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Revision

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Keywords

Basal ganglia, behavior, cognition, emotion, reward.

Basal Ganglia and Behavior

Ganglios basales y conducta

Abstract

Historically, the function of the basal ganglia has been a subject of debate and study. Initially it was proposed that these structures participated exclusively in the motor behavior; however, the current body of knowledge and science progress allows us to understand that these structures and their connections determine not only motor behavior, but also cognition and emotions. The present review describes the neuroanatomic and functional basis of the basal ganglia, emphasizing both the traditional schemes and the most recent models including sensorimotor, associative, and limbic circuits, along with the relevance of reward systems.

Palabras clave

Ganglios basales, conducta, recompensa, sistema límbico.

Resumen

Históricamente la función de los ganglios basales ha sido motivo de debate y de estudio. Inicialmente se consideró que estas estructuras participaban exclusivamente en la conducta motora; sin embargo, el conocimiento que se tiene hoy en día, permite entender que estas estructuras y sus conexiones son determinantes no solamente en la conducta motora, sino también en la cognición, aprendizaje y las emociones. En la presente revisión se describen las bases neuroanatómicas y funcionales de los ganglios bases, enfatizando tanto en los esquemas tradicionales como en los modelos más recientes incluyendo los circuitos sensorimotor, asociativo y límbico, así como la relevancia de los sistemas de recompensa.

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Introduction

The role of the basal ganglia has traditionally been focused on the planning, integration, and control of motor movement, as well as emotional behavior and reward systems. Functional models have changed over time. About three decades have elapsed since David Marsden described "the mysterious function of basal ganglia" and concluded that they are involved in automatic behaviors and motor learning.[1] Later, the first descriptions of functional circuits were made by DeLong, which described their function through a direct pathway to facilitate movement and an indirect pathway to inhibit it.[2,3]

Thus, basal ganglia were initially related only to motor functions; however, they are now known to play an important role, not only in motor behavior, but also in cognition, emotions, and learning.[4-6] Advances in science have made it possible to reveal profound changes in the initial model, broadening the knowledge and understanding of the role that this group of structures plays in behavior. In this review, we consider the components of the basal ganglia, the neurotransmitters involved, the way these interact, and their functions.

I. Components of the basal ganglia

The basal ganglia are a group of deep nuclear structures which are well-defined both anatomically and functionally. They are located within the telencephalon, diencephalon, and mesencephalon. The structures that are included within the basal ganglia vary according to different authors; however, it is classically considered to be neostriatum or striatum (caudate and putamen), globus pallidus, substantia nigra, and subthalamic nucleus.[7]

From the anatomical point of view, they can be subdivided into dorsal and ventral. The nuclei of the dorsal portion include the striatum, external globus pallidus (GPe), internal globus pallidus (GPi), subthalamic nucleus (STN), and substantia nigra (SN) with its pars compacta (SNc) and pars reticulata (SNr). The nuclei of the ventral portion include the substantia innominate (SI), the nucleus basalis of Meynert, and the nucleus accumbens (NAc). The latter is subdivided in the central zone (Core) of the nucleus accumbens (NAcC) and the cortical zone (Shell) of the accumbens (NAcS).

Moreover, given the interconnections and circuits to be described below, it is relevant to identify the structures involved in the limbic circuit and reward system. The limbic system is a group of cortical interconnections and subcortical structures dedicated to linking visceral and emotional states with the cognitive and behavioral parts.[8] There is no universal agreement on the structures that comprise the limbic system. There is some consensus, however, that the cerebral regions that constitute the limbic system include:[9] limbic cortex, cingulate gyrus, parahippocampal gyrus, hippocampal formation, dentate gyrus, hippocampus, subicular complex, amygdala, septal area, hypothalamus, and habenula. The term "extended amygdala" includes the nucleus of the amygdala and the bed nucleus of the stria terminalis.

II. Neurotransmitters involved in basal ganglia physiology

The final function of each nucleus depends on the neurotransmitter used. Table 1 summarizes the main neurotransmitters used by each nucleus. In general, it can be considered that there are excitatory nuclei and inhibitory nuclei. It is important to consider that the basal ganglia do not use various neurotransmitters, and they also have different receptors.

The striatum does not express only receptors for dopamine; it also has receptors for glutamate, acetylcholine, γ-aminobutyric acid (GABA), adenosine, histamine, neuropeptide Y, somatostatin and nitric oxide, among others. All these neurotransmitters interact to modulate the final inhibitory response of the striatum; for example, adenosine type 2A receptors bind to dopamine receptors type D2 and antagonize the function of the latter.[10] Likewise, γ-aminobutyric acid (GABA) is not the only neurotransmitter

Table 1. Major efferent neurotransmitters in basal ganglia.

Neurotransmitter	Function	Nuclei
γ-aminobutyric acid (GABA)	Inhibitor	Striatum Internal globus pallidus (GPi) External globus pallidus (GPe) Substantia Nigra pars reticulata (SNr)
Glutamate	Excitatory	Subthalamic nucleus (STN)
Dopamine	Dependent on the type of receptor	Substantia Nigra pars compacta Ventral tegmental area

released by the striatum. It is known that this nucleus expresses endocannabinoids, which interact in neuronal plasticity and help to modulate excitatory messages from the cortex.[11] Dopamine synthesized in the SNc of the mesencephalon is the neurotransmitter best represented in the physiology of the base ganglia. Different types of dopamine receptors may increase or reduce the function of the base ganglia.

The known five types of dopamine receptors (D1, D2, D3, D4, and D5) are divided into two large families: D1-like receptors (which include types D1 and D5, and are bound to stimulatory G proteins), and D2-like receptors (which include types D2, D3, and D4, and are bound to G protein inhibitors).[12]
The different interactions between each of the elements mentioned are described in more detail in the following sections.

III. Intrinsic and extrinsic interactions of the basal ganglia

a. Traditional functional model

The traditional functional model of the basal ganglia was formulated in the early 1990s and consists of two antagonistic pathways; the direct pathway that facilitates movement and the indirect pathway that inhibits movement.[2,7] In this model, the different nuclei of the basal ganglia can be categorized as 1. Input nucleus (striatum), 2. Output nuclei (GPi and SNr), and 3. Intrinsic nuclei (GPe and STN).[13]

The striatum receives excitatory afferents via glutamate of the primary motor cortex (M1), the supplementary motor area (SMA), the premotor area (PM), the somatosensory cortex, and frontal eye field (FEF).[14-15] These cortical afferents synapse with the main population of striatum neurons: the medium spiny neurons (MSNs)—named after the thorn-like ramifications seen in their dendrites. MSNs are the only projection neurons of the striatum and communicate with the intrinsic and output nuclei through γ-aminobutyric acid (GABA).[15,16]

There are two distinct types of MSNs which differ in their projection target, expressed neuropeptides, excitability, and main subtype of dopamine and acetylcholine receptors. Table 2 shows the main characteristics of each type of MSNs.

In basal conditions, the output nuclei are found to generate tonic inhibition of the Ventral Anterior (VA) and Ventral Lateral (VL) nuclei of the thalamus through GABA and, therefore, the thalamus is unable to excite the cortex.[14,15] The end result of these actions is inhibition of movement.

• Direct pathway

At the moment when the execution of a voluntary movement is planned, the cortex sends information of the desired movement to the striatum. The direct pathway MSNs inhibit the GPi and SNr, which were inhibiting the thalamus, releasing it so that this structure can excite the cortex and, finally, the desired movement is executed via the corticospinal tract.[16,17]

• Indirect pathway

The indirect pathway MSNs send inhibitory afferents to the GPe, which is tonically inhibiting

Table 2. Characteristics of the different types of medium spiny neurons (MSNs).

	Direct Pathway MSNs	Indirect Pathway MSNs
Projection target	GPi/SNr	GPe
Neuropeptides	Substance P and Dynorphin	Enkephalin
Excitability	Minor	Major
Dopaminergic receptor	D1 (Exciter)	D2 (Inhibitor)
Cholinergic receptor	M2 (Inhibitor)	M1 (Exciter)

MSNs - Medium spiny neurons, GPi - Internal globus pallidus, SNr - Substantia Nigra pars reticulata
GPe - External globus pallidus

the STN; once the latter is released it is able to send excitatory afferents to the GPi and SNr, causing greater inhibition on the thalamus, resulting in the inhibition of movements antagonistic to those desired.[16,17]

The correct function of both pathways is facilitated by the dopamine present in the neurons of the SNc located in the mesencephalon. The direct pathway MSNs express D1-dopaminergic receptors, which, upon binding to dopamine, activate stimulatory G proteins and, through the cascade of second messengers, promote the function of the direct pathway. On the other hand, the indirect pathway MSNs express dopamine receptors type D2, which when they bind to dopamine they activate inhibitory G proteins, finally resulting in the inhibition of the indirect pathway.[18] The net result of the dopaminergic action is the facilitation of movement.

• Hyperdirect pathway

At the beginning of the millennium, the so-called hyperdirect pathway was described. In this pathway, the information of the different cortical areas arrives directly at the STN, without passing through the striatum. That is, the STN ceased to be considered a relay station for the indirect pathway. The net result is the rapid excitation of GPi and SNr, with subsequent inhibition of movement.[19] We currently know that the traditional model and its unidirectional flow represents a simplification of the motor functions of the basal ganglia, nevertheless, understanding it is fundamental for the study of Parkinson's disease and other movement disorders.

b. Recent models

More recent studies have allowed the proposition of a model in which the PFC and the different motor areas communicate and maintain a "dialogue" with the striatum through different types of neurons with a different excitability pattern. Thus the information of the different cortical areas reaches the striatum through two types of neurons: intratelencephalic (IT) and pyramidal neurons (PN). IT neurons carry information from the PM, the SMA and the somatosensory cortex areas, are primarily involved with planning movement, and communicate primarily with direct pathway MSNs. Meanwhile, PNs carry information from the cortex M1 to the motor neurons of the corticospinal tract, and at the same time to the indirect pathway MSNs and the STN; the final result is the transmission of a copy of the movements in execution to the striatum, which results in the inhibition of undesired movements.[15,20]

c. Other nuclei involved

There are other important nuclei, such as the centromedian (CM) and parafascicular (Pf) nuclei of the thalamus. These nuclei send excitatory signals to the cholinergic interneurons of the striatum to "warn" about relevant sensory stimuli. In addition, these nuclei send projections directly to the SNc and the ventral tegmental area (VTA) to facilitate the release of dopamine. In addition, other brainstem nuclei such as the superior colliculus (SC), the red nucleus (RN), and the pedunculopontine nucleus (PPN), have connections to the striatum directly and through the thalamus, to modulate movement.[21] Finally, there are intrinsic connections; these microcircuits

between the different nuclei have the function of obtaining feedback and a constant evaluation that keeps each part of the circuit informed, thus avoiding unnecessary responses.[15,21]

IV. Functional circuits in the basal ganglia

In addition to the connections explained above, such as direct, indirect, and hyperdirect pathways, research using micro-stimulation, microregistration, and functional images has demonstrated the existence of regions in the basal ganglia with functional implications. As already mentioned, basal ganglia are composed of closed circuits that originate in the cerebral cortex, which later pass through the basal ganglia, pass through the thalamus, and finally return to the frontal cortex.[22,23] Accordingly, three functional circuits have been described according to their site of origin: 1. Sensory-motor circuit (motor), 2. Associative circuit (cognitive), and 3. Limbic circuit (motivational and emotional). The sensory-motor circuit has a dorsolateral localization, it is related to habitual or automatic behaviors. The associative circuit is dorsomedial, it is related to the goal-directed, decision-making, and planning behaviors. The limbic circuit, which is rostroventral, is related to behaviors guided by emotions and motivation.[17,23] Next, we will briefly describe each of the circuits.

Figure 1 shows the nuclei, afferences, efferences, and main neurotransmitters involved in the functional circuits of the basal ganglia.

a. Motor Behaviors

Basal ganglia and their connections are involved in the selection of habitual or goal-directed motor behaviors according to the needs and responses of the external and internal environment.[17] Figure 2 summarizes the types of motor behaviors. Evolution has led to a specialization within the basal ganglia structures so that the response systems can be carried out quickly and with less computational demand. In this way, it is possible to obtain effective motor responses that allow survival and appropriate interactions with the environment.

To understand these circuits it is important to consider that there are two types of motor responses: a goal-directed response, which implies an explicit or conscious processing with a high attentional demand; and a habitual or automatic behavior that involves implicit, parallel, and rapid processing.[17,24] Depending on the required motor responses, the sensory-motor circuit will be active for quick responses and previously-acquired motor behaviors such as walking or blinking, and the associative circuit will, if the motor behaviors required are the result of previous deliberation and decision-making in a continuous dialogue with the cortex.

b. Sensory-motor circuit

As previously mentioned, the sensory-motor circuit has a dorsolateral location. It originates in the M1 cortex, SMA, PM area, and FEF, then goes in the dorsolateral region of the striatum, especially the posterior putamen, traverses the STN and output nuclei in its dorsolateral portion, and finally to the thalamic nuclei VA, VL and CM, which connect again with the M1, SMA, and PM area, completing a closed circuit. This circuit is involved in the selection of habitual or automatic behaviors.[17,25]

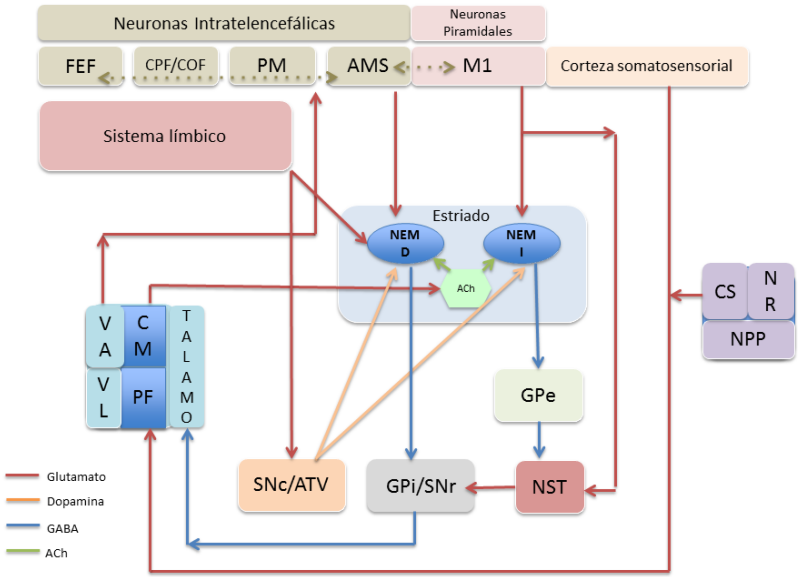
c. Associative circuit

On the other hand, the associative circuit is dorsomedial, its origin is in the dorsolateral prefrontal cortex (DLPFC) and medial and lateral orbitofrontal cortex (OFC), then it has connections with the dorsomedial region of the striatum, especially with the caudate nucleus, crossing the STN and output nuclei, and finally, in the thalamus in the VA, VL, and Pf nuclei. This circuit is related to goal-directed behaviors, decision making, and planning.[17,25]

d. Role of dopamine

Dopamine, as in the modulation of direct, indirect, and hyperdirect pathways, which in turn are part of the sensory-motor, associative, and limbic functional circuits, has a determining role. Dopamine is key in the selection, execution, and change of motor behaviors, as well as for learning by reinforcing new behaviors, for motivation, and in the reward system. At baseline, dopaminergic

Figure 1. Functional circuits of the basal ganglia.



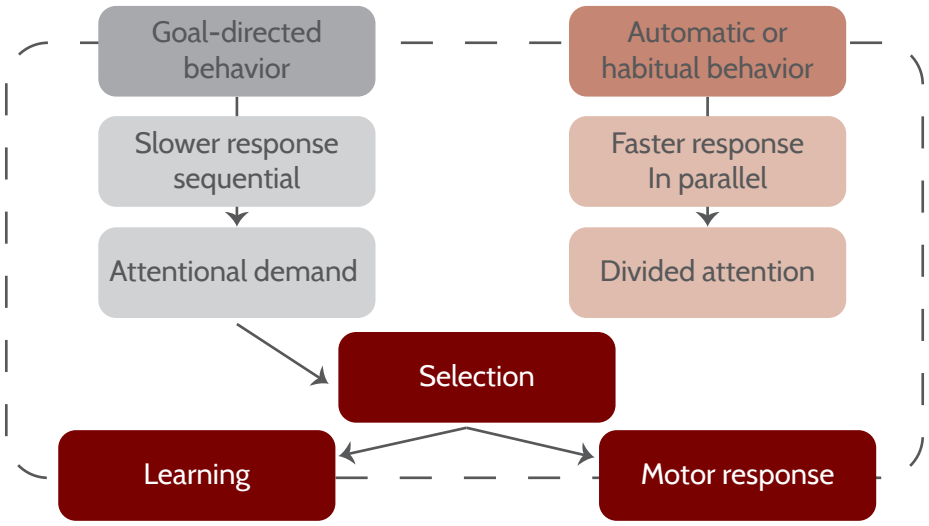
Main nuclei, afferents, efferents, and neurotransmitters of the functional circuits of the basal ganglia. Detailed description in the text. ACh = Acetylcholine (Cholinergic Interneuron). SMA = Supplementary Motor Area. VTA = Ventral Tegmental Area. CM = Centromedian Nucleus. SC = Superior Colliculus. PFC = Prefrontal Cortex. OFC = Orbitofrontal Cortex. FEF = Frontal Eye Field. GPe = External Globus Pallidus. GPi = Internal Globus Pallidus. MSNs D = Direct pathway Medium Spiny Neurons. MSNs I = Indirect pathway Medium Spiny Neurons. RN = Red Nucleus. STN = Subthalamic Nucleus. PPN = Pedunculopontine Nucleus. PFN = Parafascicular Nucleus. SNc = Substantia Nigra pars compacta. SNr = Substantia Nigra pars reticulata. VA = Ventral Anterior Nucleus. VL = Ventral Lateral Nucleus.

neurons in the SNc have a tonic firing frequency of 2-10 Hz, while the output nuclei fire at a tonic frequency of 60 to 80 Hz. When there is a salient stimulus in the environment or a deliberation in our frontal cortex, the dopaminergic neurons in the SNc respond by changing their tonic activity to a phasic activity composed of bursts of high frequency firing, up to 80 Hz in humans, that stimulate the direct pathway through D1 receptors and inhibit the indirect pathway through D2 receptors, facilitating a change in previously established behavior and the selection of a new motor pattern.[17,26]

By way of example, we will use a salient visual stimulus. In this case, a visual stimulus arrives through the optic tract to SC, which in turn sends an excitatory signal to the CM and Pf thalamic nuclei, which send projections to the SNc and the cholinergic interneurons in the striatum.[27,28] The dopaminergic neurons of the SNc respond by changing their tonic activity to a phasic activity. On the other hand, the cholinergic interneurons that are tonically active respond by means of a pause that allows a stop in the motor act, followed by an excitatory response. These changes in the firing patterns allow the direct pathway to be stimulated and the indirect pathway inhibited, allowing the selection of a new motor act, usually automatic when rapid responses are required—in this case, a saccadic eye movement towards the outward visual stimulus.[28] Following the selection of the most relevant motor pattern, the motor cortex constantly excites the striatum and STN through the indirect and hyperdirect pathways respectively, so that through the output nuclei the unwanted motor patterns are inhibited and the chosen motor pattern is maintained. This processing occurs in parallel.[28,29]

In contrast, when there is a deliberation in the

Figure 2. Types of Motor Behaviors.



Basal ganglia and their connections are involved in the selection of daily motor behavior or goal-directed motor behavior. These behaviors differ in response speed and need for attention.

PFC to carry out a goal-directed behavior, a dialogue occurs between the PFC, the PM area, the SMA, and the basal ganglia to select the most appropriate response according to the desires, memories, emotions, and context. Subsequently, a response is produced that is again facilitated by a phasic dopamine discharge that allows the change and the selection of a new motor behavior. When a new motor pattern is efficient, dopamine performs a positive reinforcement, so that by means of long-term potentiation mechanisms (LTP) new motor acts are learned. These new motor acts can be selected in the future more quickly and without attentional demand as habitual behaviors.[29]

By means of electrophysiological experiments with field potentials measurement, this variability in the dopamine-guided responses has been demonstrated by the registration of high frequencies, usually in the gamma band (>60Hz), as well as desynchronization in these potentials. The aforementioned reflects the diversity of responses and changes in the firing rate of dopaminergic neurons that modulate circuits and, consequently, the selection and changes in motor behavior.[30]

e. Limbic Circuit

Behavior can be considered as a mechanism where the brain manages the input of information and immediately generates an output order that allows the organism to adapt to the circumstances of the environment.[31] The information received through the senses is translated mainly inside the cerebral cortex and this directs an output behavior. To process the information coming from the senses and to allow a behavior to be performed, regulatory levels are required. The highest level is integrated by the cerebral cortex; the second level is made up of the basal ganglia, including the extended amygdala; the third level is the mesencephalon; and, finally, a fourth level is regulated by the habenula.

1) First level of regulatory behavior

The first regulatory level is the cerebral cortex. The limbic system receives three main sources of input: a) from the posterior association cortex, the cingulate gyrus, the insula, the hippocampus, and the fornix, which in turn connect the hippocampus with the mammillary bodies in the posterior

hypothalamus; b) the inferior temporal cortex, via the entorhinal cortex; c) the PFC. Each of these input sources provides information from the association cortex and provides the limbic system with highly processed information about the environment.[31]

Within the PFC, a similar information flow occurs, which leads to the activation of specific regions, for example, the M1 cortex and other more distant regions. Each neuronal connection is able to learn throughglutamatergictransmission—whichincreases or decreases the sensitivity of the connecting synapses by inducing LTP or long-term depression (LTD). Through these mechanisms, the cortex can "learn" to transmit detailed sensory information to a specific output unit through a "preferred" cortical tract. Consequently, the cerebral cortex and the networks it integrates interpret sensory information and produce a specific behavioral response through networks that in turn connect with deep structures such as the basal ganglia.[32,33]

2) Second level of regulatory behavior

The processing units in the cerebral cortex send information to the basal ganglia.[34,35] The route through the basal ganglia and the thalamus is directed to the corresponding processing units in the anterior cortex. This parallel circuit, as previously mentioned, has stimulatory pathways (direct pathway) and inhibitory pathways (indirect pathway), and its glutamatergic synapses can also induce LTP and LTD. Therefore, this parallel pathway through the basal ganglia allows the brain to correct and guide the information as well as select the motor behavior to give it a final destination.[31]

The amygdaloid complex, formed by the basolateral and centromedial (or nuclear) region, together with its connections constitutes the main pathway to regulate behaviors guided by emotions. The basolateral region can be considered as a receptor area; on the other hand, the centromedial region (ganglionar or nuclear) functions as an emitting or output area.[35] The terminal stria connects the nuclear amygdala with the diencephalon and with the anterior dorsomedial frontal areas; additionally, a large part of this circuit has connections that are directed towards the brainstem where they synapse with nuclei of the autonomic nervous system, to produce the visceral responses involved with the emotions. Through these connections, the amygdala affects motor output signals, guiding behaviors driven by emotions, as well as impulses needed for survival such as seeking food, warmth, comfort, escaping pain, quenching thirst, and fleeing danger, among others.[31]

In a very general way, sensory-motor and associative circuits regulate rational behavior, while the limbic circuit regulates emotional behaviors.[36,37] The two systems can be inhibited or activated, depending on the situation, even in parallel. The dorsolateral PFC is important in particular to control the goal-directed responses while the medial PFC controls the emotional responses. Within the medial PFC, the OFC is essential to regulate the direction of the motivation.[32] This motivation requires the participation of two specific structures in the nucleus accumbens: the NAcC and the NAcS.[38-40]

3) Third level of regulatory behavior

The NAcC motivates the individual towards a behavior that can lead to a feeling of reward, while the NAcS motivates the individual towards behaviors that can lead to escape a feeling of misery.[41] The activities of the NAcC and the NAcS are controlled by monoaminergic nuclei within the mesencephalon. These nuclei transmit signals through dopaminergic (VTA), adrenergic (norepinephrine, locus coeruleus), and serotonergic (5-hydroxytryptamine, raphe nuclei) pathways.[40,41]

4) Fourth level of regulatory behavior

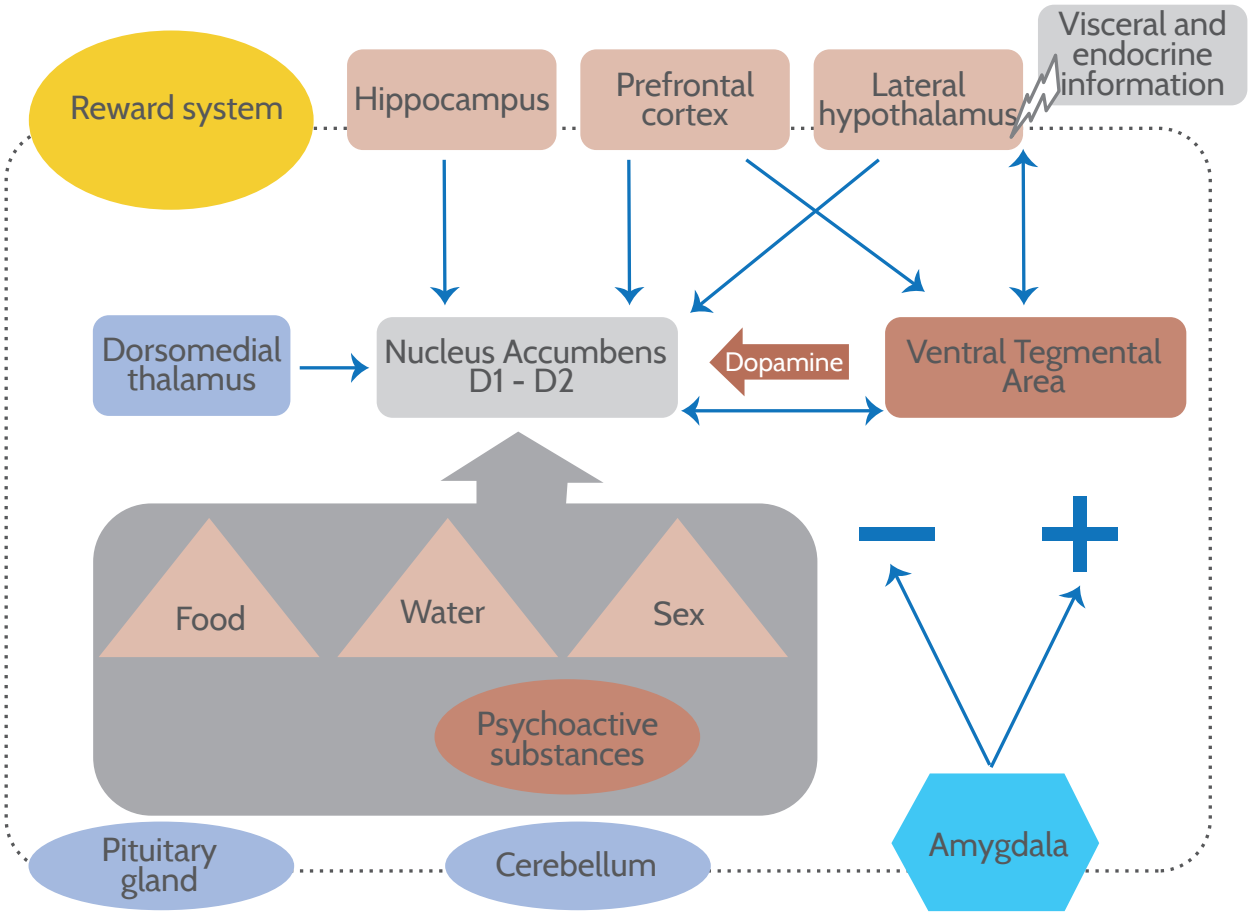
The fourth level of regulation is given by the coupling between the cerebral cortex and the mesencephalon. Here, a very old structure within the diencephalon stands out: the lateral habenula (LHb)—located in the dorsomedial portion of the thalamus.[33] The dopaminergic neurons that project from the VTA to the NAc are activated by an unexpected reward (or stimuli predicting a reward), and inhibited by the omission of the expected rewards. This inhibition seems to depend on the contributions from the LHb.[33,42]

f. Reward system

Reward systems are centers in the central nervous system that obey specific and natural stimuli, allowing the individual to develop learned behaviors that respond to pleasant or unpleasant events. Figure 3 describes in a simplified way the main nuclei, afferents and efferents in the reward system.

Activation of the NAc by the release of dopamine from the VTA occurs in the presence of natural (e.g. food, water, sex) or artificial (e.g. psychoactive drug substances) boosters. The NAc receives projections from the lateral hypothalamus (LH), PFC, dorsomedial thalamus (DMT), hippocampus (HC), and VTA. The NAc, in turn, sends projections to the VTA and the LH while the VTA sends and receives projections from the PFC and the LH. We should mention the cerebellum, which allows the control of muscular functions, and the pituitary gland, which is responsible for pain relief and establishing positive bonds, among others. These structures form the reward system, which is also called the limbic-motor circuit. This entire circuit is in turn modulated by the amygdala.

Figure 3. Reward System.



Reward system's main nuclei, afferents and efferents. Detailed description in the text.

Table 3. Clinical correlation and alterations in circuits and neurotransmitters of the basal ganglia.

Disease	Motor symptoms	Behavioral and psychiatric symptoms	Main Circuit or affected structures	Main Neurotransmitters involved
Parkinson's Disease	Bradykinesia, stiffness, tremor at rest, changes in posture and gait.	Apathy Depression Anxiety Executive dysfunction. Alterations in working memory. Impulse Control Disorder.	Loss of dopaminergic neurons in substantia nigra. Nigrostriatal pathway alteration, in the sensory-motor, associative, and limbic circuits. Direct and indirect pathway alteration, resulting in hyperstimulation of subthalamic nucleus and GABAergic exit nuclei (GPi and SNr). Pedunculopontine nucleus and nucleus basalis of Meynert alteration. Reward circuit alteration.	Dopamine↓ Acetylcholine↓ Serotonin↓ Noradrenaline↓ Adenosine↑
Huntington's disease	Chorea, Tics, Dystonia, Bradykinesia, Rigidity	Depression, Irritability, Impulsivity, Dysphoria, Anxiety, Mania, Apathy, Psychosis, Executive Dysfunction	Neuronal loss in caudate, putamen, prefrontal cortex, cingulate and amygdala. Failure in the indirect pathway and in the inhibitory role of the basal ganglia. Alteration of the medial orbitofrontal cortical circuit. Alteration of the frontostriatal circuit.	GABA↓ Glutamate↓ Enkephalin↓ Dopamine↑ Substance P↓
Generalized Primary Dystonia	Dystonia	Depression, Anxiety, Impulsivity	Loss of Intracortical Inhibition and Increased Brain Plasticity. Altered sensorimotor integration. Failure in inhibition around. Excessive direct pathway activity, Decreased indirect pathway activity. Decreased GPe and GPi activity Decreased subthalamic nucleus activity. Overactivity of prefrontal cortex during movement.	GABA ↓ Acetylcholine↓ Dopamine↑

GPi - Internal globus pallidus SNr - Substantia Nigra pars reticulata GABA - γ-aminobutyric acid GPe - External globus pallidus

Conclusions

Basal ganglia and their connections are determinant in the selection, execution, and learning of new behaviors that have their expression through motor acts, thoughts, and emotions. These connections allow to act according to internal and external environment requirements. According to these requirements, the answers can be automatic, goal-directed, or guided by our emotions. Table 3 summarizes the clinical and anatomo-functional correlations of some of the most common basal ganglia diseases to illustrate the relevance of these circuits and their neurotransmitters.

Although science has allowed a better understanding of the functioning and integration of these structures, it would be pretentious to ensure that everything has been explained because some of these are theoretical models. In addition, there are still gaps in knowledge that do not allow a complete understanding of their functionality and their relation to a concept as complex and broad as behavior. However, the advances made today highlight the importance not only of their individual components but also of their connections, that is, neural networks, neurotransmitters, and functional circuits. The aforementioned allows an understanding of the behaviors from a pragmatic point of view and helps us comprehend not only their normal functioning but also a wide variety of neurological syndromes that carry motor and neuropsychiatric symptoms derived from their alterations.

Conflict of interest statement
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