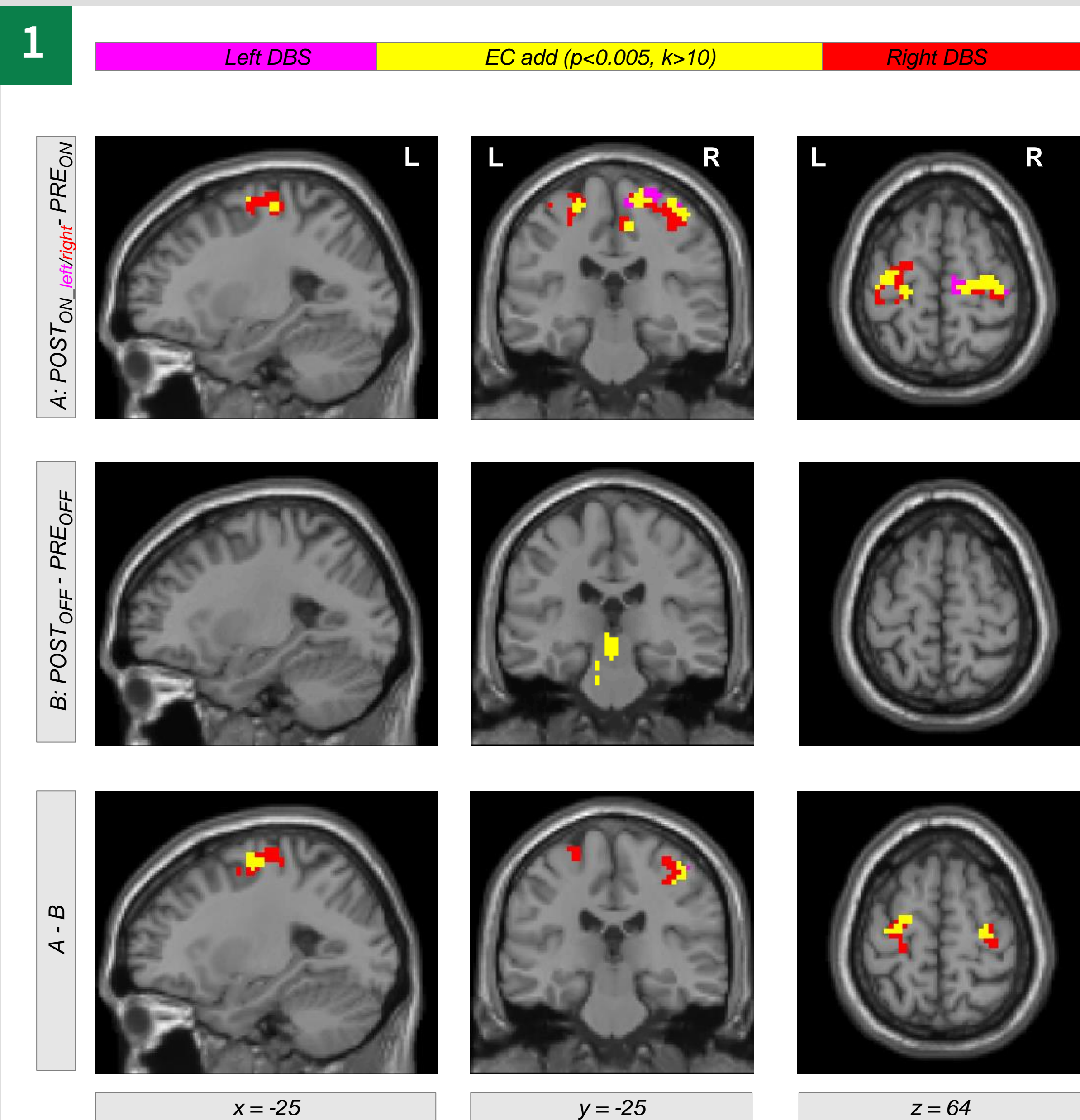


Figure 1. Differential effects of levodopa medication and deep brain stimulation (DBS) in the subthalamic nucleus (STN) on functional connectivity in motor networks affected by Parkinson's disease. The upper row shows eigenvector centrality (EC) differences between both treatment approaches when comparing levodopa medication with DBS of the left and right STN (color-coded in magenta and red, respectively; overlap in yellow). The second row shows the result for the same analysis comparing both OFF-conditions without DBS and without levodopa. The bottom row shows the difference between the contrasts shown in the top and middle row.

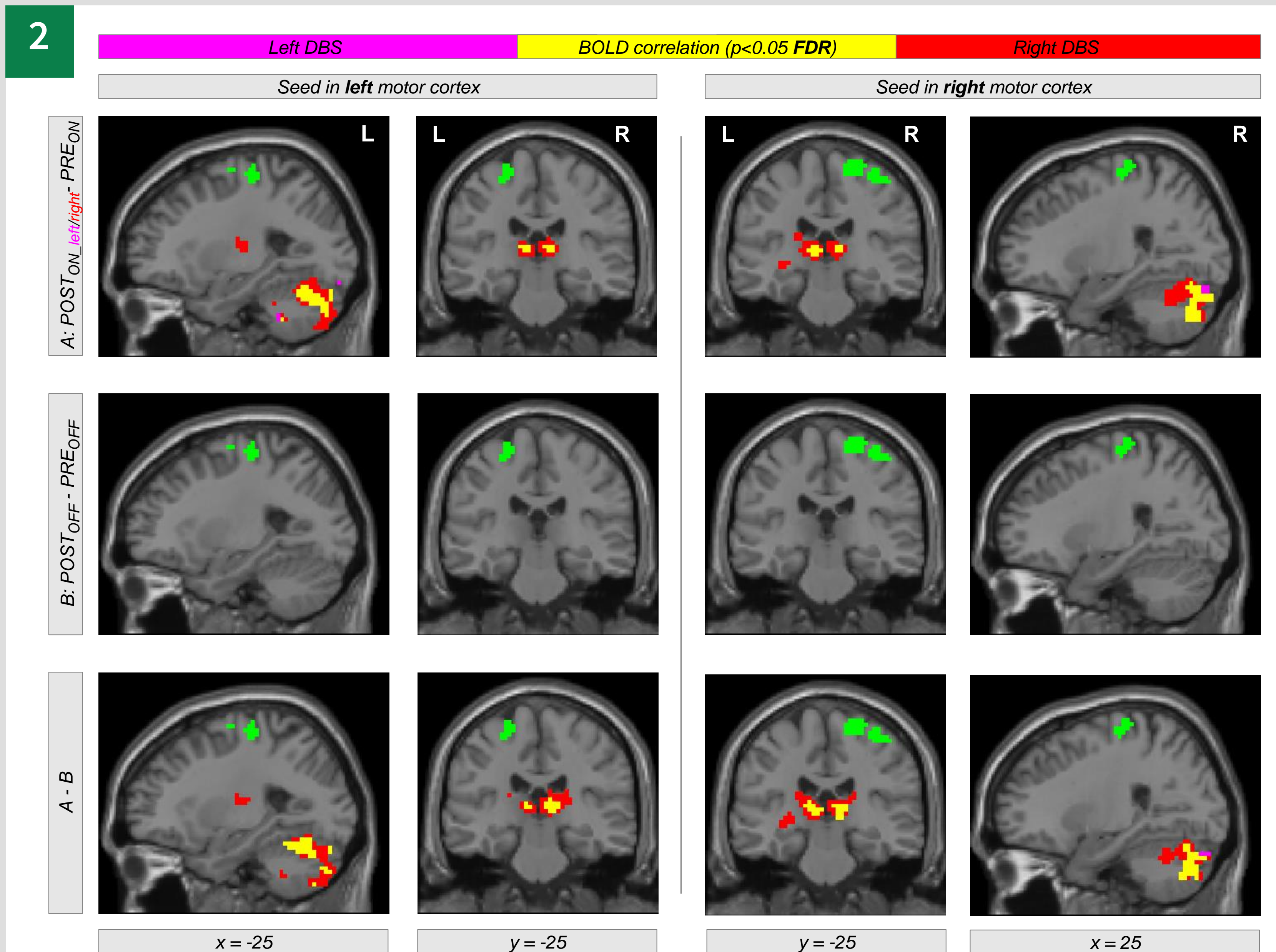


Figure 2. Differential effects of levodopa medication and deep brain stimulation (DBS) in the subthalamic nucleus (STN) on seed-based functional connectivity in motor networks affected by Parkinson's disease. The top row shows an increased correlation between BOLD time courses of the motor cortex (green color) with other brain regions within the motor mask during the STN DBS condition in comparison with the levodopa medication (color-coded in magenta and red, respectively; overlap in yellow). Comparing DBS with levodopa treatment, we found an increased correlation between the BOLD signal of the motor cortex with the BOLD signal in thalamus and cerebellum in both hemispheres irrespective of using left or right unilateral STN DBS. The second row shows the result for the same analysis comparing both OFF-conditions without DBS and without levodopa. The bottom row shows the difference between both contrasts shown in the top and middle row.

Results and Discussion

- We found a major increase of interconnectedness in the left and right motor cortex when comparing DBS to levodopa (Fig 1, top row).
- We also obtained a significant difference between the treatment method and the microlesion effect using an interaction approach (Fig 1, bottom row).
- Our EC findings were accompanied by an increase of connectivity of these motor hubs with the thalamus and cerebellum (Fig 2).
- We observed significant functional connectivity changes when comparing the effects of STN DBS and oral levodopa administration, revealing different treatment-specific mechanisms linked to clinical benefit in PD.
- In contrast to levodopa treatment, STN DBS was associated with increased connectivity within the cortico-thalamo-cerebellar network.
- Understanding the observed connectivity changes may be essential for enhancing the effectiveness of DBS treatment, and for better defining the pathophysiology of the disrupted motor network in PD.

References

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