Abstract
Deep brain stimulation (DBS) achieves symptomatic relief in various brain disorders by restoring neural circuit function. To explore remote DBS effects on distributed circuitry at the macroscale, connectivity metrics from structural or functional neuroimaging may be related to clinical stimulation impact as a function of variably placed electrodes. At the cohort level, optimal whole-brain connectivity profiles of effective DBS electrodes can be modeled using this approach whose modulation associates with substantial relief within a given symptom domain. As such, this strategy is capable of systematically mapping out the spatial distribution of therapeutic connections across different circuitopathies. We applied this concept to the diverse cardinal dysfunctions present in four different brain circuit disorders, which all profit from subthalamic DBS. The resulting organization of therapeutic mappings spanned from circuits involving sensorimotor (dystonia), motor/premotor (Tourette’s syndrome), supplementary motor (Parkinson’s disease), toward cingulate cortices (obsessive-compulsive disorder). A comparable yet critically downscaled organizational scheme was observed at the focal sites of optimal subcortical stimulation. Retrospective and prospective evidence supports the potential of identified mappings in guiding clinical decision making.

An increasing spatial resolution at sub-symptom or somatotopic levels promises flexibility in addressing circuit dysfunctions that extend beyond a given disorder’s core symptomatology. This can be illustrated on the example of obsessive-compulsive disorder where we identified a set of therapeutic DBS symptom networks relevant to phenotypical heterogeneity among patients, amongst others including compulsivity, depression, or anxiety circuits. Within a transdiagnostic perspective, the therapeutic properties of such networks for specific symptoms may further cut through distinct disease categories.

In conclusion, neuromodulation-derived circuit mappings may bear relevance as targets for stereotactic neurosurgery, and potentially for non-invasive neuromodulation, through their association with prior therapeutic effectiveness. They could also play a role in managing symptoms that transcend cardinal diagnoses, or for tailoring treatments to individual symptom constellations.

Research Category and Technology and Methods
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Deep brain stimulation, Connectivity, Psychiatric disorders, Neurological disorders

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