Title: Multiscale modeling of cortical information flow in Parkinson's disease

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The deep brain structures of the basal ganglia play a crucial role in the execution of movements, as demonstrated by the severe motor deficits that occur when one of these structures, the substantia nigra pars compacta, degenerates during Parkinson's disease (PD). However, motor commands themselves originate from the cortex, leading to the question of how the basal ganglia influence cortical information flow, and how this influence becomes pathological in PD.To address this issue, we developed a multiscale neuronal network/neural field model. The neuronal network consisted of 4950 event-driven rule-based neurons, divided into 15 excitatory and inhibitory cell populations in the thalamus and cortex, representing a patch of cortex approximately 1 mm in diameter. This model was then embedded in a neural field model encompassing the whole brain (roughly 30 cm in diameter), including the cortex, thalamus, and basal ganglia. Both network and field models have been separately validated in previous work, with both shown to produce realistic firing rates and spectra. Two field models were explored: one with parameters based on data from healthy individuals, and one based on data from individuals with PD. Spikes generated by these field models (which represent inputs from large-scale brain areas) were then used to drive the network model (which represents a small-scale region of association cortex). We then explored the multiscale influence of the field drive on the information flow and dynamics of the network. Compared to the network driven by the healthy field model, the PD-driven network had lower firing rates and increased power at low frequencies, consistent with clinical PET and EEG findings; it also had more spike bursts, indicating pathologically increased intracortical coherence. The PD-driven network showed significant reductions in Granger causality between cortical layers. In particular, the reduction in Granger causality from the main "input" layer of the cortex (layer 4) to the main "output" layer (layer 5) represents a possible explanation for some of the characteristics of PD, such as bradykinesia. These results demonstrate that the brain's large-scale oscillatory environment, represented here by the field model, strongly influences the information processing that occurs within its small-scale subnetworks.