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Hemiballism a Case Report and Literature Review

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Abstract: The term ballism derives from the Greek word ballistēs which translates as "throw". Ballism is one of the abnormal movements reported in the medical literature, characterized by the involuntary, non-purposeful action of a limb, in a repetitive, sudden, centrifugal way, and when it affects the upper and lower limbs together ipsilaterally in a patient is called hemiballism, this neurological manifestation is part of the so-called abnormal hyperkinetic movements. The objective of our report is to present the clinical picture of a patient with hemiballism who jointly presents cerebrovascular alterations and the use of dopaminergic drugs. He is a male of 79 years old, with a history of chronic degenerative diseases such as, systemic hypertension, diabetes mellitus type II, cerebrovascular disease, hyperlipidemia, vascular cognitive deficit and apparently Parkinson's disease, which presented abnormal movements of sudden onset, of insidious progression, to the left side of the uncoordinated type, abrupt, thick, centrifugal, causing disability in their bodily functioning and deteriorating their quality of life. This picture began after the increase in the medicines used for the diagnosis of Parkinson's disease. The diagnosis of Hemiballism was established and medical treatment based on Haloperidol and reduction of the antiparkinsonic drug was provided, showing an important improvement evidenced in the attached video. A review of the anatomical, histological, physiological and pathophysiological aspects related to this type of pathology is made emphasizing the relationship of the direct and indirect pathways of the extrapyramidal system used for the modulation of the corporal movement by the primary motor system.

Keywords: Hemiballism, Basal Ganglia, Abnormal Movements

1. Clinic History

79-year-old male patient, with date of birth on 05/01/1939, married, unemployed, originally from Monterrey, Mexico.

Pathological personal history:

Systemic Arterial Hypertension of 25 years of evolution in treatment with Losartan 50 mg every 24 hours.

Type II diabetes mellitus of 15 years of evolution in treatment with Metformin 850 mg every 12 hours.

Insomnia of initial type of 4 years of evolution under treatment with Clonazepam 2 mg tab. (1/2 tab every 24 hours).

Tremor of the right upper limb with a diagnosis of Parkinson's disease of one year of evolution under treatment with Levodopa 250 / Carbidopa 25 mg every 8 hours and Pramipexole 0.5 mg every 8 hours.

Recent memory alteration diagnosed as Cognitive Deficit (Dementia Syndrome) of a vascular type of 1 year of evolution under treatment with Memantine 10 mg every 12 hours.

Ischemic cerebral infarction in the right cerebral hemisphere 1 year ago under treatment with acetylsalicylic acid 100 mg every 24 hours and Atorvastatin 40 mg every 24 hours.

Alcohol consumption of 1 to 6 beers per week up to 2 months before your review.

Reason for consultation June 16, 2018 abnormal movements of the left hemibody of 3 months of evolution.

The patient's family reports that his symptoms began in March 2018 when they made adjustments to his medications, increasing the dose in his treatment for the diagnosis of Parkinson's disease, (Levodopa 250mg every 8 hours and Pramipexole 0.5mg every 8 hours) noticing the occasional involuntary orolingual gesticulation movements appeared, which increased in intensity in the following four weeks causing dysarthria and inability to eat. In addition to being added progressively and insidiously over 5 months, uncoordinated involuntary movements of the left upper and lower thoracic limb, centrifugal, sudden, intense, constant during vigilance that disappear in sleep, causing inability to stand and walk, as well as fatigue. (See video 1) Attending the consultation for evaluation on October 08, 2018.

Physical examination.-

Vital signs: blood pressure 130/80 mmHg in the right arm. Pulse rate 88 per minute. Respiratory rate 14 cycles per minute, Axillary temperature 36°C.

Goes in a wheelchair, conscious, obeys simple orders, disoriented in time and space, cranial nerves and fundus without alterations, dysarthric, with hypophonia, with intense, continuous oro-lingual dyskinesias, and centrifugal, intense, incoordinated, involuntary, constant movements, abrupt, proximal and distal of left upper and lower extremities. In the right hemibody, its motor function is 5/5 on the Levin scale, the tendon reflexes (+ +), the sensitivity to touch, pain and temperature are preserved bilaterally. The motor function, reflexes and coordination of the left half of the body as well as the gait cannot be evaluated.

Rest of the general physical examination without alterations.

Laboratory, office and imaging studies.

Glucose 76 mg/dl.

Glycosylated hemoglobin 7.8%.

Hematic biometry, Liver function tests, Lipid profile, General Urine Exam, are reported normal.

Brain MRI of October 22, 2018 (see figure 1) reports.

Diffuse corticosubcortical atrophy. Symmetric exvacuous ventricular dilatation. Diffuse supratentorial, periventricular and brain steam leukoaraiosis. Gliosis / encephalomalacia in the basal ganglia and region of the right occipital lobe. As well as Dolichoectasia of the basilar artery.

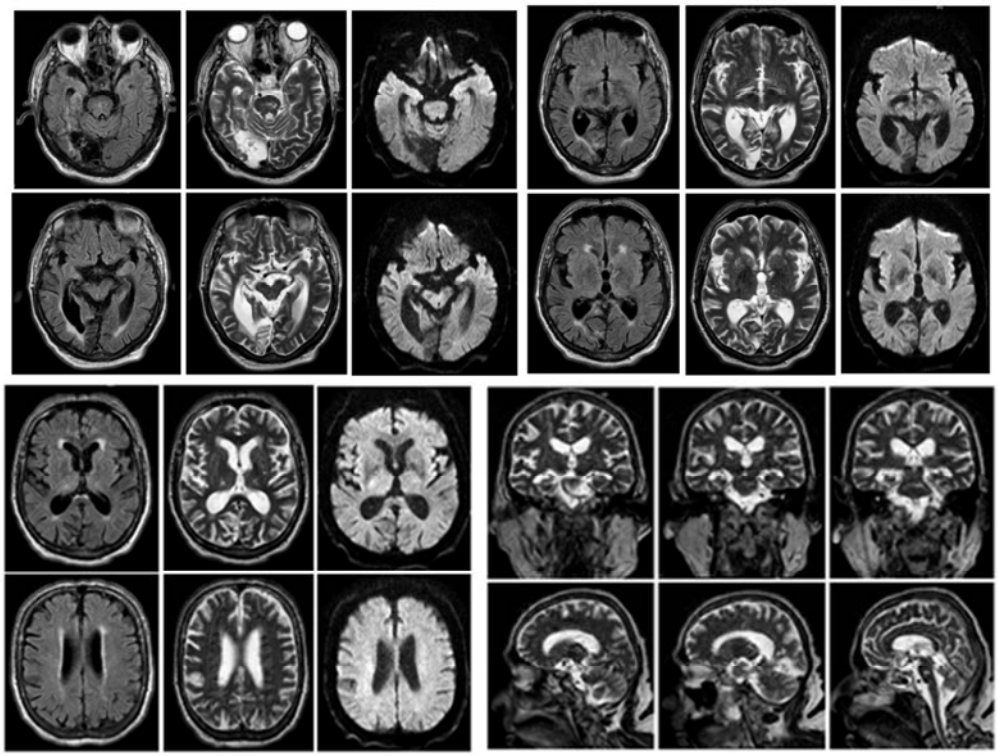

Figure 1. *Brain Magnetic Resonance studies. A, B and C) Axial in T1, T2 and FLAIR dependent images. D) Coronal and Sagittal in T2-dependent images. That demonstrate data of diffuse cortico-subcortical atrophy, exvacuous ventricular dilatation, diffuse supratentorial, periventricular and brain steam leukoaraiosis. As well as Gliosis / encephalomalacia in the basal ganglia and region of the right occipital lobe. Basilar artery dolichoectasia.*

Diagnosis.

Multifactorial left hemiballism secondary to diffuse ischemic cerebral vascular disease and use of antiparkinsonic drugs.

Current treatment:

Losartan 50 mg half tab every 24 hours

Metformin 850 mg every 12 hours

Atorvastatin 40 mg every 24 hours

Acetylsalicylic acid 100 mg every 24 hours

Levodopa 250 / Carbidopa 25 mg half tab every 12 hours

Biperiden 2 mg half tab every 8 hours

Haloperidol dropper 2.5mg / ml 6 drops am and 3 drops

pm (October 2018)

Evolution.- Partial response to the control of involuntary movements, with progressive reduction in accordance with the decrease in parkinsonic drugs and increase in the dose of haloperidol.

November 2018.- Total control of abnormal movement. (See video 2).

2. Review of Literature

When physicians are confronted with patients with alterations in the control of movement, it is very important to have the maximum knowledge of the anatomical, histological and physiological structures of the extrapyramidal system, in order to detect and analyze the clinical manifestations that appear in the alterations of this via, in order to be able to adequately select the appropriate diagnostic and therapeutic measures. Disorders of the extrapyramidal system cause neurological diseases known as abnormal movements or movement disorders. These alterations are divided into two major categories: a) Hypokinetic disorders (reduction of movement, for example the rigid phase of Parkinson's disease) and b) Hyperkinetic disorders (exaggerated movements, for example Huntington's chorea or Hemiballism). Not to mention the association of alterations in the correct tone, posture or reflexes among others [1].

Within the diagnostic approach of these alterations, it is relevant to obtain a detailed clinical information of the referred symptomatology to be able to establish if the movement deficit presented by the patient is of voluntary or involuntary type, the affected area or areas, the presentation form, if there is some trigger mechanism, the aggravating factors since anxiety and / or depression accentuate the affectation and sleep reduces them; likewise, establish the type of dysfunction, frequency, rhythm, speed, duration, presentation pattern, induction mechanism, movement complexity or if they are reduced or suppressed by some specific maneuver.

The system or extrapyramidal route is considered as an interconnected and interrelated multineuronal network, which participates in the control of the motor system, modulating the functions of the pyramid system, which is responsible for the production of voluntary movements. It is considered phylogenetically as an "old" system and some authors have referred to this system as a functional concept rather than as a specific anatomical or physiological structure, however, the basal ganglia (BG) and their interconnections are considered the main structures since the organic point of view. Other structures involved in the extrapyramidal motor system include: red nucleus (RN), reticular formation of the brainstem (RFB), lower olivary nucleus in the medulla oblongata, incerta zone (IZ), vestibular nuclei, peduncle pontine nucleus (PPN), and the gray matter of the quadrigeminal plate. Likewise, some thalamic nuclei are involved in these functions and are called "motor thalamus", includes the nucleus ventralis lateralis (VL), the pars oralis (VLo); ventralis lateralis, the pars caudalis (VLc); the posterior lateral ventral, pars oralis (VPLo); and portions of the anterior ventral (VA). There are several anatomical structures outside the pyramidal system important in the control of movement that are not related to the basal ganglia, such as the rubral- spinal, vestibule-spinal, olive-spinal and reticulum-spinal, as well as the cerebellum [1, 2].

The basal ganglia that are considered most important from the clinical physiopathological point of view are the caudate nucleus (CN), the putamen (P), the globus pallidus (GP), the substantia nigra (SN) and the subthalamic nucleus of Luysii (STN). The caudate nucleus and the putamen make up the so-called corpus striatum (CS). Globus pallidus and putamen make up the lenticular or lentiform nucleus (LN). (Figure 2).

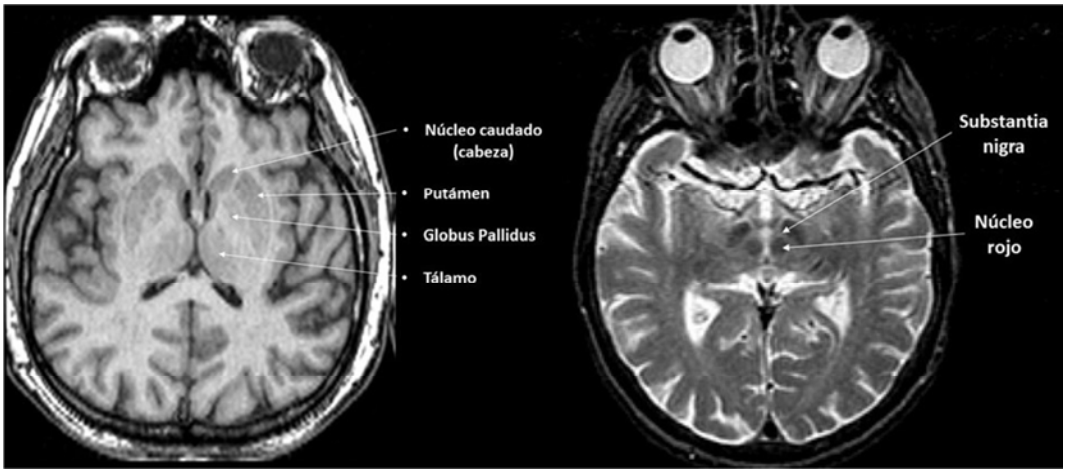

Figure 2. *Magnetic resonance imaging of the brain in axial section showing the structures of the basal ganglia.*

It is reported in the neurological literature that in addition to the motor circuits that control voluntary movement, the basal ganglia have connections with the oculomotor system and with the limbic area, which is related to the emotional aspects of movement. It is important to mention, that the basal ganglia have multiple interconnections, these are related to the cerebral cortex motor (precentral region, supplementary area and premotor region), brain stem nuclei and spinal cord regions [1, 3].

The caudate nucleus and the putamen have a common

embryological origin, anatomically considered semi-continuous, structures that are separated by the nerve fibers of the anterior arm of the so-called internal capsule. (Figures 3 and 4), in addition to being considered histologically identical; they are made up of large and small neurons, with 20:1 predominating small cells, where their dendrites can be spiny or non-spiny. The small non-spiny cells are mainly cholinergic. In the striatum the most common type of cell is of the small-spiny type, contains the neurotransmitter gamma aminobutyric acid (GABA), as well as enkephalin (ENK), dynorphin or substance P (P) and are considered the main source of the striatal efferent pathway. The microscopic structure of the striatum consists of a group of cells that stain from the histochemical point of view for the neurotransmitter acetylcholine (ACh) (cholinergic pathway), they are facilitators of the projection neurons inhibited by Dopamine, in said matrix are interspersed in the form of mosaic cellular islands called striosomes containing substance P type neurotransmitters with D1 type dopaminergic receptors and enkephalin with D2 type dopamine receptors. Some histological variations are observed in the caudate nucleus where the striosomes have a higher concentration of neurotransmitter Dopamine, the putamen consists mainly of matrix, and striosomes predominate in the ventral striatum. The striatum (caudate-putamen nucleus) receives glutaminergic-type afferent fibers that originate from small pyramidal cells located in layers 5 and 6 of the cerebral cortex on the same side, as well as thalamic fibers. The caudate nucleus is formed by three parts, first a head that bulges in the anterior horn of the lateral ventricle forming part of the floor of the same. It continues with the thinner body, which forms the central part of the floor of the lateral ventricle, is located lateral to the superior surface of the thalamus. Finally, the tail rotates down along the outer margin of the posterior surface of the thalamus and makes a turn towards the interior of the roof of the lower horn of the lateral ventricle. It receives multiple afferent nerve fibers that are distributed as follows: in the head region, afferent nerve fibers are received from the frontal lobe, in the body region they come from the parietal-occipital lobes and in the tail region they come from the lobe temporal, in addition to receiving afferent nerve fibers from the dorsomedial and anterior ventral region, nuclei of the thalamus and putamen. On the other hand, in the putamen afferent fibers are received from zones 4 and 6 of the parietal lobe and the substantia nigra. The striatonigric afferents of the striatum use the neurotransmitters GABA and substance P or enkephalin. The caudate nucleus sends efferent fibers towards the thalamus (striatum-thalamic fibres), putamen and globus pallidus [1, 3].

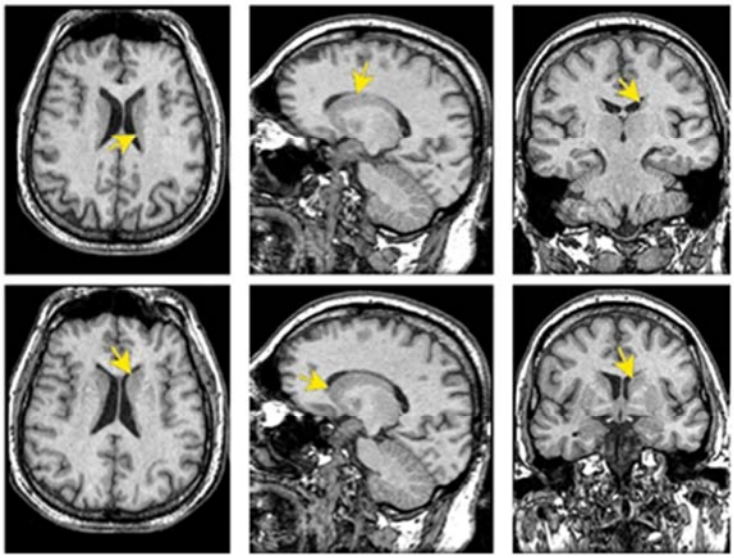

Figure 3. *Axial, sagittal and coronal image of the brain with magnetic resonance imaging showing (yellow arrow) the body (upper images) and head (middle images) of the caudate nucleus and the putamen (lower images) components of the body fluted.*

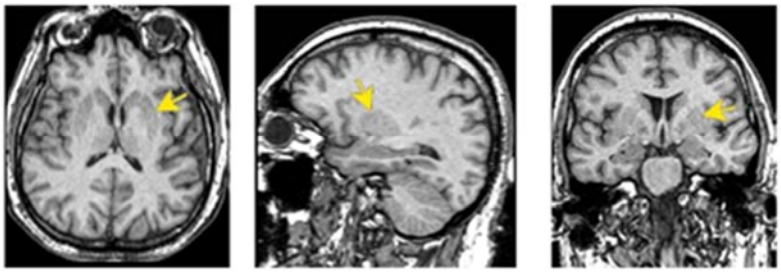

Figure 4. *Magnetic Resonance Image in Axial, Sagittal and Coronal sections that demonstrates the characteristics of the Putamen.*

The globus pallidus is located between the third ventricle and the putamen, separated by an external lamina of the latter. It is subdivided into external globus pallidus (GPe) and internal globus pallidus (GPi) (Figure 5). It is formed mainly of large neurons predominating the neurotransmitter gamma aminobutyric acid (GABA) and as associated neuropeptide is substance P in the GPi and enkephalin in the GPe. The globus pallidus receives afferent fibers mainly from the caudate nucleus and the putamen, in addition to the subthalamic nucleus, the pars compacta of the substantia nigra, the dorsomedial and ventral anterior nuclei of the thalamus, in addition to the cortical areas 6 and 4. The efferent fibers of the globus pallidus are the main exit route of the basal ganglia. There are four main routes: (a) the lenticular fascicle; (b) the ansa lenticularis; (c) the palidotegmental fibres, (they arise from GPi); and (d) pale-subthalamic fibers (arise from GPe) [1, 3].

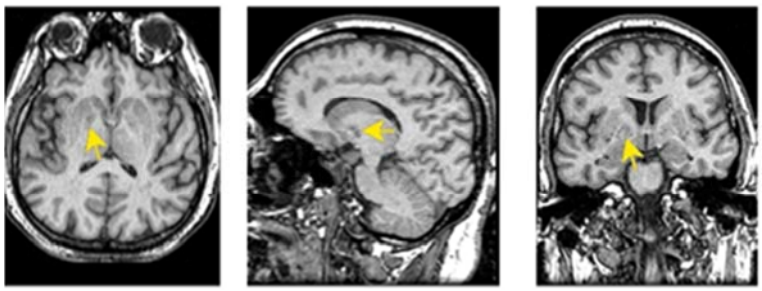

Figure 5. *Axial, sagittal and coronal image of the brain magnetic resonance imaging where the Globus Pallidus is indicated (yellow arrow).*

The substantia nigra (SN) is located at the level of the superior colliculi in the region of the cerebral peduncle exactly between the crus cerebri and the tegmentum in the midbrain. (Figure 6). It constitutes the population of primary dopaminergic cells of the mescencephalon. It is composed of two regions: the pars compacta (SNc) where there are large dopaminergic cells with a high concentration of melanin and the pars reticular (SNr) that contains large non-pigmented multipolar neuronal cells with a predominance of the GABA neurotransmitter and is related to the efferent functions of the basal ganglia. In the substantia nigra, the reticular pars receives striatonígricas afferents from the striatum, the globus pallidus and the subthalamic nucleus. The primary efferent pathways of the substance nigra are towards the striatum, the midbrain tectum, and the thalamus. The nigrostriatal dopaminergic fibers project from the pars compacta to the striatum. The pars reticularis functionally related to the internal globus pallidus; its efferent pathways are GABAergic type. The nigrotectal tract is the structure that connects the substantia nigra with the superior ipsilateral colliculus and could be involved in the control of eye movements. The nigrothalamic tract extends towards the ventral and dorsomedial nucleus of the thalamus [1, 3].

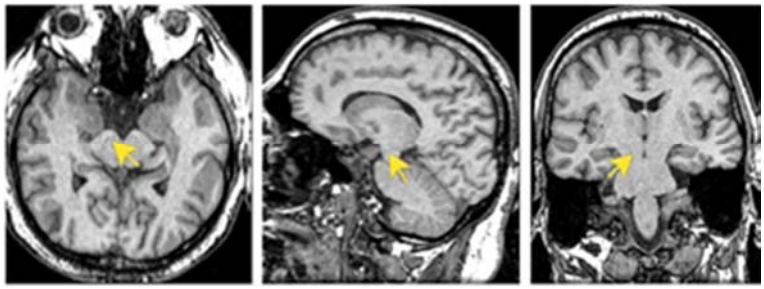

Figure 6. *Image in axial, sagittal and coronal section where the Substantia Nigra is indicated (yellow arrow).*

The subthalamic nucleus of Luysii (STN) is located in the ventral area of the thalamus, being located dorsal and medial to the cerebral peduncle. This structure is reciprocally connected (efferent-afferent fibers) with the globus pallidus through the subthalamic fascicle. The connection with the subthalamic nucleus of Luysii (STN) is the only efferent pathway of the globus pallidus that emerges from GPe.

In some neuroanatomy texts other structures of gray matter located at the base of the brain are mentioned as part of the basal ganglia; although, they do not have a functional importance, and that for clinical purposes are not considered part of the extrapyramidal system, these are: the innominate substance, the nucleus accumbens, the claustrum, the amygdala, the perforated anterior substance and the olfactory tubercle.

From the physiological point of view it is mentioned in the literature that there are two main interconnections with the cerebral cortex for the control of movement that are with the basal ganglia and the cerebellum. We will refer to the relationship of the motor cortex with the basal ganglia. The main connections form the following circuit: striated bark-body-globus pallidus-thalamus-cortex [1].

It is very important to remember that currently physiological models of the primary function of the basal ganglia include two main pathways: a direct pathway and an indirect pathway in relation to their functional interconnections. (Figure 6). Where the direct route is of the excitatory type, it serves to facilitate the excitation of the cortical region and perform voluntary movements, and the indirect route is of the inhibitory type, and it serves to inhibit the excitation of the cortical region and prevent unwanted movements. These important pathways interconnect the nuclei of entry and exit of the structures called basal ganglia. The entry nuclei are formed by the caudate nucleus, the putamen and the subthalamic nucleus and their function is to facilitate the motor activity of the cortical region by disinhibiting the thalamus, or, they inhibit motor activity by increasing the inhibition of the thalamus. The internal globus pallidus (GPi) and the nigra reticular substance (SNr) are the exit nuclei and tonic inhibit the motor thalamus. The outflow of the striatum and globus pallidus are mainly inhibitory. Therefore, the route from the striatum to the thalamus can be excitatory or inhibitory, depending on the route used [1, 3].

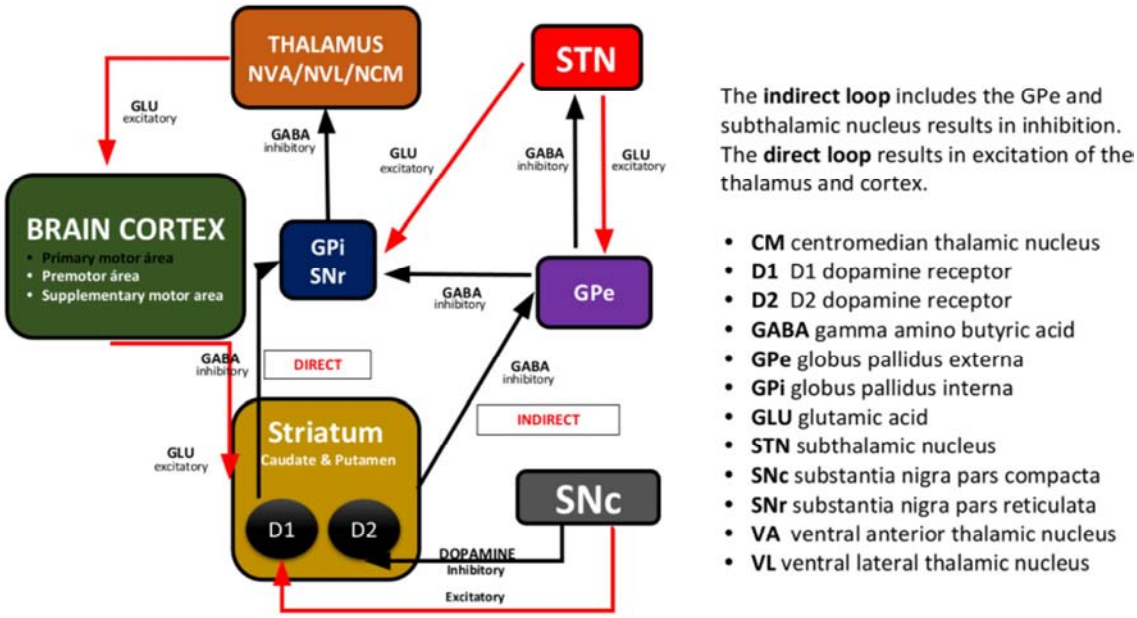

Figure 7. *Image where the direct and indirect pathways and their interconnections of the basal ganglia are schematized. (Exciting red arrows, inhibiting black arrows).*

It is known that another important component in the functionality of these neurological interconnections is the region called pars compact of the substantia nigra (SNc) that projects dopaminergic fibers towards the striatum, causing excitation or inhibition depending on the type of receptor that has been stimulated. Five subtypes of dopamine receptors, designated D1 through D5, have been described. Being the receivers D1 and D2 the main ones related in the regulation of the movement. The effect that the neurotransmitter dopamine has on D1-type receptors is primarily excitatory; used by the direct route generating facilitation and increased thalamic-cortical excitation. Similarly, the excitation of D1-type receptors by the neurotransmitter dopamine via the direct pathway increases the inhibitory effect of striatum in the internal globus pallidus and the pars reticularis of the substantia nigra (GPi / SNr), resulting in in a decrease of the inhibitory effect in the thalamus and an increase in the excitation of the thalamic-cortical interconnection. The result obtained is that the nigrostriatal system facilitates activity in the direct pathway, which increases thalamic-cortical excitation and inhibits activity in the indirect inhibitory pathway, which also increases thalamic-cortical excitation. The observed effect on dopamine D2 receptors is inhibitory. The indirect route works through D2-type receptors, at this site the inhibitory action of dopamine on D2 receptors decreases the inhibitory effect of the striatum in the external globus pallidus through the indirect route, resulting in consequence in a decrease of the inhibitory effect of the same in the subthalamic nucleus. (Figure 6). Disinhibition of the subthalamic nucleus of Luysii causes an increase in its ability to excite the internal globus pallidus and the pars reticularis of the substantia nigra, thus increasing the inhibitory production of both and causing a net decrease in thalamocortical excitation. When there is dopamine deficiency, cortical activation is reduced by the reduction of the facilitation through the direct excitatory pathway as well as by the lack of inhibition of the indirect inhibitory pathway. Therefore, alterations of the direct pathway will produce diseases where hypokinesia predominates, for example in Parkinsonism, and alteration of the indirect pathway will produce diseases where hyperkinesia predominates, for example, in chorea or hemiballism. To date, it has been established that hypokinetic movement disorders, such as parkinsonism, are the result of a significant increase in the normal inhibitory effects of the basal ganglia output neurons and that hyperkinetic movement disorders, as in the case of

chorea, hemiballism and dystonia, are possibly due to a reduction or impairment of the normal inhibition of the "motor thalamus" by the internal globus pallidus-substantia nigra pars reticularis.

In the reports of the neurological literature, it has been proposed that the clinical picture of hemiballism is the result of a lesion of the contralateral subthalamic nucleus of Luysii, generally due to damage to the neuronal structures due to a cerebral vascular lesion of the ischemic infarction type [1, 3, 4]. Injury to this structure eliminates the normal facilitation of the inhibitory effects of the substantia nigra pars reticularis of the internal globus pallidus, which disinhibits the motor thalamus and the motor cortex, which would cause the presence of hyperkinetic movements of the affected limbs [5]. (Figure 8).

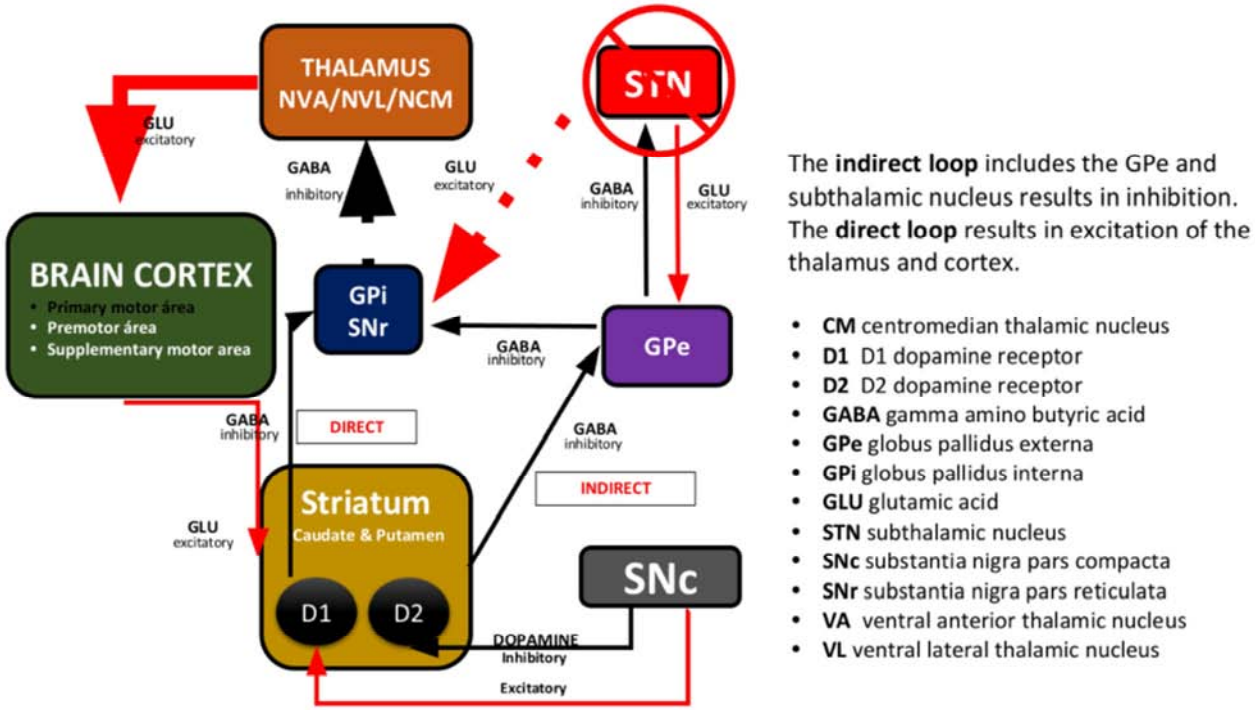

Figure 8. *Image where the direct and indirect pathways of the basal ganglia and their main interconnections are schematized. A lesion in the subthalamic nucleus of Luysii is exemplified that causes a reduction in the excitatory function on the internal globus pallidus (GPi) causing a decrease in the inhibition of GPi towards the thalamus causing an excitatory increase in the motor cortex producing a picture of hemiballism.*

Ballism is characterized by violent centrifugal movements of great amplitude, usually involving the proximal region of some limb and when both limbs on one side of the body are affected it is called hemiballism. The term derives from the Greek word *ballistēs* which means "to jump, dance, throw" [6].

It has been defined as "uncoordinated, violent and continuous involuntary activity that involves the proximal and axial appendicular musculature, so that the extremities are thrown away". Rarely, it can occur bilaterally (biballism or paraballism). The alteration It is usually caused by a lesion in the contralateral subthalamic nucleus of Luysii, but it has also been associated with alterations in other subcortical areas, it has been reported in the literature that ischemic infarction in the caudate nucleus, striatum, lenticular nucleus or thalamus also It has been associated with the presence of the clinical picture of hemiballism [7, 8]. However, there are reports in the literature that this disorder can appear even in the absence of a lesion in the subthalamic nucleus of Luysii [7, 9].

At the ultrastructural level (cellular and molecular), ballism can be caused by multiple pathologies that could include: ischemia-type injuries, infections, demyelination and neoplasms [9-15].

There is sufficient information to show that many patients with hemiballism also present with distal choreic movements and, as the recovery phase occurs, the hemiballism often progresses to hemichorea and even hemidystonia [7-13].

All this information must be considered for the adequate selection of the treatment where a practical approach individualized and adapted to the needs of the patients is crucial to obtain the optimal response of the substance used, in order to improve the symptoms, reduce the disability, dependence on caregivers and improve the quality of life. As it is considered a highly complex pathology, the main objectives of drug treatment are to reduce morbidity and prevent complications. Therapeutic, pharmacological or rehabilitation strategies are guided not only by information or data based on evidence, but also by long-term observational and personal experience, because in reality we often lack more reliable data and well designed and randomized clinical protocols. Currently the new drugs used, the use of botulinum toxin and the surgical treatments implemented also need to be critically reviewed.

The most widely used pharmacological agents in the control of abnormal hyperkinetic movements are the so-called neuroleptics (see Table 1). The basis of its mechanism of action has been considered to be directly related to the blockade of receptors for the neurotransmitter dopamine. Neuroleptics or antipsychotic substances can be classified into two large groups: typical neuroleptics and atypical neuroleptics.

Typical neuroleptics include haloperidol and fluphenazine [16]. On the other hand, the neuroleptics called atypical include, among others, risperidone, olanzapine, clozapine and quetiapine [16]. Another option in the treatment of chorea is represented by agents that reduce dopamine, such as reserpine and tetrabenazine [17, 18].

Some chemical substances that can be used in a complementary way in the management of these patients are GABAergic drugs, such as clonazepam, gabapentin and valproic acid [19].

Table 1. *Table showing the main drugs and their mechanism of action used in the therapeutic management of ballism and hemiballism.*

Drugs	Mechanism of action
Antipsychotic agents	
They block dopamine receptors and have antispasmodic-like effects.	
Haloperidol (Phenylbutylpiperazine)	1. Antagonizes the D1 and D2 dopamine receptors. 2. Depress the reticular activation system. 3. Inhibits the release of hypothalamic and pituitary hormones.
Flufenazine (Phenothiazine)	1. Antagonizes the D1 and D2 dopamine receptors. 2. Depresses the release of hypothalamic and pituitary hormones. 3. Blocks postsynaptic mesolimbic dopamine receptors. 4. It has alpha-adrenergic and anticholinergic effects. 5. Depresses the reticular activation system.
Clozapine (Neuroleptic atypical)	1. Shows blocking activity of receiver D2 and receiver D1 2. It also possesses antiserotoninergic properties (5-HT1C, 5-HT2, 5-HT3) 3. Affinity for the mesolimbic dopamine D4 receptor. 4. It blocks cholinergic, histamine, serotonergic, norepinephrine, and dopamine receptors.
Olanzapine	1. It can act through the combination of antagonism of the dopamine-type 2 receptor site and serotonin. 2. It can inhibit the effects of serotonin, muscarinic and dopamine.
Risperidone	1. High affinity for type 2 serotonin receptors (5-HT2) 2. Reduced binding affinity for D2 (dopamine) receptors, 20 times lower than 5-HT2 receptors 3. Antagonism at alpha1-adrenergic, alpha2-adrenergic and histaminergic-like receptors 4. Moderate affinity for type 1 serotonin receptors (5-HT1A, 5-HT1C, 5-HT1D) 5. Weak affinity for D1-type dopamine receptors 6. No affinity for beta1- and beta2-adrenergic receptors, as well as muscarinic ones 7. Binding to the dopamine D2 receptor (20 times less than that of the 5-HT2 receptor).
Quetiapine (Antipsychotic atypical)	1. Antagonism of the receptors for neurotransmitters dopamine type D1 and D2, adrenergic alpha1 and alpha2, histamine type H1 and serotonin types 1 and 2 (5-HT1A, 5-HT2)
Monoamine depleting agents	
The antichorea effect of agents that deplete central monoamine is believed to be related to their effect on the reversible depletion of monoamines (eg, dopamine, serotonin, and norepinephrine) of nerve endings.	
Reserpine	1. Antagonist of peripheral adrenergic neurons through depletion of catecholamine tissue store (norepinephrine, dopamine) that produces lower blood pressure and sedative effects. 2. Exhausts norepinephrine and epinephrine
Tetrabenazine	1. It causes reversible inhibition in the human vesicular monoamine transporter type 2 (VMAT2), to produce a decrease in the uptake of monoamines (eg, dopamine, histamine, serotonin and norepinephrine) at the level of synaptic vesicles and generates depletion of the monoamine reserves of nerve endings.
Deutetrabenazine	1. It is an inhibitor of the vesicular monoamine transporter-2. (VMAT-2). 2. Reduces the absorption of monoamines (eg, dopamine, norepinephrine, serotonin and histamine) at the level of synaptic vesicles.
Benzodiazepines	
Used to reduce the concentrations of GABA in the caudate nucleus, the putamen, the substantia nigra and the globus pallidus.	
Clonazepam (Benzodiacepina de vida media larga)	1. Increases presynaptic GABA inhibition. 2. Reduces monosynaptic and polysynaptic reflexes. 3. Suppresses muscular contractions by facilitating the inhibitory neurotransmission of GABA.
Anticonvulsants	
They help through various neuropharmacological mechanisms. Valproic acid is a GABAergic type agent and helps in the same way as benzodiazepines. The mechanism of action of carbamazepine is the stabilization of the inactive state of voltage-gated sodium channels, reducing neuronal activation in many systems and thus nonspecifically reducing abnormal movements in patients.	
Valproic Acid	1. Increases the levels of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) in brain tissue 2. May enhance or mimic the action of the neurotransmitter GABA at receptor sites at the postsynaptic level 3. May inhibit sodium and calcium channels.
Carbamazepine	1. Stabilizes the inactive state of sodium channels, making neurons less excitable 2. Reduces the activity of the ventral nucleus of the thalamus. 3. Decreases synaptic transmission or the sum of temporary stimulation that leads to neuronal firing.

3. Conclusion

As a general overview of the functions of the basal ganglia and their interconnections, we can summarize that the direct pathway is mediated by dopamine D1 receptors and results in facilitation of movement. In this pathway, the motor cortex sends signals of glutaminergic activation to the caudate nucleus and to the putamen exciting the D1 receptors. Its activation inhibits the activity of the internal globus pallidus and the reticular pars of the substance nigra. That the projection fibers from the striatum to the internal globus pallidus inhibit the pale-thalamic inhibitory pathway and result in excitation and cortical facilitation. Likewise, it generates excitation of the thalamic projections towards the cerebral cortex, causing inhibition in the pale bundle-thalamus. As a consequence, the activity in the so-called direct pathway causes as a final result an evident increase in excitation at the cortical level and when it is at a normal level, voluntary movements are of normal characteristics. On the contrary, when there is a pathological decrease in cortical activation due to a disease or dysfunction involving the direct route, voluntary movements are inhibited; this situation will cause typical hypokinetic movement disorders, as in Parkinson's disease. That the indirect pathway is mediated by type D2 dopaminergic receptors and its stimulation produces an inhibition of movement. Where the motor cortex sends signals of glutaminergic activation to the caudate nucleus and to the putamen activating the D2 receptors; that the striopalidal fibers then project to the outer globus pallidus (GPe), causing the inhibition (GABAergic); and likewise that the external pallidus globus projects GABAergic inhibitory fibers by means of the subthalamic fascicle to the Luysii subthalamic nucleus (STN) and this facilitates the inhibitory projection of the globus pallidus internal to the thalamus, which results in a decrease in the activity in the thalamo-cortical pathways.

The striopalidal fibers in the internal globus pallidus and the reticular pars of the superficial substance nigra as well as the fibers of the globus pallidus interna to the thalamus are GABAergic type inhibitors. At rest, the connections of the internal globus pallidus and the reticular pars of the substance nigra exert an inhibitory influence on the thalamus, which diminishes the exciting influence of the thalamus in the cortex. We have mentioned that the activity in the indirect route avoids the activation of cortical motor areas that could interfere with the voluntary movement executed by the direct route. Recognizing that when there is a pathological increase in cortical activation due to a disease that involves the indirect pathway, movements are increased causing hyperkinetic type disorders, such as chorea or hemiballism. Considering the information mentioned with the data obtained in the clinical evolution and the paraclinical studies of neuroimaging that show very important diffuse encephalic involvement of vascular type in the cortical, subcortical and basal ganglia regions it is necessary to consider that the picture that the patient developed of abnormal movements of hyperkinetic type (hemiballism) of the left side of the body would be the result of a combination of the structural alteration evidenced and potentiated by the increase that was made in the drugs for the management of their apparent Parkinson's disease. The favorable response that he presented when carrying out the reduction of parkinsonian drugs and the use of neuroleptic substances (haloperidol) confirms and supports us to support the arguments expressed in the diagnostic conclusions.

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