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Learning and Memory Mechanisms of the Basal Ganglia: from Habits to Cognition

The same brain that can construct language, music and mathematics also lets us develop habits of thought and action. These semi-automatic routines free us to think and attend to the world. But the habit system can also be hijacked by disease and drug exposure. The Graybiel Laboratory focuses on the habit system of the brain and our remarkable ability to switch from conscious activity to nearly non-conscious behavior. The goal of this research is to understand how we make and break habits and how the neurobiology of the habit system is helping to advance understanding of human problems ranging from Parkinson's disease to obsessive-compulsive spectrum disorders and addiction. Clinical and experimental evidence suggests that our ability to acquire habits depends on the basal ganglia, deep forebrain structures that are interconnected with the frontal cortex in a series of loop circuits. The development of recording techniques for monitoring neural activity in awake, behaving animals now makes it feasible to investigate what forms of neuronal representation are built up in the basal ganglia and cortico-basal ganglia loops as habits are acquired. The lab's recordings from the striatum, the largest input side of the basal ganglia, suggest remarkable plasticity in the response properties of striatal neurons as animals learn sequential procedures and also as they undergo bouts of learning, extinction and reacquisition training. Single unit activity changes systematically through these bouts and so does ensemble activity. These results suggest that there is a form of 'neural exploration' followed by 'neural exploitation' in the basal ganglia as procedures are learned. After learning, the ensemble activity tends to emphasize the beginning and end of such procedures, as though setting up boundary states in higher-order representations. Such action-boundary representations can be found also in multi-electrode chronic recordings from the prefrontal cortex and striatum of primates. These and other findings support the

view that basal ganglia-based circuits can build representations of sequential actions that facilitate their release or inhibition. Emotion is an important guide to these behaviors, and the lab studies how the emotional and motor systems of the brain interact. The lab has developed the view that the basal ganglia can influence not only motor pattern generators, but also cognitive pattern generators. Evidence suggests that the laying down of such representations involves genes expressed in basal ganglia-related networks, and the lab is also pursuing promising molecular approaches to understanding learning mechanisms of the basal ganglia. The lab is actively working on genes that were cloned by the lab and that appear to be important for controlling behavioral exploration and repetitive behaviors. These findings are proving to have direct relevance to clinical disorders involving the basal ganglia. Disorders of such basal ganglia plasticity could contribute to behavioral fixity and difficulty of initiation of behavior, as in Parkinson' s disease, or to the excessive release of behaviors, as in Huntington' s disease, or to the repetitive behaviors and thoughts characteristic of many neuropsychiatric disorders.

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