CRC 1451: Project C07: Characterization of neural networks underlying motor tic formation and suppression

We analyzed a multicenter dataset of individuals with Tourette syndrome undergoing Deep Brain Stimulation (DBS) and demonstrated that DBS is most effective when targeting specific functional resting-state networks.
In particular, connectivity to action-related networks - the cingulo-opercular action-mode network (AMN) and the somato-cognitive action network (SCAN) - is associated with optimal clinical outcomes. We replicated this finding in an independent DBS cohort and further showed that brain lesions leading to secondary tic syndromes, exhibit similar connectivity patterns to these networks.
Together, our results underscore the critical role of action-related networks in both the treatment and pathophysiology of Tourette syndrome

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A critical role of action-related functional networks in Gilles de la Tourette syndrome

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Gilles de la Tourette Syndrome (GTS) is a chronic tic disorder, characterized by unwanted motor actions and vocalizations. While brain stimulation techniques show promise in reducing tic severity, optimal target networks are not well-defined. Here, we leverage datasets from two independent deep brain stimulation (DBS) cohorts and a cohort of tic-inducing lesions to infer critical networks for treatment and occurrence of tics by mapping stimulation sites and lesions to a functional connectome derived from 1,000 healthy participants. We find that greater tic reduction is linked to higher connectivity of DBS sites (N = 37) with action-related functional resting-state networks, i.e., the cingulo-opercular ($r = 0.62$; $p < 0.001$) and somato-cognitive action networks ($r = 0.47$; $p = 0.002$). Regions of the cingulo-opercular network best match the optimal connectivity profiles of thalamic DBS. We replicate the significance of targeting cingulo-opercular and somato-cognitive action network connectivity in an independent DBS cohort (N = 10). Finally, we demonstrate that tic-inducing brain lesions (N = 22) exhibit similar connectivity to these networks. Collectively, these results suggest a critical role for these action-related networks in the pathophysiology and treatment of GTS.

Tics are typified by repetitive, sudden actions in the form of unwanted motor behaviour or vocalizations. Gilles de la Tourette syndrome (GTS) is a chronic tic disorder, wherein both motor and vocal tics occur. Tics can become so intrusive that they profoundly impede daily functions. This disruption may stem from interruptions of goal-oriented behaviour, the tics' social inappropriateness, or even the pain and self-harm they potentially induce. Deep brain stimulation (DBS) has repeatedly demonstrated potential in mitigating tic severity in treatment-refractory cases that do not respond sufficiently to pharmacotherapy and behavioural therapies. However, DBS outcomes remain heterogeneous[1,2]. One significant limitation of DBS for GTS has been the insufficient understanding of the optimal brain networks to be targeted.

Among movement disorders, tics have a unique phenomenology. Typically, tics are preceded by an aversive sensory phenomenon, the premonitory urge, that diminishes after tic execution[3]. Consequently, it is debated whether tics are involuntary or if they form a volitional motor response to an unwanted, pathological sensation[4]. The severity of tics fluctuates in response to environmental influences and mental states, e.g., aggravating during stress or mitigating during mindfulness

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