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TRR 295 ReTune

A brain network for deep brain stimulation induced cognitive decline in Parkinson‘s disease.

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Cognitive decline, as a stimulation-induced side effect, can diminish the therapeutic success of DBS (deep brain stimulation) in Parkinson's disease. There is often a delay before this side effect is apparent, and the mechanism remains unknown, making it difficult to identify patients at risk or select appropriate DBS settings. We test whether connectivity between the stimulation site and other brain regions is associated with cognitive decline following DBS.

First, we studied a unique patient cohort with cognitive decline following subthalamic DBS for Parkinson's disease (n = 10), where re-programming relieved the side effect without loss of motor benefit. Using resting state functional connectivity data from a large normative cohort (n = 1000), we showed that connectivity between each stimulation site and the subiculum, an a priori brain region functionally connected to brain lesions causing memory impairment, is significantly associated with DBS induced cognitive decline. A data-driven analysis confirmed that DBS sites causing cognitive decline (versus those that did not) were more functionally connected to the anterior cingulate, caudate nucleus, hippocampus, and cognitive regions of the cerebellum. The spatial topography of this DBS-based circuit for cognitive decline aligned with an a priori lesion-based circuit for memory impairment, and only aligns 9 % of spatial variance with our previously published DBS-based motor improvement network.

To begin translating these results into a clinical tool that might be useful for DBS programming, we generated a "heatmap" in which the intensity of each voxel reflects the connectivity to our cognitive decline circuit. We validated this heatmap using an independent dataset of PD patients in which cognitive performance was measured following subthalamic DBS (n = 33). Intersection of DBS sites with our heatmap was highly correlated with changes in the Mattis dementia rating scale one year after lead implantation. Finally, to illustrate how this heatmap might be used in clinical practice, we present a case that was flagged as "high risk" for cognitive decline based on intersection of the patient's DBS site with our heatmap. These results lend insight into the mechanism of DBS induced cognitive decline and suggest that connectivity-based heatmaps may help identify patients at risk, and who might benefit from DBS reprogramming.

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Martin Reich is a consultant neurologist and group leader at the Julius-Maximilians-University Hospital Würzburg. His laboratory, visualDBSlab, tackles clinical questions related to deep brain stimulation and the pathophysiology of movement disorders through computer visualisation, modelling and imaging with a multidisciplinary neuroscience team. He was awarded the David Marsden Award in 2021.

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