

Structural network fingerprints for GPI-DBS in dystonia

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Objective: Here, we investigate whether patients who respond to GPI-DBS present different brain global and local network organization and structural MRI fingerprints as derived from 3D MP-RAGE-T1 images, and if these markers could act as predictors for the DBS outcome.

Background: Deep brain stimulation (DBS) on the globus pallidus internus (GPI) is an effective evidence-based therapy for dystonia. However, no unequivocal and independent predictors of the clinical response to DBS exist. Moreover, only little is known about the neuromodulatory effects of DBS over the brain networks.

Methods: Fifty-one patients diagnosed with segmental and generalized dystonia who underwent bilateral GPI-DBS were recruited for this study. Patient's neurosurgical procedure and clinical data are described elsewhere [1-3]. DBS clinical outcomes were quantified as the improvement percentage in the movement scale, assessed before and 3 years after surgery. The improvement percentage at follow-up was then used to classify the patients as having a moderate- or superior-outcome (threshold of 70%). All patients underwent MRI (1.5T) and a validation cohort was acquired at 3T. MRI data were pre-processed in FreeSurfer to obtain cortical thickness (CT). Network reconstruction from CT estimates was based on the anatomical delimitations of the Desikan-Killiany atlas[4]. The network topology was assessed within the graph theoretical framework using the brain connectivity toolbox[5].

Results: Decreased small-worldness ($t=4.7$, $p = 1.8e-5$) and normalized path length ($t=3.82$, $p = 0.0002$), with increased normalized clustering coefficient ($t=3.81$, $p = 0.005$) and local efficiency ($t=1.6$, $p = 0.05$) arose for the superior-outcome, indicating long-range disconnection and higher local connectivity. The regional analyses showed that frontal, sensori-motor, temporal and parietal regions had higher degree centrality and clustering in the moderate-outcome network than in the superior-outcome. The structural integrity of cortical regions showing network differences could best discern the clinical responsiveness 3 years after GPI-DBS (AUC=88%).

Conclusions: Our study shows that the analysis of morphologic MRI markers and its derived network architecture can be developed into independent predictors for GPI-DBS outcomes at the group and single subject level, which in turn can be used to guide personalized therapeutic approaches when selecting patients who will benefit from this therapy.

References: 1. Volkmann J, Wolters A, Kupsch A, et al. (2012) 'Pallidal deep brain stimulation in patients with primary generalised or segmental dystonia: 5-year follow-up of a randomised trial', *The Lancet Neurology*. Vol. 11, no. 12. pp. 1029-1038. 2. Volkmann J, Mueller J, Deuschl G, et al. (2014) 'Pallidal neurostimulation in patients with medication-refractory cervical dystonia: a randomised, sham-controlled trial', *The Lancet Neurology*. Vol. 13, no. 9. pp. 875-84. 3. Starr PA, Turner RS, Rau G, et al. (2006) 'Microelectrode-guided implantation of deep brain stimulators into the globus pallidus internus for dystonia: techniques, electrode locations, and outcomes', *J Neurosurg*. Vol. 104, no. 4. pp. 488-501. 4. Desikan RS, Segonne F, Fischl B, et al. (2006) 'An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest', *NeuroImage*. Vol. 31, no. 3. pp. 968-80. 5. Rubinov M, Sporns O (2010) 'Complex network measures of brain connectivity: Uses and interpretations', *NeuroImage* 52:1059-69.