Complementary Cognitive Roles for D2-MSNs and D1-MSNs

Abstract:
Striatal pathways control motivation and movement; however, their role in cognition is unclear. We studied dorsomedial striatal cognitive processing during interval timing, an elementary cognitive task that requires mice to estimate intervals of several seconds. Interval timing involves working memory for temporal rules and attention to the passage of time. We discovered that both pharmacological and optogenetic disruptions of D2-dopamine receptor-expressing medium spiny neurons (D2-MSNs) or D1-dopamine receptor-expressing MSNs (D1-MSNs) delayed timing. Disrupting D2-MSNs or D1-MSNs did not affect task-specific movements. Furthermore, pharmacological blockade of D2-dopamine receptors or D1-dopamine receptors degraded dorsomedial MSN temporal encoding. We compared the timing-related firing of optogenetically-tagged D2-MSNs and D1-MSNs. Strikingly, we found that D2-MSNs and D1-MSNs exhibited opposite dynamics over temporal intervals despite similar effects of D2-MSN and D1-MSN disruptions. MSN dynamics helped construct and constrain a four-parameter drift-diffusion computational model that captured interval timing behavior and D2-MSN and D1-MSN perturbations. Despite opposing dynamics, disrupting either D2-MSNs or D1-MSNs slowed timing, implying that D2-MSNs and D1-MSNs make complementary contributions to interval timing. These data provide novel insight into basal ganglia cognitive operations beyond movement. Our findings carry implications for a broad range of human striatal diseases and for therapies targeting striatal pathways.

Bio:
Dr. Narayanan is the Juanita J. Bartlett professor of Neurology Research and Vice Chair for Basic and Translational Research in the Department of Neurology at the Carver College of Medicine in the University of Iowa. He also is an Associate Professor an Associate Director of the Iowa Neuroscience Institute, and Associate Director of the Clinical Neuroscience Training Program.

He is originally from Seattle, Washington. He received BA from Stanford University and received an MD and PhD from Yale Medical School, where he also completed a residency in neurology. He came to the University of Iowa in 2012 to launch his lab studying the basic mechanisms of prefrontal dopamine. He leads a multidisciplinary clinic focused on Parkinson’s disease.

He received the Donald B. Lindsley Prize for the best dissertation from the Society for Neuroscience, the S. Weir Mitchell Award for best residency research from the American Academy of Neurology, and the Jon Stolk Award for movement disorders research from the American Academy of Neurology.