Review

Computational Models of the Basal Ganglia

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Summary: Computer simulation studies and mathematical analysis of models of the basal ganglia are being used increasingly to explore theories of basal ganglia function. We review the implications of these new models for a general understanding of basal ganglia function in normal as well as in diseased brains. The focus is on their functional similarities rather than on the details of mathematical methodologies and simulation techniques. Most of the models suggest a vital role for the basal ganglia in learning. Although this interest in learning is partly driven by experimental results associating the acute firing of dopamine cells with reward prediction in monkeys, some of the models have preceded the electrophysiological results. Another common theme of the models is selection. In this case, the striatum is seen as detecting and selecting cortical contexts for access to basal ganglia output. Although the behavioral consequences of this selection are hard to define, the models provide frameworks within which to explore these ideas empirically. This provides a means of refining our understanding of basal ganglia function and to consider dysfunction within the new logical frameworks. Key Words: Basal ganglia—Computer model—Parkinson’s disease—Reinforcement learning.

Over the last decade a large number of models of the basal ganglia have been developed. A great proportion of these are demonstrated and explored through computer simulation. Many of the models not only address facets of basal ganglia dysfunction, such as Parkinson’s disease, but also attempt to place dysfunction into the context of normal basal ganglia operation. We describe three prominent classes of models, each of which can be aligned with different aspects of basal ganglia function and consequently views basal ganglia dysfunction from different perspectives. Shared among these classes is a common theme, the ability for the basal ganglia to detect contexts of cortical activity and respond to these contexts in terms of choosing sets of cortical activity, possibly for action by the motor system. The majority of models bring together the detection of cortical contexts with the selection or enhancement of cortical activity, which may be the selection of motor or cognitive actions or the modulation of activity in the generation of sequences of patterns. A broad selection of models will be outlined, demonstrating the diverse approaches in describing the functional properties of basal ganglia anatomy and physiology.

The models chosen for inclusion in this review describe basal ganglia function at the level of networks of nerve cells. This allows us to make comparisons at a similar level of functional description. All the models reviewed are based on or associated with basal ganglia pathways as shown in Figure 1. This diagram illustrates many of the predominant pathways within the basal ganglia and introduces the abbreviations used. Primary neurotransmitter types associated with each projection are also shown.

MODELS OF REINFORCEMENT LEARNING

The phenomenon of learning behaviors from rewards which act as reinforcement has been extensively modeled.¹,² Almost all models that ascribe a learning role to the basal ganglia are based on some form of reinforcement learning (a class of methods specifying how a sequence of actions can be learned through reward signals...
provided at the conclusion of the sequence). Recent experimental evidence suggests that the basal ganglia may mediate aspects of reinforcement learning. In a classic conditioning task, after a number of trials, dopamine neurons lose their response to the primary rewarding stimulus and at the same time gain a response to the conditioned stimulus. This observation has led to the adoption of a reinforcement learning algorithm of an engineering origin, called the Temporal Difference (TD) learning algorithm, as a description of basal ganglia learning.

Barto describes an application of the TD algorithm in the Actor–Critic model, which has been fitted to certain aspects of basal ganglia anatomy, physiology, and cytochemistry. The Actor–Critic model is split into two components, the actor and the critic (Fig. 2). The critic provides an “effective reinforcement” signal to the actor, which then learns behavioral responses to the environment using this signal. The objective of the actor is to learn to generate or select actions that maximize primary reward. However, the actor learns from instantaneous feedback. If the actor receives primary reinforcement directly from the environment and the arrival of reinforcement is delayed after the action that caused it (which is usually the case), the actor would then fail to associate the underlying action with the reward. This problem is called the temporal difference problem. The role of the critic is to learn to predict primary reward and produce a signal (called the “effective reinforcement”) that can be used as reinforcement by the actor so that the actor receives an effective reward to associate with the action just initiated. Thus, there are two learning systems here: the actor that learns to perform actions that maximize reward, and the critic that learns to predict rewards from the actions being performed and the current state of the environment.

It has been proposed that neural implementation of the actor is associated with striatal matrix compartments and that of the critic with striatal patch compartments and dopamine neurons of the substantia nigra pars compacta (SNC). The dopamine signal originating from the SNC plays the role of effective or predicted reinforcement. Properties of such a role have been identified in dopamine neurons. In the classic conditioning task mentioned above, dopamine responses move to the earliest predictor of reward (for example, the conditioned stimulus) providing a “critic-like” prediction of primary reward. Although the mechanisms shown in Figure 2 work through the direct pathway, the indirect pathway involving the globus pallidus external segment (GPe) and subthalamic nucleus (STN) is proposed to mediate the transfer of dopamine response from primary reinforcement to predictor.

This model of reinforcement learning has been explored in various ways in the context of basal ganglia architecture. A number of similar models examine the types of SNC dopamine neuron responses expected if
they are indeed producing the effective reinforcement signal. Properties predicted for dopamine neurons include a negative response when a reward that was predicted fails to occur at the time it was expected. Similarly, once dopamine response has moved to the earliest of a number of sensory cues that each predict reward, removal of one of the intermediate cues should result in a depression in dopamine response at the expected time of the cue. Both of these predictions have been observed experimentally. These models also make a number of assumptions. The majority of models of reinforcement learning assume a temporal representation of sensory cues. Within the cortical representation of the cue, there is a temporal component allowing the explicit representation of time from cue onset to reward. Such a representation of cue inputs to the striatum is by no means certain. Furthermore, the models require an input of primary reward signal to the nigral dopamine neurons. The origin of such a signal is unclear.

Suri and Schultz demonstrate the ability of an Actor–Critic model to learn sequences of pattern associations. For example, stimulus A requires action Q, after which stimulus B is presented requiring action R, and so on. Reward is only received when the final required action in the sequence is performed and all preceding action associations in the sequence were correct. The model illustrates how the temporal difference algorithm yields learning of long patterns of associations. They further demonstrate that replacing the effective reward signal, that is, the prediction of primary reward, with primary reward itself leads to a failure in learning long sequences of associations. This illustrates the value of a predicted reward signal in long sequence learning.

Nigral dopamine neurons respond not only to rewards, but also to novel or unexpected stimuli. Consequently, within the context of these models, novel stimuli are considered to be rewarding events. Unexpected visual stimuli lead to early dopamine responses and saccadic eye movements. Redgrave et al. argue that because the dopamine response occurs before completion of the saccade to the visual location of the stimulus, such an event should not be considered a reward before its visual identification. However, because dopamine neuron responses do not discriminate among different reward modalities, Schultz suggests the dopamine response may represent a reward alert signal rather than the reward itself. It seems likely that the “critic” would need to be biased in this way to facilitate the associations of new stimuli and the prediction of reward.

There are a small number of reinforcement learning models of the basal ganglia that are not based on the Temporal Difference algorithm. These models focus on the basal ganglia circuitry and use a simpler form of reinforcement learning. Dominey et al. demonstrate this in a model of the interaction among cortex, basal ganglia, and thalamus. The model is considered with respect to visuospatial tasks requiring saccadic actions. Figure 3 illustrates the circuitry simulated in this model. The system consists of various cortical representations of the current visual field. In the model, saccades may be controlled through a direct projection from the frontal eye fields (FEF) to the superior colliculus (SC). The basal ganglia modulates this effect in response to learned cortical contextual activity. For example, in a conditional visual discrimination task in which the model must learn to generate saccades to one of two cues (only one of which is rewarded), the basal ganglia learns through reinforcement learning to disinhibit only the correct response represented in the superior colliculus. In learning sensorimotor sequences, the model prefrontal cortex architecture is designed so that each point in the sequence holds a unique pattern of activity. This provides a novel context for the striatal neurons to differentiate one item in the sequence from the next.

Reinforcement learning has become a major component of many contemporary models of the basal ganglia. However, these same models highlight many issues yet to be addressed. For example, there is no clear consensus for the role of the indirect pathway. The simplicity and elegance of the reinforcement learning paradigm is more easily associated with the direct pathways as sites for implementation. The indirect pathway may be better described as an indirect network within which there is the likelihood of complex dynamics, and its role in reinforcement learning models remains unclear.
At first sight, models that emphasize a role for learning in the actions of dopamine in basal ganglia function argue against the clinical data. What has learning to do with the obvious neurologic problems of Parkinson’s disease? Surely, no one thinks that not being able to get up from an armchair or freezing in the middle of the road is a problem of learning. One solution to this dilemma has been to assign dopamine two roles in the striatum. One role is phasic, requiring a burst of activity in nigral cells, perhaps with actions at D$_1$ receptors, being the one involved in learning. The other role is tonic, in which low-level dopamine is the result of the resting firing level of dopamine cells. 1-Dopa, probably acting more on D$_2$ receptors, replicates this action. The absence of this tonic activity is likely to be the cause of the neuropathology. This dual functional role of dopamine is implemented explicitly in the models of Dominey et al.

A more elegant solution is to assume that the presence of low dopamine levels is a valid reinforcement signal. For example, in the absence of reward presentation, yet when the reward is expected (that is, predicted), there is a suppression of dopamine activity. Under the TD interpretation, this is an error signal that indicates that less reward than expected has occurred. Consequently, the actions that led to this will be less prone to be chosen in the future. Under parkinsonian conditions, such an interpretation would label every selection of a corticostriatal connection delays, the activity pattern across the STN is at least one time step behind that being imposed on the GPi. Thus, learning associates the previous step in a temporal sequence across the STN with the current step over the GPe and the output units of the globus pallidus internal segment (GPi). The GPi then feeds back to the STN, thus becoming the previous step in the sequence. As the GPi feeds back to the STN, this allows the learning and generation of sequences. Once learned, the activity of the STN (the previous step in the sequence) generates the activity pattern of the current step over the GPi and the output units of the globus pallidus internal segment (GPi). The GPi then feeds this current step onto the STN, thus becoming the previous step, and the cycle continues. Learning is implemented through a reinforcement algorithm allowing the effects of dopamine to be assessed in a simple manner. Loss of dopamine is modeled through a global reduction in learning rate, leading to deficits in the sequence learning.

MODELS OF SERIAL PROCESSING

One of the characteristic anatomic features of the basal ganglia is the observation of loops. Cortical-basal ganglia-thalamic-cortical loops have raised the idea of a functional role in serial processing. Early neural network models of loops have been used to learn and perform serial tasks, and they have given rise to some early models of the basal ganglia. The possible involvement of the basal ganglia in movement control and planning has long provided a motivation for predicting serial processing capabilities. Planned sequences of motor actions not only require sequential processing abilities, but also representations of sequential events. A role in motor operations and the nature of basal ganglia loops taken together have provided a powerful motivation for basal ganglia models of serial processing.

Like we have seen above, the roles of serial processing and reinforcement learning in the basal ganglia are compatible. In the Suri and Schultz model, the environment provided the cue to the next item in the sequence, whereas in the models of Dominey et al. an internal representation of a sequence is generated across the prefrontal cortex. This internal representation can then be used to reproduce the sequence. Beiser and Houk present a model of the direct pathway being used in the generation of representations of such temporally serial events. They propose that the basal ganglia acts as an encoder, processing serial events into a spatial representation of prefrontal cortex activity. Medium spiny neurons of the caudate play the role of context detectors. Because each receives up to 10,000 different corticostriatal afferents, this places these striatal neurons in an optimal position for such a role. The model prefrontal cortex receives (preprocessed) stimuli from the environment resulting in an initial pattern of activity. Lateral inhibition among medium spiny cells in the caudate allows only a limited number of medium spiny neurons to respond to this activity pattern. Those that do respond disinhibit thalamic neurons, engaging a sustained recurrent activity between the thalamus and cortex. The thalamic input, together with new stimuli to the prefrontal cortex, modifies its pattern of activity. This new prefrontal pattern of activity in turn augments the caudate responses. Beiser and Houk demonstrate how this continued looping process builds unique representations of the serial stimuli in the prefrontal cortex.

An alternative to the cortical location for short-term memory in the production and encoding of sequences is illustrated in a model by Berns and Sejnowski. In this model, the subthalamic–pallidal loop is proposed as a site for such short-term memory. During learning, the striatum repeatedly imposes a temporal sequence pattern on the GPi (through direct inhibition). As the input to the STN arises from the GPi and is given significant connection delays, the activity pattern across the STN is at least one time step behind that being imposed on the GPi. Thus, learning associates the previous step in a temporal sequence across the STN with the current step in the GPi. As the GPi feeds back to the STN, this allows the learning and generation of sequences. Once learned, the activity of the STN (the previous step in the sequence) generates the activity pattern of the current step over the GPi and the output units of the globus pallidus internal segment (GPi). The GPi then feeds this current step onto the STN, thus becoming the previous step, and the cycle continues. Learning is implemented through a reinforcement algorithm allowing the effects of dopamine to be assessed in a simple manner. Loss of dopamine is modeled through a global reduction in learning rate, leading to deficits in the sequence learning.
The capacity to generate sequences of activity patterns has also been proposed solely within the architecture of the striatum. Wickens and Arbuthnott demonstrate that lateral connectivity within the striatum can be used to generate spatiotemporal patterns. In their model, inhibition by one medium spiny neuron of another occurs through axon collaterals among medium spiny cells sufficiently close to one another (termed the "domain of inhibition"). The model demonstrates that with uniform random input, usually only one medium spiny neuron is active within a domain as a result of the mutual inhibition. Furthermore, as a consequence of a slowly increasing after-hyperpolarizing conductance, the active neuron may eventually become inactive, allowing an alternative neuron within the domain to begin firing. Although the generation of these spatiotemporal patterns is strongly dependent on external input, this model demonstrates the ability for a lateral inhibitory network to generate local spatiotemporal patterns. The nature of the patterns depends on the strength of the after-hyperpolarizing conductance. Inclusion of inhibitory interneurons increases the stability of the spatiotemporal patterns. This idea has been extended to use the up and down state properties of medium spiny neurons in a model of basal ganglia control of cortical sequential activity.

Connolly and Burns describe a model that represents matrix compartments within the striatum as a network of linked resistors. Anatomically this would assume electrotonic coupling between the medium spiny neurons. There is evidence for a weak electronic coupling as a result of dye spread to several neurons from intracellular electrodes. However, gap junctions have primarily been seen in the electron microscope between parvalbumin-positive interneurons. In this model, the corticostriatal input sets up goal and boundary conditions over the resistance network corresponding to, for example, target and obstacle positions, respectively, in the real world. The goal and boundaries are represented by clamped trough and peak voltages, respectively, setting up a voltage landscape. Under the assumption of a direct representation of limb position in the striatum, this creates a trajectory of activity following a gradient and avoiding the boundaries (voltage peaks). It is proposed that the temporal activity sequence generated provides an optimal movement trajectory within the context of the imposed boundaries. This model depends critically on a direct representation of limb position in the striatum.

Contreras-Vidal and Stelmach present a model that places the basal ganglia circuitry directly as a "GO" signal for movement (Fig. 4). Although in this model the basal ganglia does not generate sequential activity, it plays the role of providing a measured gating signal to a theoretical model that computes the differences between a target position vector and a present position vector of a limb. The output of the model basal ganglia circuitry gates the rate of the integration between target and present position vectors. As the system captures the influence of basal ganglia circuitry on the vectors representing changing limb position, direct comparisons can be made to experimentally measurable phenomena such as reaction time and movement time. This model includes both direct and indirect pathways and consequently, the effects that parkinsonism-type conditions have on these experimentally measurable parameters can be gauged. The parkinsonian conditions simulated follow that described by Albin et al., in which striatal activity along the direct pathway (that is, the pathway associated with substance P) is diminished and striatal activity along the indirect pathway (that is, associated with enkephalin) is enhanced. Under these conditions, the model replicates certain parkinsonism phenomena. For example, as dopamine levels decrease, both task reaction time and movement time increase. For low levels of dopamine, the model fails to gate all movements and akinesia-type behavior results. The model thus demonstrates a single mechanism for both bradykinesia and akinesia.

Because the mechanisms underlying these various models of serial processing are different, so too are their descriptions of how basal ganglia disorders influence processing. For example, Wickens et al. explore the effects of dopamine on the activity within domains of inhibition in the striatum as described above. By modeling particular channel conductances within striatal me-
medium spiny neurons and incorporating the influence of the large aspiny cholinergic interneurons, Wickens et al. demonstrate a dramatic change in the functioning of the domains of inhibition under conditions of low dopamine. As described above, a single neuron within such a domain is likely to be active as a result of competition from the inhibitory lateral interactions. Under conditions of reduced levels of dopamine, the model demonstrates co-activation of neurons within a domain. It is proposed that adjacent neural populations may represent antagonistic muscles and consequently, coactivation may be associated with symptoms such as rigidity.

MODELS OF ACTION SELECTION

The major output nuclei of the basal ganglia (GPi, substantia nigra pars reticulata [SNr]) exhibit a tonic activity that exerts an inhibitory influence over their targets. Because activity along the direct pathway leads to disinhibition of these targets, it has been proposed that this allows the selection of specific motor programs.34,35 A focused disinhibition surrounded by inhibition on targets would allow this process to be finely tuned. In this theoretical model, the tonic inhibition can be maintained or enhanced through the STN by way of the indirect pathway providing widespread excitation to the output nuclei.35 Such an elegant center-surround model of basal ganglia processing has provided motivation for the role of the basal ganglia in selection of actions or motor programs. This idea has been extended by Redgrave et al.11,36,37 so that the basal ganglia may be considered a general resource selection mechanism.

The arguments for such a centralized resource selection system are posited from an engineering efficiency perspective. A central system saves the need for combinatorially massive connections between each competing resource. It simply requires each resource area to connect to the central mechanism. The projections from widespread cortical areas to the striatum certainly encourage such a view. Figure 5 illustrates the central selection model presented by Gurney et al.36 within the context of the basal ganglia circuitry. Cortical input to the striatum is described in terms of “channels,” where each channel refers to a competing resource or action, and originates from the (cortical) neural substrate responsible for processing it. Channels are assumed to carry salience information so that at the striatal level, competition among medium spiny neurons is determined by salience. The model is split into selection and control mechanisms. The direct pathway in cooperation with signals from the STN mediates selection. Local competition within the model striatum solves local resource conflicts leaving a single channel active. For example, under a somatotopic representation this may resolve conflicts for a common motor resource. The activity of the local winning active channel represents that channel’s salience. Consequently, output from the striatum can be used in global resource competition. The direct projection from the striatum to the output nuclei (GPi, SNr) inhibits the channel zones in these nuclei in proportion to the saliences of the competing channels. The STN provides a diffuse and uniform excitation to channel zones over the output nuclei. This diffuse excitation from the STN combined with inhibition from the GPe scales the activity of the output nuclei so that only the channels with the highest saliences remain sufficiently depressed to disinhibit the targets and thus perform selection. Within the control pathway, feedback from the GPe to the STN scales STN activity making it independent of the number of competing channels.

The effects of dopamine are included in the model through the division of striatum into medium spiny neurons with D1 or D2 receptors. In agreement with Albin et al.,32 dopamine inhibits the D2-mediated pathway and facilitates the D1-mediated pathway. Thus, a reduction of dopamine enhances the control mechanisms and suppresses the selection mechanisms. As the level of dopamine is reduced in the simulations, the possibility of multiple channel selection also reduces. If the selection of multiple channels corresponds to the selection and operation of two or more simultaneous behaviors, then the effects of reduced dopamine in the model is consistent with the phenomenon of “loss of associated movements” in early Parkinson’s disease. Low levels of do-

FIG. 5. Schematic diagram indicating the connectivity in the model of Gurney et al.36 Solid lines indicate an inhibitory connection; dotted lines indicate an excitatory connection.
pamine in the model prevent selection of any action or resource. This has been proposed as being consistent with akinesia. As dopamine levels increase, so do the possibilities for several anomalies. In addition to the correct selection of the highest salient channels, in the model with intermediate dopamine levels there is a possibility that two highly salient channels cause each other to fail to be selected. This results in neither channel being chosen. In the conditions of high levels of dopamine, many competing channels with high salience may be selected. These behaviors can be undesirable in a selection system. Although these anomalies may be loosely associated with certain behavioral conditions (for example, possibly schizophrenia), their interpretation as experimentally predictable behavior is still unclear.

**DISCUSSION**

The models reviewed range not only in their functional descriptions of the basal ganglia, but also in their method of description. For example, in the models of Dominey et al.,13,14 a single neuron is described as a continuous time differential equation, whereas in the Suri and Schultz9 model, a single neuron is a summation unit and time is discrete. Modeling a single neuron as a simple differential equation or as a logic function imposes limitations on how the resulting network models should be interpreted. For example, as mentioned above, depletion of dopamine is modeled simplistically. With one exception, none of the models capture the effects of dopamine on striatal cells. Consequently, these models have limited informational value at this level. It is increasingly possible to model neurons at more detailed biochemical levels; however, this is only in the early stages of being extended into networks of cells. As another example, all of the models include pathways between structures without recourse to the known anatomic variations within these pathways such as preserved topology.38 Thus, the brush strokes with which the models currently describe basal ganglia function are broad. Nonetheless, they provide a unique framework on which to build.

The three themes of models presented here share much in common. Collectively, there is an emphasis on the importance of learning, in particular, reinforcement learning, to the function of the basal ganglia. Reinforcement learning is not only posited as a function in itself, but is also consistent with models of the serial processing and action selection themes. Learning through reward plays a key role in the development of context detection or selection of cortical activity. Cortical activity related to a future increase in reward is hypothesized to evoke a stronger striatal response on subsequent occurrences. This stronger response may influence its chance of behavioral selection or enhance the original cortical activity in the production of learned cortical activity. However, the mechanisms of learning, such as the representation of error in reward prediction in dopamine responses, are still debated.

At a functional level, sequencing and action selection models are compatible. It is possible that the selection of cortical activity would also involve its modification, consequently influencing its future selection. This may stabilize selections as suggested by Redgrave et al.37 or alternatively allow selection of the appropriate next behavioral set in a sequence.

These extensions of ideas extracted from the models have the same limitations as the models themselves. Not only are the models pitched at a high level as described above, but they also make implicit or explicit assumptions yet to be experimentally verified. The majority of models rely primarily on the direct pathway. The complexities of the indirect pathway and the current shifting of our understanding of its anatomy and physiology make it a difficult system to model. However, it is clear that the indirect pathway plays a crucial role in basal ganglia function, and it is important that this be increasingly addressed in basal ganglia models. Another common feature of many of the models is the assumption of lateral inhibition within the striatum. All the current models rely to a greater or lesser extent on the interconnectivity of the striatal neurons. Although anatomic data supports this,39 there is no physiological confirmation of mutually inhibitory connections between cells in the neostriatum.40 Other aspects of the anatomic pathways underlying many of the models (see Fig. 1) are similarly subject to criticism. For example, there is increasing evidence for multiple corticostriatal pathways20,41,42 in which functional significance is not yet addressed in any of the models. In addition, the interpretation of the loss of dopamine in Parkinson’s disease, as described by Albin et al.,32 is also still under active debate.

However abstract, all the models reviewed have important ideas to convey. Although the physical models have many operational inconsistencies with each other, they provide a framework within which basal ganglia functions are beginning to be structured. The development of models needs to be extended to lower levels. For example, only the models of Wickens et al.33 capture detailed anatomy within a single nuclei. Recent models of the STN and GPe16,43 have demonstrated that the anatomic arrangements within a nucleus can be crucial to how the nucleus operates within the basal ganglia as a whole. Models of lateral connectivity within the STN
demonstrate that this can functionally lead to widespread switch-like behavior across the nucleus. This has important consequences for how other basal ganglia nuclei may operate in this context. For example, it has further been shown that under parkinsonian conditions, as described by Albin et al., this switch-like behavior in the STN can lead to continuous oscillations of bursting-like activity in both the STN and GPe. These models demonstrate not only functional constraints on STN operation, but also the importance of considering multiple levels in model development. It is an exciting prospect that modeling will continue to provide increasingly detailed frameworks within which the full extent of basal ganglia function may eventually emerge.

REFERENCES


