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Presentation Abstract

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Title: Striatum as a possible source of exaggerated beta oscillations in Parkinson's disease: Insights from computational models

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Abstract: Prominent beta frequency oscillations appear in the cortex, pallidum and subthalamic nucleus (STN) in Parkinson's disease. Treatment with L-dopa both reduces Parkinsonian motor symptoms and decreases the beta rhythm. However, the mechanism by which these beta oscillations arise is unknown. We hypothesize that the source of these exaggerated beta rhythms may be due to alterations in the dynamics of the striatum. We construct conductance-based models of striatum to investigate the relationship between decreased striatal dopamine and the emergence of beta frequency oscillations. We simulate loss of dopamine indirectly through its effect on acetylcholine (ACh). Our models consist of combinations of medium spiny neurons (MSNs) and low-threshold spiking interneurons (LTS cells). We find that beta oscillations are already present in our model striatum in a normal, non-Parkinsonian state. The beta rhythm is brought about by an interaction between the MSN GABA_A current and the M-current. The M-current allows the MSNs to rebound spike in response to inhibition, and due to the time-constant of decay of the M-current, the MSNs as a population spike in the beta frequency range. Increasing ACh leads to increased beta power in the model LFP. ACh works in our models by lowering M-current conductance, thus increasing network excitability. Higher ACh allows individual MSNs to spike more frequently and therefore additional MSNs spike on each cycle of the beta rhythm. We also investigate a second potential source of beta frequency generation in striatum through the interaction of reciprocally connected LTS cells and their influence on MSNs. Through the same GABA_A/M-current interaction, LTS cells will spike anti-synchronously at a population beta frequency,

which in turn patterns MSNs into the beta frequency rhythm.

We have begun to test this model by directly manipulating the cholinergic influences in the striatum of awake mice, leaving other parts of the neural circuit unaffected. Preliminary data show that the addition of a muscarinic agonist to the striatum can evoke the beta oscillation. Further testing will pinpoint the regimes of cholinergic activation that enhance the striatal beta oscillation, and test the extent to which the striatum can support direct generation of beta oscillations. These results suggest that the exaggerated beta frequency oscillations in Parkinson's disease may be an amplification of normal striatal dynamics and that the effect of increased striatal ACh on MSN M-current may be responsible for their prominence in Parkinson's disease.

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Keyword(s): PARKINSON'S DISEASE

STRIATUM

BETA OSCILLATIONS

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