The Basal Ganglia in Human Learning

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For many years, the basal ganglia were described in anatomy courses as strictly motor structures. Certainly, some of the most obvious and debilitating symptoms shown by persons with basal ganglia disorders are problems in motor control. However, the basal ganglia are not limited to motoric aspects of behavior: recent research shows that they are involved in most areas of cognitive and emotional functioning, consistent with their anatomical connections with all areas of the cortex. This review will focus on the roles of the basal ganglia in human learning, particularly sequence learning and category learning. Current areas of research that are discussed include the differing roles of different basal ganglia regions, patterns of interaction between the cortex and basal ganglia, differences in positive and negative association learning, effects of dopaminergic medication on learning, whether basal ganglia–mediated learning is implicit or explicit, and how the basal ganglia learning systems interact with other learning systems, particularly within the medial temporal lobe. NEUROSCIENTIST 12(4):285–290, 2006. DOI: 10.1177/1073858405285632

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The basal ganglia are interconnected with all lobes of the cortex and subcortical structures such as the superior colliculus. They are in a key position to modulate all aspects of mental life. Many common neurological and psychiatric disorders, such as Parkinson disease, attention deficit-hyperactivity disorder, Huntington disease, and Tourette syndrome are primarily due to basal ganglia dysfunction, and many other diseases such as schizophrenia and drug addiction have a large basal ganglia component.

Anatomy and Diseases of the Basal Ganglia

The basal ganglia consist of the caudate nucleus, putamen, globus pallidus, subthalamic nucleus, and substantia nigra; the caudate and putamen together are collectively known as the striatum. The basal ganglia interact with the cortex through independent processing loops in which cortex projects to striatum, striatum to pallidum, pallidum to thalamus, and from there back to cortex. These processing loops have functions that complement those of the cortical areas they interact with. Four loops that are relevant for human learning are diagrammed in Figure 1.

The two diseases of the basal ganglia that are most frequently studied are Parkinson disease and Huntington disease. In Parkinson disease, the dopamine projections from the substantia nigra to the striatum are lost. Without this dopamine input, the corticostriatal loops function abnormally. Degeneration of the substantia nigra in Parkinson disease typically begins in lateral portions of the substantia nigra and progresses to more medial portions (Dauer and Przedborski 2003). As a result, Parkinson disease initially affects the putamen and motor loop, then the head of the caudate and executive loop, and only in late stages of the disease reaching the visual and motivational loops. In Huntington disease, the striatum itself degenerates. Disease progression in the striatum is dorsal to medial, anterior to posterior, and medial to lateral (Lawrence and others 1998). The executive loop through the head of the caudate is one of the first affected areas.

Sequence Learning

Sequence learning is learning a relative sequence of events across time. It is vital for all aspects of human functioning, including sequencing of component movements in complex motor plans (e.g., dance), sequencing of grammatical elements in language, and sequencing of subgoals in complex reasoning (e.g., mental arithmetic).

The most common laboratory sequence learning task is the serial reaction time task. In this task, participants view four locations on a computer screen that correspond to four response keys. They are instructed to respond by pressing the corresponding response key whenever a stimulus appears at each location. Unbeknownst to the participants, the stimuli appear in a sequence, for example, 132431234214, where 1 to 4 denote the leftmost to rightmost screen locations, respectively. Learning is typically measured by comparing reaction time to stimuli presented in sequence with reaction time to randomly ordered stimuli.

Patients with Parkinson and Huntington diseases are impaired on the serial reaction time task, even when using variants of the task in which motor response demands are minimized (Smith and McDowall 2006). Neuroimaging studies using positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) typically report activation of the anterior putamen and head of the

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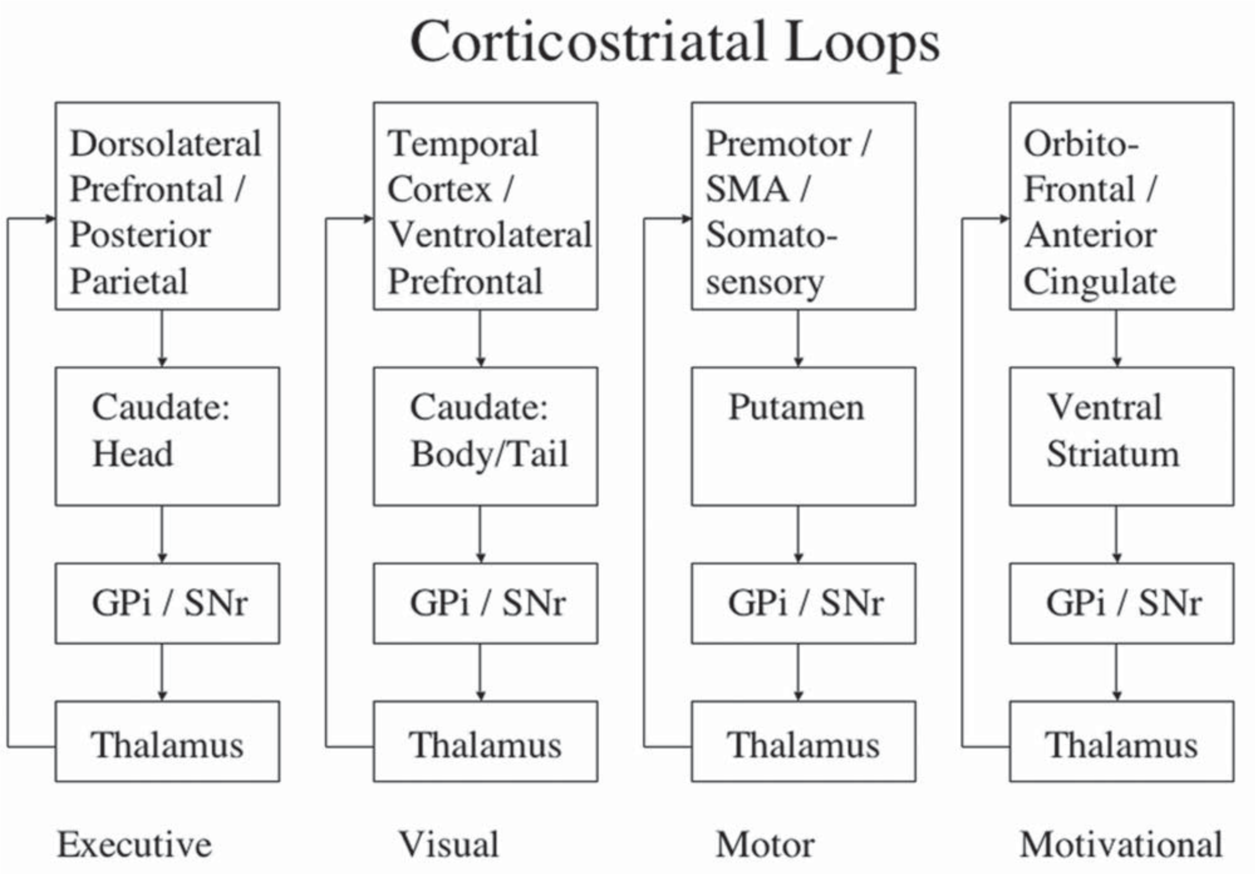

Fig. 1. Diagrammatic representation of four corticostriatal loops. Each loop connects cortical areas (*top* box) with striatal areas (second from *top*) and the output structures of the basal ganglia (*bottom* two boxes). For simplicity, only primary cortical projection sources are listed for each loop. SMA = supplementary motor area; GPi = globus pallidus, internal part; SNr = substantia nigra pars reticulata.

caudate (Peigneux and others 2000; Hazeltine and Ivry 2003), implicating the motor and executive loops in task performance.

In addition to the serial reaction time task, patients with basal ganglia damage are impaired on sequencing in other domains. Both Huntington and Parkinson disease patients are impaired in production of linguistic syntax (Lieberman 2000). The FOX-P gene, which has been linked to difficulties in sequencing during speech production, is expressed mainly in basal ganglia (Lai and others 2003).

Category Learning

Learning to categorize stimuli and associate them with appropriate responses is an important human capacity. It underlies our ability to choose appropriately (e.g., choose foods categorized as safe but avoid those categorized as poisonous) and to perform abstract inferences (e.g., if a particular food is categorized as poisonous, then a similar food may also be poisonous and should be avoided). The striatum, particularly the caudate nucleus, plays a key role in such learning.

Category learning is customarily examined in the laboratory by a variety of tasks in which participants view stimuli and learn which stimuli belong in which category by trial and error, that is, by making a response indicating the proposed category membership and then receiving feedback. Categorization tasks often vary, however, in the number of stimuli mapped to each response, the rules or patterns relating stimuli within each category, and whether the relationships between stimuli and responses are deterministic or probabilistic.

At its simplest, categorization is similar to stimulus-response learning studied in nonhuman animals. In both, the participant learns to respond to a particular stimulus with a particular response; the main difference is that in categorization many stimuli are mapped to each response, whereas in stimulus-response learning, there is typically a one-to-one mapping. Caudate lesions in rats and monkeys impair performance in tasks that require learning to repeatedly choose the same location or object in a particular testing context (Fernandez-Ruiz and others 2001; Packard and Knowlton 2002). Stimulus-response learning has been termed “habit learning” to differentiate it from forms of learning mediated by the medial temporal lobe, termed “memory” (Mishkin and others 1984).

Patients with compromised striatal functioning due to Huntington disease and Parkinson disease have been shown to be impaired on classification learning (Knowlton and others 1996; Shohamy and others 2004; Ashby and Maddox 2005). fMRI and PET studies in humans have found caudate activity in many classification tasks, which range in complexity from learning to respond to individual stimuli with arbitrary responses (Toni and others 2002) to associating multiple stimuli with varying features into two common categories (Poldrack and others 1999, 2001; Seger and Cincotta 2005).

Some kinds of category learning do not involve the basal ganglia (see Ashby and Maddox 2005 for a review). Learning single categories in which the stimuli are all visually similar to each other (sometimes termed prototype learning) can be learned without caudate involvement and is thought to rely on plasticity in extrastriate visual areas (Reber and others 2003). It is also possible to learn to categorize by memorizing the category membership of individual stimuli. Shohamy and others (2004) showed that people with Parkinson disease could learn to categorize stimuli via explicit memorization but were impaired in learning via feedback. Learning categories through memorization most likely relies on the medial temporal lobe (Poldrack and others 2001).

Current Areas of Research

Initial research in the field of basal ganglia contributions to learning focused simply on showing that the basal ganglia do play a role. Recent research has begun to ask more detailed questions. Here I will focus on six particularly interesting questions driving recent research: Do different corticostriatal loops contribute to different processes in learning? How do the cortex and striatum work together within the corticostriatal loops? Are positive associations learned via different mechanisms than negative associations? Does dopaminergic medication affect learning? Is learning mediated by the basal ganglia conscious (explicit) or unconscious (implicit)? How do basal ganglia learning systems interact with other learning systems, in particular, that performed by the medial temporal lobe?

Functional Specialization of Striatal Regions

Because each region of the striatum interacts with different cortical areas, it is plausible that different basal ganglia regions will be recruited during different learning tasks. Several recent studies have found that different types of learning are related to different corticostriatal loops. For example, learning about rewards involves the affective loop (including the ventral striatum and orbitofrontal cortex; Galvan and others 2005), and learning visual categories involves the visual loop (including the inferior temporal cortex and body/tail of the caudate; Ashby and Maddox 2005).

An emerging area of research identifies the roles of multiple corticostriatal loops within a single task. Using a visual categorization task, Seger and Cincotta (2005) dissociated the roles of the executive and visual loops. As illustrated in Figure 2, the body/tail of the caudate, which participates in the visual loop, was associated with learning: activity in this area was greater during correct classification than during baseline trials. In addition, activity increased along with the time course of learning, and good learners recruited this area more than poor learners. In contrast, the head of the caudate, which participates in the executive loop, was associated with executive functions such as feedback processing: this area was relatively more active when participants received positive feedback than when they received negative feedback.

Using the serial reaction time task, Poldrack and others (2005) found a distinction between the caudate and putamen. They compared performance before and after extensive training, in both single- and dual-task conditions. Activity in the putamen was affected by the presence of a sequence after training, but not before, indicating a role in sequence representation and skill performance. In contrast, caudate activation was greatest during dual-task learning conditions, indicating it was associated with executive functions involved in coordinating performance of two tasks at once.

Interaction between the Striatum and Cortex

Recently researchers have begun to ask how the striatum and cortex work together to support learning. Procedural learning theories of corticostriatal interaction postulate that habits are represented in the striatum and that the striatum is gradually "taught" what to do by the cortex (Graybiel 1998; Packard and Knowlton 2002). These theories imply that cortical activity should precede striatal activity across the course of learning. Other models argue that the striatum is important for recognizing the context of the situation, which then allows the cortex to choose and implement the proper learning strategy (Houk and Wise 1995; Frank and others 2001). These models imply that striatal activity should precede cortical activity. Recently, research using single-unit recording in monkeys (Pasupathy and Miller 2005) and fMRI with humans (Seger and Cincotta in press) has found evidence that striatal activity precedes frontal activity in the executive corticostriatal loop connecting the head of the caudate and lateral frontal areas. These results support the model that the striatum is important for recognizing the behavioral context and modulating activity in the cortex. Future research is necessary to see if the same pattern holds in other corticostriatal loops.

Positive and Negative Associations

The striatum is connected with the output structures of the basal ganglia via two parallel pathways, diagrammed in Figure 3: the direct pathway and the indirect pathway. The direct pathway has been termed the "Go" pathway because it facilitates expression of responses. In contrast, the indirect pathway, termed the "NoGo" pathway, inhibits expression of responses. Although dopamine is the neurotransmitter used in both pathways, the dopa-

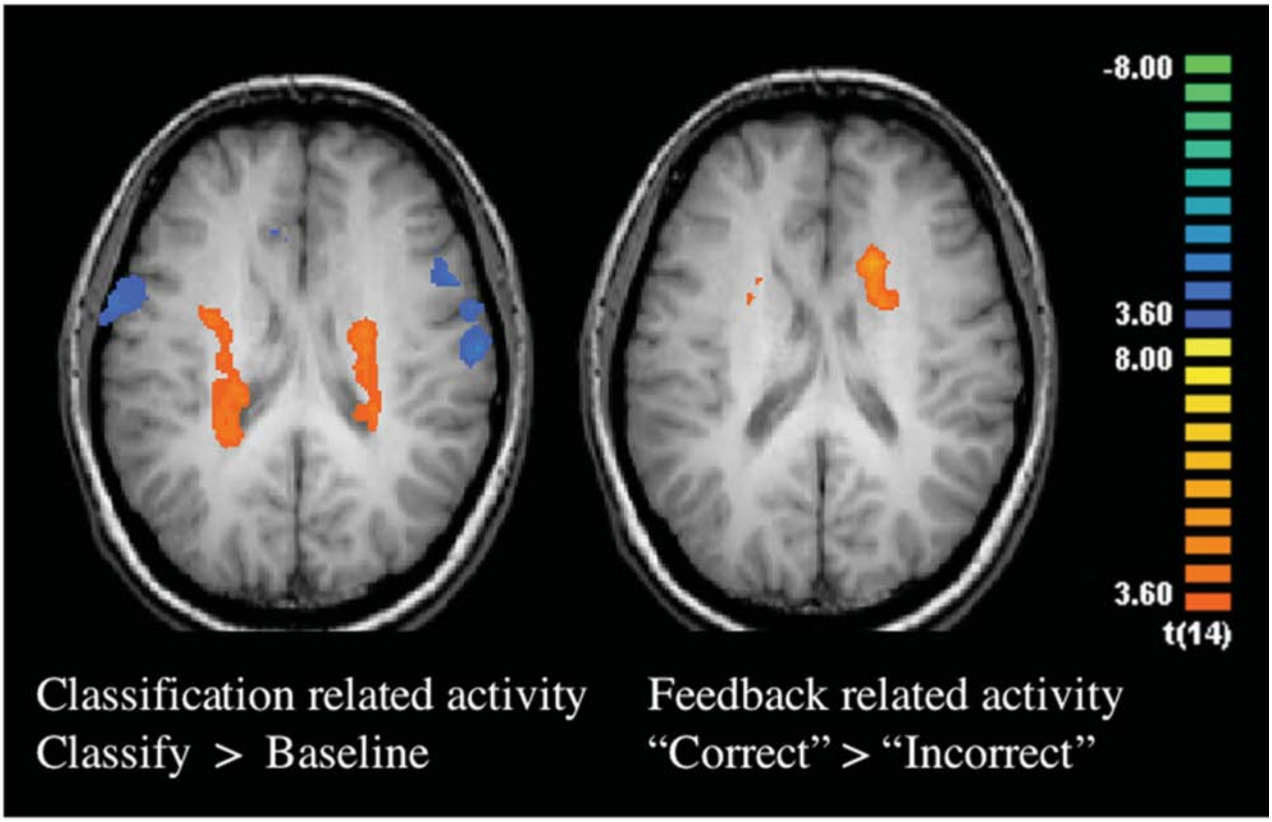

Fig. 2. Activity in different parts of the caudate nucleus associated with different aspects of task performance. *Left*, Activity in the body and tail of the caudate nucleus, elicited by a comparison of correctly categorized trials with baseline trials. *Right,* Activity in the right head of the caudate nucleus, elicited by a comparison of positive versus negative feedback to random trials. Activations are overlaid on a normalized high-resolution anatomical image from a single subject, at z = 19 in the coordinate system of Tailarach and Tournoux.

mine receptors differ: the D1 receptor is present in the direct pathway, whereas the D2 receptor is present in the indirect pathway. Recent research by Frank and colleagues (2004) has investigated how these pathways are involved in learning. They proposed that learning positive associations with stimuli (i.e., which stimuli to choose) should be controlled by the Go pathway, and negative associations (i.e., which stimuli to avoid) by the NoGo pathway. Frank and colleagues (2004) found that unmedicated Parkinson disease patients, who have particularly low activity in the direct pathway, were significantly impaired at learning positive associations but were able to learn negative associations at or above control levels.

Effects of Dopaminergic Medication on Learning

Typically Parkinson disease is treated with dopaminergic medication, which alleviates the bradykinesia and freezing that are so disabling. However, dopamine depletion in Parkinson disease is not equally severe in all portions of the striatum. The putamen and head of the caudate typically show higher levels of depletion than the body/tail of the caudate and ventral striatum. Dopaminergic medication raises dopamine levels in all areas of the striatum, with the result that some regions may reach higher than normal dopamine levels. Researchers have wondered what effects these medications might have on the functions mediated by the basal ganglia, particularly those that rely on neural systems that may experience higher than normal dopamine levels in medicated patients.

The literature so far is consistent with the hypothesis that if medication returns dopamine levels to normal in a particular region, learning associated with that region will be less impaired than when off medication. However, if dopamine levels are abnormally elevated in a region, learning will be impaired in comparison with off medication. Probabilistic reversal learning, a form of reward learning that relies on the motivational loop linking the orbitofrontal cortex and ventral striatum, is impaired in medicated Parkinson patients (Cools and others 2001). Sequence learning, dependent on the head of the caudate and putamen, is impaired in unmedicated Parkinson patients but normal in medicated patients (Shohamy and others 2005). Medication also improves performance on task shifting, a function of the head of the caudate and executive loop (Cools and others 2001).

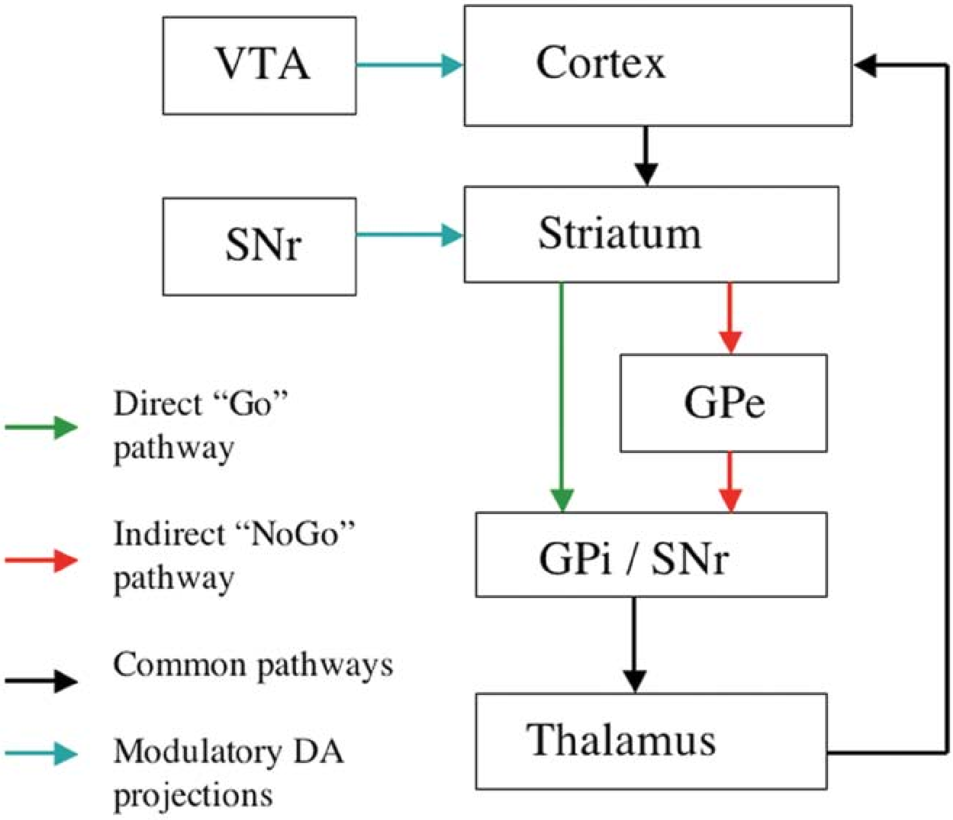

Fig. 3. Diagrammatic representation of the circuitry within each corticostriatal loop, including the indirect and direct paths and modulatory dopamine projections. DA = dopamine; GPe = globus pallidus, external part; GPi = globus pallidus, internal part; SNr = substantia nigra pars reticulate; VTA = ventral tegmental area.

In addition, dopaminergic medication differs in its effects on the direct and indirect pathways. Frank and colleagues (2004) found an opposite pattern of learning of positive and negative associations in medicated and unmedicated Parkinson patients: unmedicated were impaired at learning positive associations but unimpaired at learning negative associations; medicated were impaired at learning negative associations but unimpaired at learning positive associations. Further research is needed to identify the conditions under which medication enhances or impairs learning and whether these effects are large enough to have clinical significance.

Implicit and Explicit Learning

When the basal ganglia were initially identified as a locus of learning, they were categorized as an "implicit" learning system, in contrast with the "explicit" memory system supported by the medial temporal lobe. Explicit memory tasks are those in which patients are aware of and can verbalize what they have learned, whereas implicit learning involves learning without fully conscious, verbalizable knowledge of what has been learned (Seger 1994). Because the serial reaction time task and some categorization tasks were well established as implicit learning tasks via behavioral research, the equation between basal ganglia and implicit learning made sense at the time. However, recent functional imaging research challenges the view that medial temporal lobe–mediated learning is necessarily explicit and basal ganglia–mediated learning is necessarily implicit. Several studies have found medial temporal lobe activation during implicit sequence learning (Schenden and others 2003) and in implicit associative learning (Degonda and others 2005). Additional studies have found that the basal ganglia are recruited in explicit sequence learning tasks (Destrebecqz and others 2003; Hazeltine and Ivry 2003; Aizenstein and others 2004) and explicit categorization learning tasks (Seger and Cincotta in press) in addition to implicit versions of these tasks.

Interactions with the Medial Temporal Lobe Memory System

The existence of at least two human learning systems, the basal ganglia system and medial temporal lobe system, raises the interesting question of how these systems interact during learning. Do they cooperate in a synergistic way? Do they learn independently, in parallel? Or are they antagonistic, activating the system best suited for learning in each situation and suppressing the other system? There is functional neuroimaging evidence that indicates that at least in two tasks, a categorization task (Poldrack and others 2001) and an explicit rule-learning task (Seger and Cincotta in press), the striatum is recruited while the medial temporal lobe is suppressed. Further research is required to see if this pattern extends to other learning tasks before we can conclude that the systems are always antagonistic or whether the degree of antagonism varies dynamically depending on task demands.

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