Listening to dopamine: a corticostriatal circuit model of auditory hallucinations

Kaushik Lakshminarasimhan[1], Justin Buck[2], Sean Escola[1,2], Guillermo Horga[1,2]

[1] Zuckerman Mind Brain Behavior Institute, Columbia University, New York, NY 10027

[2] Department of Psychiatry, Columbia University, New York, NY 10032

Abstract

Auditory hallucinations are a core symptom of schizophrenia. Although a leading theory implicates excess dopamine in the ventral striatum (VS), studies in patients demonstrate elevated dopamine in more dorsal regions. Parallel studies in rodents show that dopamine in caudal parts of the dorsal striatum – tail of striatum (TS) – is critical for auditory perception and stimulating TS dopamine afferents induces hallucination-like percepts characterized by high-confidence false alarms. Grounded in neuroanatomical findings showing segregated dopaminergic projections to VS and TS, we built a neural-level circuit model of corticostriatal loops for detecting the presence of a signal embedded in noise. In this model, VS-projecting dopamine encodes reward prediction errors to facilitate value learning, while TS-projecting dopamine encodes state prediction errors to facilitate learning of signal statistics from stimulus history both within and across trials. A recurrently connected cortical population combines sensory inputs with the TS output to dynamically compute a probabilistic belief about the presence of a signal, which is broadcast to striatal neurons thereby closing the corticostriatal loop. This model recapitulates experimentally observed differences between dopamine transients as well as neural dynamics in VS and TS, including their dependence on reward magnitude, signal probability and signal-to-noise ratio. Furthermore, stimulating dopamine in the TS but not the VS induced hallucination-like percepts in the model. Paradoxically, chronic TS stimulation yielded weaker effects than intermittent stimulation due to compensation by corticostriatal plasticity in the VS. The proposed model highlights the interplay between plasticity mediated by distinct dopamine pathways and provides a mechanistic basis for guiding the selection of novel targets for improving treatment efficacy.

Funding/Acknowledgement

The study was supported by the NSF NeuroNex Award DBI-1707398 and the Gatsby Charitable Foundation.