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Reversible pathway selective inactivation in the macaques: behavioral and brain-wide functional effects

Rodent studies have demonstrated the role of the mesoaccumbal circuit in reinforcement-based learning. Importantly, however, while phasic activity of the ventral tegmental area (VTA) contributes to reinforcement learning, rodent evidence suggests that slow changes in tonic VTA activity and associated accumbal dopamine release help regulate motivational behavior. I my talk I will discuss results from a series of experiments performed in collaboration with the laboratory of Tadashi Isa from Kyoto University. In short, the consequences of sustained blockage of the mesoaccumbal circuit for motivation and reinforcement learning in macaque monkeys. Using a double-infection viral vector technique, we demonstrated that selective, unidirectional and reversible blockage of the primarily dopaminergic mesoaccumbal circuit in monkeys profoundly increased network-level functional connectivity as measured with resting state fMRI. Surprisingly, these global network changes were not associated with deficits in reinforcement learning during an object discrimination reversal task. In contrast, sustained mesoaccumbal inactivation greatly reduced motivation for performing an effort-based decision-making task. We can conclude that the mesoaccumbal pathway in primates is critical for high-effort motivation, but not for all forms of reinforcement-based learning.