Role of Basal Ganglia in Initiation of Voluntary Movements

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Abstract. A motor system called the basal ganglia facilitates movement initiation by receiving its powerful influence on other motor areas. It may also facilitate activity in the cerebral cortex with disinhibition and ensure sequential processing of sensory signals.

Multiple brain areas related to saccadic eye movement

A brain structure called the basal ganglia is an assembly of several nerve cell nuclei located at the base of the brain. It has been well known that nuclei of the basal ganglia are indispensable for us to move our body parts. A number of brain diseases, such as Parkinson's disease or Huntington's disease, affect the basal ganglia and thus render victims unable to move or unable to suppress involuntary movements. Different types of approaches have clarified that the basal ganglia are intimately connected with the cerebral cortex and that neurons in different nuclei of the basal ganglia indeed carry saccadic signals [1]. Given many beautiful brain images repeatedly revealed with modern anatomical techniques, however, I am aware that our understanding of the brain is far from complete. It is probably in the connection of neurons as a whole, rather than fine structures of individual brain nuclei, where we can find appropriate language to describe the functions of the brain. In this article I attempt to characterize the major function of the basal ganglia, especially with reference to the neuronal networks between the basal ganglia and the cerebral cortex.

A suggestion that the basal ganglia might be related to eye movement came from the discovery that the substantia nigra, a part of the basal ganglia, has fiber connections to the superior colliculus [3, 14]. A number of brain areas are related to saccadic eye movements. In the cerebral cortex are the frontal eye fields [1], parietal association cortex, and the recently found supplementary eye field [19]. The frontal eye field, especially, has been related to "voluntary initiation" of saccadic eye movements. A subcortical structure in the midbrain called the superior colliculus has optic tectum in another important area for saccadic eye movements [21, 22].

The output of the superior colliculus is disinhibited in the brainstem reticular formation which conveys brainstem neurons generating a saccade to a saccadic eye movement. The signal processing occurring along this sub-cortico-reticulo-thalamic pathway is purely motor. The question I wanted to solve was any further upstream in the oculomotor signal processing. It was how a saccadic eye movement is initiated, not just how it is generated.

Superior colliculus mediates saccadic oculomotor signal

Before going into the basal ganglia, I would like to show the basic function of the superior colliculus (Fig. 1). The superior colliculus is a small portion of the brainstem and is a laminated structure. The superficial layer consists of direct fiber connections from the retina in a retinotopic manner, and the cells here respond to a visual stimulus within a small area in the contralateral
visual field called "visual receptive field" and are therefore purely visual.

The intermediate layer, on the other hand, is largely motor. The cells show a burst of spike activities before a saccadic eye movement if it is directed to an area in the contralateral visual field called "movement field." This saccadic motor signal is sent to the brainstem reticular formation and is shaped up to be a pulse output to the extracocular muscles. There is a beautiful matching between the visual receptive field in the superficial layer and the movement field in the underlying intermediate layer.

It might appear from this scheme that a visual signal originating from the retina could be converted to a saccadic motor signal via a top-to-down tectoreticular connection. This might occur in special occasions, especially in lower animals, but what's happening is not really that simple [21]. The superior colliculus is a crossroad of sensory-motor signals and has massive, heterogeneous connections with other cortical and subcortical structures. Two major inputs to the intermediate layer have been identified, those from the frontal eye field [12] and thence from the substantia nigra [14], and they have contrasting effects on the superior colliculus.

![Diagram of fixation and saccade](image)

Fig. 1 Role of the superior colliculus in the initiation of visually guided saccade. If a light stimulus (target) is presented in the right visual field (left), cells within a small area in the superficial layer of the left superior colliculus (designated by V) are activated. This is followed by a burst of spikes in the cells in the underlying intermediate layer (S)(right). This information is sent to the brainstem saccade generator on the right side and is used to generate a saccade to the target. The temporal activities of these cells are shown schematically on the bottom.

It is not easy to demonstrate that a neuron has a motor role. The animal must be free to move voluntarily, yet the relationship between the electrode and the neuron must be kept stabilized. The animal's head must be immobilized especially when eye movements are studied. The animal must be trained to repeat voluntary movements. Robert H. Wurtz [24] devised an ingenious method to
counsel animal's eye movements, as shown in Fig. 2. Here, if a monkey, sitting in a chair, press a lever, a small spot of light appears at the center of the screen in front of the monkey. After a random period of time the light spot becomes slightly dim for a brief period, and if the monkey releases his hand from the lever he gets rewarded with a drop of water. If the spot jumps to another location, the monkey naturally moves his hand of light to reilluminate the spot by making a saccadic eye movement. While the monkey was performing this kind of task, we inserted a microelectrode into the retinal ganglion to record electrical activity of single neurons. This is how we investigate function carried by neurons.

**Substantia nigra interna superior colliculus**

The pars antagonista of the substantia nigra (SNi) is one of the most active areas in the brain. Neurons in this region show saccadic potentials (slowly) with the rate of up to 100 times per second. They do so even when the animal is sleeping. Such high background activity points to an important aspect of basal ganglia function, which I will show later.

![Fig. 2 Saccade task. A and V indicate saccadic horizontal and vertical eye positions.](image)

Fig. 3 shows spike activity of a single substantia nigra neuron. The monkey repeated successions of visual target contrasts to the side where the neuron was recorded. The results are shown as a raster display. Like other substantia nigra neurons, this neuron showed tonic high frequency theta discharges, but stopped discharging after the onset of the target (6-8). The creation of the cell activity was followed by a saccade to the target. Nearly half of substantia nigra neurons showed essentially the same pattern of activity change. It could be a visual response to the saccade target or could be a motor response time locked to the saccade itself. Now, what does this mean?
I can answer this question by comparing the substantia nigra activity with superior colliculus activity, as illustrated in Fig. 4. The upper part shows activity of another substantia neuron, and the lower part shows activity of a superior colliculus neuron. They are aligned on the onset of saccade, but in this case saccade to a remembered target. I compared these two neurons because Robert Wurtz and I were able to prove electrophysiologically that the substantia nigra neuron projected its axon to the site where the superior colliculus neuron was recorded, therefore presumably connecting to this very neuron [9].

![Diagram of eye position and saccade-related activity of substantia nigra and superior colliculus neurons](image)

A striking feature is evident from this comparison. While the substantia nigra neuron was cortically active, the superior colliculus neuron was nearly silent. Before the saccade, the substantia nigra neuron stopped discharging while the colliculus neuron showed a burst of spike activity. This result strongly suggested that the nigrocollicular connection is inhibitory [15].

When the monkey is not making an eye movement, substantia nigra neurons keep inhibiting superior colliculus neurons with their high background activity. In fact, the relationship is probably re-versed: because of the tonic inhibition, the superior colliculus neurons are disabled so that no saccade is elicited. Once the substantia nigra neurons stopped discharging and the tonic inhibition is removed, the superior colliculus neurons get ready to be excited and therefore are likely to produce a saccade.

The next question was obviously how the substantia nigra neurons stop discharging. The substantia nigra is one of the two major output stations in the basal ganglia, and is known to receive fiber connections from other parts of the basal ganglia. The caudate nucleus is one of these areas.
Basal ganglia may initiate a movement by disinhibition

In contrast to the substantia nigra, the caudate nucleus is an extremely quiet area. When inserting a microelectrode into the caudate, we passed by many neurons without noticing their presence simply because they did not show a single action potential. Nonetheless, Masahiro Sakamoto and I found a cluster of neurons that were related to saccadic eye movements [4].

![Diagram showing SNr and SC connections]

**Fig. 4.** A substantia nigra cell (SNr) decreases while a superior colliculus cell (SC) increases its activity before a conjunctional saccade. A vertical bar on each plot line indicates the onset of target.

![Activity plots showing neuronal response to saccades]

**Fig. 5.** Activity of a caudate cell selectively related to memory-guided saccades. On the left, while the monkey was fixating, another spot of light (T) was flashed indicating the position of a future target. The monkey remembered its position and, when the fixation point (F) disappeared, made a saccade to the position. On the right, the target appeared as the fixation point was off; a following saccade was guided by the visual information. Calibration: 50 and 100 spikes/sec/trial.
Fig. 5 shows an example. This typically quiet caudate neuron showed spike discharges just before a saccade to a contralateral target, only when it was remembered (fly). If we stimulated the site where this caudate neuron was recorded, the activity of saccade-related nigra neurons was suppressed. This experiment strongly suggested that the saccade-related depression of substantia nigra cell activity is the result of an inhibition by caudate neurons including this one.

From these experiments emerged a scheme shown in Fig. 6. The caudate nucleus and the substantia nigra are both included in the basal ganglia. They constitute two serial inhibitions: caudate-nigral and nigro-collcular. The nigro-collcular inhibition is tonic type whereas the caudate-nigral inhibition becomes active only phasically. Therefore, disinhibition is the way in which the caudate acts on the superior colliculus, and the substantia nigra determines the depth of the inhibition to be released. Functionally, this disinhibition acts to open the gate for saccade initiation. But this is not the sole function of the basal ganglia, as I will show later.

![Diagram](image)

Fig. 6. Neural mechanisms in the basal ganglia for the initiation of saccades. Excitatory and inhibitory axons are indicated by open and filled circles, respectively. SC: superior colliculus. FEF: frontal eye field. PS: putamen area. SN: substantia nigra. SC: saccade generator in the brainstem reticular formation. The 'stem' of substantia nigra (SN) neuron is more darker than others to indicate its high background activity.

Fig. 7 extracts the basic mode of operation of the basal ganglia, that is, disinhibition. There are two important aspects in this scheme: a tonic component and a phasic component. The tonic component acts to suppress the output. This is necessary because the superior colliculus is continually under exogenous bombardments from a number of brain areas and without this suppressive mechanism the animal would be forced to make saccadic eye movements inexcusably and uncontrollably. In pharmacological experiments Robert Wurtz and I have shown that this is indeed the case. [10, 11]. The strongest the tonic component, the more effective is the suppression.
The second, phasic component opens the inhibitory gate, producing an output. Interestingly, the effectiveness of the phasic component depends on the strength of the tonic component; the stronger the tonic inhibition, the more effective and more cut-off becomes the output which is released from the tonic inhibition.

**Basal ganglia activity selective for memory-guided movement**

We now face the fact that the basal ganglia system is only a part of the brain, as illustrated in Fig. 8. It interacts with other brain areas in a number of ways, and this is where the basal ganglia system reveals its unique role. As indicated before, the superior colliculus is the site where many different types of information converge: the retina and the cerebellum, including the frontal eye field and parietal association cortex.

The unique feature of the basal ganglia input is its suppressive nature. Most of the other areas provide the superior colliculus with excitatory signals; each of them tells or suggests the colliculus to make a saccade. Motor signals are distributed everywhere in the brain; there is probably no area that emits a holistic motor command. From such chaotic urges to move comes the necessity and importance of the basal ganglia suppressive mechanism.

![Diagram of Basal Ganglia Activity](image)

As I have shown, the suppression is not the sole function of the basal ganglia: it removes the suppression and thereby contributes to the movement initiation. An important question is, “How unique is the motor signal originating in the basal ganglia?”

I have indicated that the basal ganglia contains number of saccade-related neurons. However, as already shown in Fig. 5, the neural activity in the basal ganglia was often selective for a saccade which was made to the remembered position of a visual stimulus. Such a neuron showed no activity if the monkey made saccades to a visual target no matter where the target appeared (Fig. 5, right).

This kind of selectivity at first appeared peculiar, probably because we have been implicitly posulating holistic command neurons. If we look at the signal from the input side, not from the output side, the selectivity may not be peculiar or surprising: a memory-related signal is directly used to initiate a saccadic eye movement and the saccade anticipates the appearance of the target (Fig. 5, right).
Fig. 8. Hypothetical neural mechanisms underlying initiation of movement.

Basal ganglia may modulate activity in cerebral cortex.

A question then arises: "Is such memory-related or anticipatory activity used just for preparation or initiation of movement?" I have characterized the basal ganglia as a serial disinhibitory mechanism through which information is passed from the cerebral cortex to lower motor centers. However, if we look at the fiber connections of the basal ganglia, a different and more complex scheme emerges, as shown in Fig. 9.

In addition to the superior colliculus, the substantia nigra projects to parts of the thalamus [13]. A considerable portion of the thalamic functions as relay stations of specific sensory information, but the parts receiving basal ganglia information are called non-specific thalamic nuclei. In short, their functions are unknown. They are mainly connected with the cerebral cortex [14]. The non-specific thalamic nuclei in turn project back to the caudate [15], the cerebral cortex, especially the non-specific association cortex, also projects to the caudate [17, 20]. These connections would complete the neural circuits involving the basal ganglia. Although admittedly oversimplified, this scheme gives us many hints about how the basal ganglia might work.

The first hypothesis derived from this scheme is that the basal ganglia have access to neural events in the cerebral cortex. The basal ganglia activity may not simply be the result of the cortical activity; it could change the cortical activity by the return connection. Here I assume that the return connections between the thalamus and the cerebral cortex are excitatory. Also, I assume that there are excitatory mutual connections within the cerebral cortex. Such mutual excitation or positive feedback would act to hold neural information and subserve the neural basis of memory.

Now let us concentrate on the connections from the basal ganglia to the cerebral cortex (Fig. 10). Here the surge of the basal ganglia disinhibitory mechanism is the thalamo-cortical circuit. The substantia nigra [22], and probably also the globus pallidus [23], would normally keep suppressing the thalamo-cortical activity. If caudate neurons fire, the tonic inhibition would be removed transiently and the thalamo-cortical activity would be set off. Is there such activity in the caudate?
Masahiro Sakamoto and I found an interesting group of caudate neurons [5], and an example is shown in Fig. 11. In the delayed saccade task, a spot of light is flashed while the monkey is fixating to give him a future target position. A number of caudate or substantia nigra neurons responded to such a target cue if it was in the cell’s receptive field (Fig. 11, left); but if the same spot was given at the end of the fixation period so that the monkey no longer needed to remember its location and just simply responded to it by making a saccade, the neuron never responded to the spot of light (Fig. 11, right). It was as if the cell’s activity was used to encode the stimulus location into memory so that the monkey could use it afterwards.

I speculate that the caudate activity might be explained by the scheme in Fig. 10. The basal ganglia normally suppress the activity of thalamo-cortical circuits underlying memory, but selectively releases some of them. With a transient removal of inhibition, the thalamo-cortical activity may be maintained for a while so that it can be used for mnemonic preparation or event anticipation.

![Diagram of brain connectivity](image)

Fig. 9. Interaction between the basal ganglia and the cerebral cortex. The cerebral cortex and the thalamus are assumed to be mutually connected in an inhibitory manner so that they are shown as a single area with an inhibitory feedback. SNc indicates the substantia nigra pars compacta which exerts strong disinhibition effects on a large part of the basal ganglia, thus disassociating the striatum (SNr) which has a major output area of the basal ganglia.

I would like to point out another aspect of this collateral projection. Since the main stream of the basal ganglia is directed to the lower motor neuron, the information directed to the thalamo-cortical circuit could be regarded as "corollary discharge." The corollary discharge is often postulated such that the sensory systems know what kind of movement is going on and thereby can change their coordinate systems or sensitivities beforehand. I agree that this function would be important, but it is still bound to the present and past. In view of the predictive nature of basal ganglia activities, the function of this corollary discharge should be extended to the future. Since basal ganglia activity is already anticipating future events and preparing for next movements, the corollary discharge would evoke cortical activity anticipating further in the future. This kind of process would go on sequentially, and this is probably what underlies a complex movement.
Fig. 10. The cerebral cortex-thalamus as a target of the basal ganglia.

Fig. 11. Memory-contingent visual response of a caudate cell. The neuron responded to a spot of light (C) only when the monkey had a memorandum in its locustae as the target for a future staircase (A/F), but not when the monkey responded to a luminousity (Light).
Neural mechanisms of learned/voluntary movement

If we incorporate the pathway returning to the basal ganglia, yet another mode of basal ganglia operation could be speculated (Fig. 12). This is a loop including two inhibitions, and could act as a flip-flop circuit. In the resting state, the thalamo-cortical activity would be suppressed and hence the caudate receives no excitation. If somehow the caudate is excited, the substantia nigra output would be suppressed and the thalamo-cortical activity would be released from the inhibition. This state is stable because the substantia nigra would be kept inhibited by the caudate. This mechanism would ensure that a selected cortical activity is maintained for a while, probably until a new trigger signal is set in.

![Diagram](image)

Fig. 12. Basal ganglia-cortex loop systems may set to stabilize neural information as a step of sequential execution.

In fact, some of the caudate neurons maintain activity as if holding specific information, as illustrated in Fig. 13. For example, this neuron's activity was set off when the target disappeared and the monkey made a saccade to search for it, and continued until the expected target appeared. This is the period when the monkey had to concentrate on searching, presumably with the search image of the target. It would be unwise to switch to another state, and the basal ganglia flip-flop pathway would prevent this.
Fig. 13. Caustic neural activity related to perception of visual target. A target appeared after elongating gap after the shadowing went off and the mouse, after making a move to the neuromotor position (small vertical bar), waited for the target; the mouse showed discharges continually until the target appeared.

A considerable portion of caustic neurons show activity before an external event they know what happens next. With such predictive information, the basal ganglia may allow a movement to be triggered.

Fig. 14 summarizes this review. There could be complex interactions between sensory input, basal input, internal cortical activity, basal ganglia activity, and motor output.

1. Sensory input may trigger internal cortical activity.
2. Cortical activity may allow sensory signal to go through (stimulus selection or selective attention).
3. Basal ganglia may allow cortical activity (by disinhibition).
4. Basal ganglia may hold cortical activity (by flip-flop operation).
5. Basal ganglia activity is influenced by cortical activity.
6. Basal ganglia and hence cortical activity are modulated by limbic input.
7. Basal ganglia may open the gate for movement based on predictive, internal information.

I have described short-term changes of basal ganglia neural activities. However, prediction or anticipation is based on long-term memory of task procedures. One might think that long-term memory is just the result of cortical activities. But now just as we have gone through several possible interactions in the brain, it seems no longer tenable that memory is created solely in the cerebral cortex. Even if we accept the hypothesis that plastic changes in synapses occur in the cerebral cortex, but not in the basal ganglia, the basal ganglia could still be as important as the cerebral cortex for the formation of memory since it ensures the signals go through repeatedly in the cerebral cortex until the involved synapses are structurally enhanced.
The prediction of future events is based on experience that has been repeated many times. How the basal ganglia react in a given circumstance, therefore, depends on such experience and determines how the animal reacts. This aspect is especially important when a young, growing animal acquires a variety of movement patterns. It may determine "habit" or "movement repertoire." Furthermore, in view of the possible contribution of the basal ganglia to internal, cortical activity, this process may involve how the animal reacts internally or mentally. It may even determine "way of thinking" or "character."

References


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