Chapter 7

Anatomical, Biological, and Surgical Features of Basal Ganglia

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Abstract

Basal ganglia refers to the deep gray matter masses on the deeply telencephalon and encompasses a group of nuclei and it influence the information in the extrapyramidal system. In human they are related with numerous significant functions controlled by the nervous system. Gross anatomically, it is comprised of different parts as the dorsal striatum that are consisted of the caudate nucleus and putamen and ventral striatum which includes the nucleus accumbens, olfactory tubercle, globus pallidus, substantia nigra, and subthalamic nucleus. Nucleus accumbens, is also associated with reward circuits and has two parts; the nucleus accumbens core and the nucleus accumbens shell. Neurological diseases are characterized through the obvious pathology of the basal ganglia, and there are important findings explaining striatal neurodegeneration on human brain. Some of these diseases are induced by bacterial and/or viral infections. Surgical interference can be one alternative for neuronal disease treatment like Parkinson's Disease or Thiamine Responsive Basal Ganglia Disease or Wilson's Disease, respectively in addition to the vascular or tumor surgery within this area. Extensive knowledge on the morphological basis of diseases of the basal ganglia along with motor, behavioral and cognitive symptoms can contribute significantly to the optimization of the diagnosis and later patient's treatment.

Keywords: anatomy, biology, surgery, basal ganglia

1. Structure and function of human basal ganglia

The term "basal ganglia" refers to the deep gray matter masses on the deep telencephalon and encompasses a group of nuclei [1]. Generally, basal ganglia influence information in the extrapyramidal system and in human beings they are related with numerous significant functions

controlled by the nervous system, including control of the voluntary motor movements, procedural learning, and habitual behaviors such as eye movements, cognition, and emotions. The nuclei group is placed deep beneath the cortical area of the brain.

Additionally, the basal ganglia specialize in processing data on movement and in fine adjustment of the brain circuit activity that defines the best suitable response in specific habitual conditions/actions such as riding a bicycle, playing a piano, and so on. They also play a major role while planning movement and learning novel actions in new situations [2, 3]. From an embryological point of view, the central nervous system (CNS) develops in early stages of embryological development in many of mammals, including humans, from the neural plate. In humans, at the middle of the third week of development, ectodermal cells from epiblast fold to form a neural groove and then differentiate into the neural tube. At the 24th day, the anterior neuropore and then at the 27th day the posterior neuropore are closed [4–6], while the cerebrospinal fluid is secreted by the ependymal cells, which are lining within the ventricular system, prosencephalic, mesencephalic, and rhombencephalic vesicles that develop from the rostral part of the neural tube and also the spinal cord from the caudal part of the neural tube. While telencephalic vesicles developed from a part of the prosencephalic vesicle at the late 34th day, at the 36th day, anlage primordium of the future cerebral cortex, basal ganglia, and olfactory bulb can be clearly identified. At the eighth week of the development of the basal ganglia, neuroepithelium is clearly defined near the other epithelial structures such as thalamic, hippocampal, and hypothalamic epitheliums. Basal ganglia neurons are derived from this epithelium [4–6]. Between the 19 and 22 gestational weeks, the neuroepithelial cell layer becomes thicker and new neurons are generated, which migrated into the striatum. Between the 23 and 28 gestational weeks, in basal ganglia, the neuroepithelial cell layer over some places of caudate nucleus became faint. Again, at week 27 of the development in the basal ganglia, neuroepithelial cellularity is scant. Between the 29 and 33 gestational weeks in the basal ganglia, neuroepithelium was thicker over the striatum and nucleus accumbens. At the 32nd week of the development process, the number of the glial cells increased [4–6]. On the other hand, during this period, the onset of myelinization was very silent. At the 35th week, it can be detected microscopically in the subventricular zone, neuroepithelial cells are limited and the glial cell number is increased. In addition, there is a slight onset of myelinization in the internal capsule. At term, proliferating neuroepithelial cells can be detected in the subventricular zone, while the numbers of astrocytes decrease in the internal capsule and basal ganglia. In the postnatal period, basal ganglia and diencephalic neurons were well organized, and myelinization of the internal capsule is complete approximately at the 6th week postnatally. Two years postnatal, in basal ganglia, all of the mature histological structures can be clearly detected in the caudate and putamen, and myelinization of internal capsule appeared completely [4–6].

In our investigation, we aimed to highlight the anatomical, biological, and surgical importance of cortical-basal ganglia circuits and their role in the pathogenesis of neurological process. Depending on the facts available nowadays and our experience, we developed an opinion that detailed anatomy related information in embryology, histology, and gross anatomy as well as molecular and surgical information on the basal ganglia and neighborhood structures may cause confused clinical outcomes and possibly the option of renovating the morphological brain structure after intervention to the region of intervention [4–6].

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Gross anatomically, the basal ganglia are composed of different parts including the dorsal striatum consisting the caudate nucleus and putamen and ventral striatum, which includes the nucleus accumbens, olfactory tubercle, globus pallidus, substantia nigra, and subthalamic nucleus. Each of these parts possesses defined, complex internal morphological and biological features. Basal ganglia are composed of several subcortical nucleus groups that are located deep on each of the cerebral hemispheres. They are called "lentiform nucleus," which includes both the putamen and globus pallidus; the "striatum," which includes the nucleus caudatus and putamen; and "corpus striatum," including the caudate nucleus and the nucleus lentiformis, and the others including the claustrum, subthalamic nucleus, nucleus accumbens, and their projections. The substania nigra is also a basal nucleus, which is placed on the mesencephalon [4–6]. This nuclear group carries heterogeneous formations, functionally, terminologically and phylogenetically. Details are presented in **Figure 1**.

According to the previous classification, the amygdaloid body was considered to be a part of the basal ganglia (archistriatum). Due to the acquisition of new scientific data associated with it, anatomists considered it as a functional educative part [8].

Clastrum is located on the lateral to the putamen and medial to the insula, which was noted by some sources to be a part of the basal ganglia [8]. The globus pallidus externus was originally revealed as a simple relay within the basal ganglia [9].

The nucleus accumbens is also associated with reward circuits that are located in the basal forebrain region superior to the preoptic region of the hypothalamus, while the prefrontal area was on both cerebral hemispheres, whose mission is planning and motivating movement performed by the body. The nucleus accumbens has two parts: the nucleus accumbens core and the nucleus accumbens shell, which consist of their own morphology and functions [10–15].

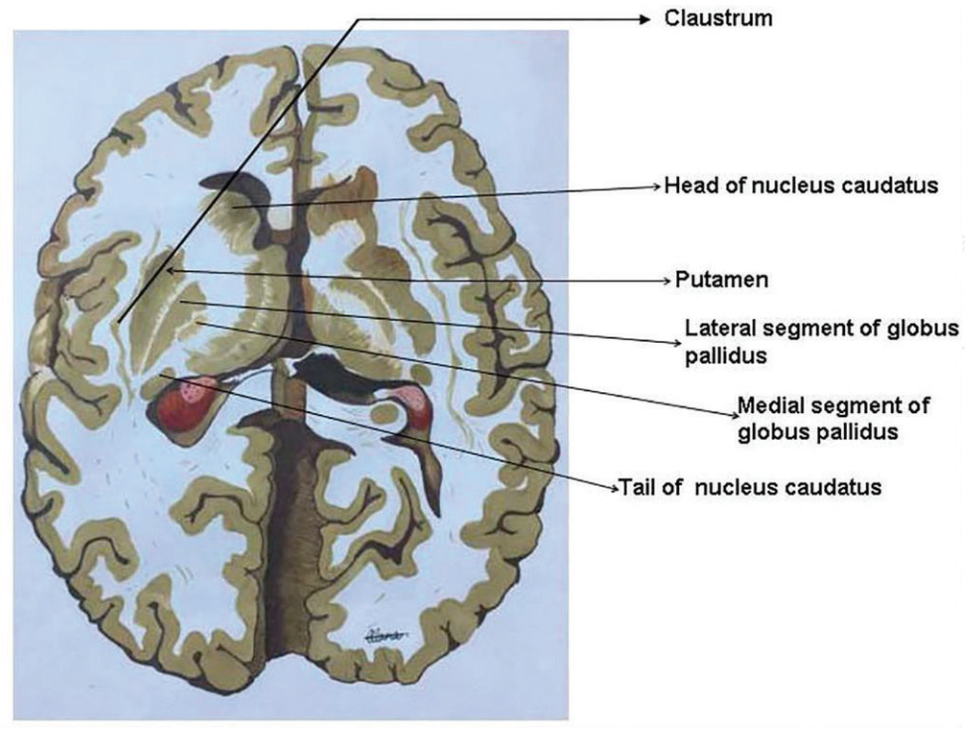

Figure 1. Nuclei of the basal ganglia showing the different components [7], with modifications.

From the histophysiological point of view, basal ganglia circuits contain an assortment of cell types that mediate synaptic interactions within and between basal ganglia nuclei [16]. Neurotransmitters also play an important role in the different areas of the basal ganglia. For example, dopamine, which has a very important function within the basal ganglia, is the source of the striatal input in the substantia nigra (**Figure 2**).

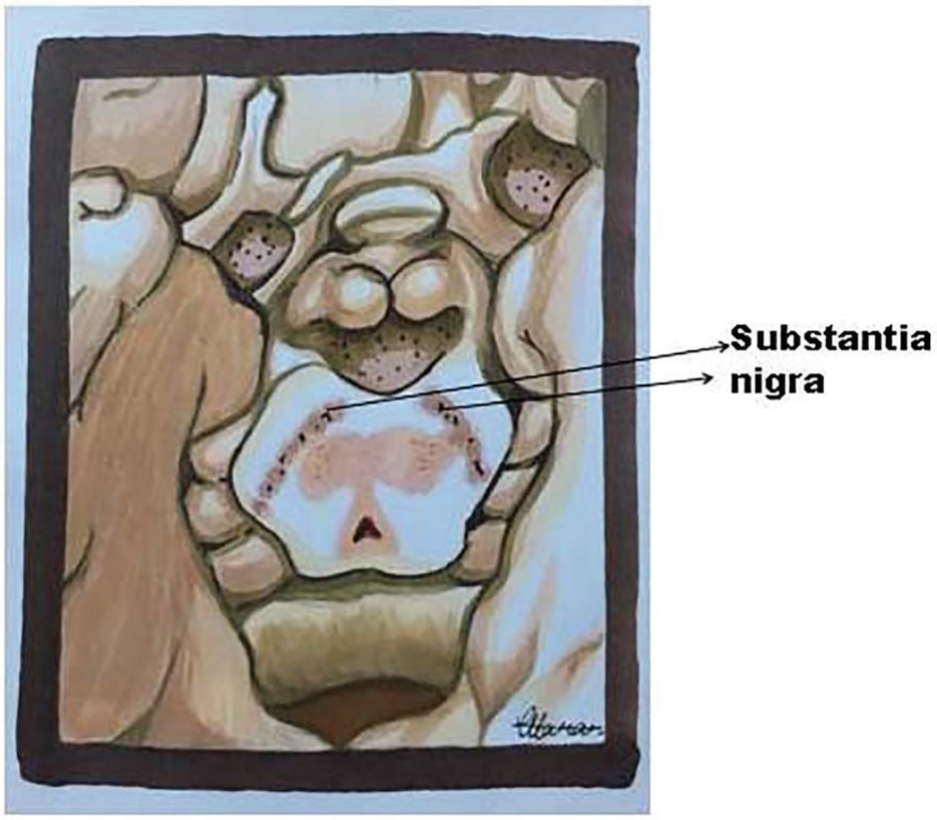

Figure 2. Illustrations showing the substancia nigra, according to [8] with modifications.

2. Pathogenic conditions of the basal ganglia

Huntington' and Parkinson's diseases are caused by the degeneration of dopamine-producing cells in the substantia nigra [4, 17]. On the other hand, most of the neurons in the basal ganglia use *gamma*-Aminobutyric acid (GABA) as a neurotransmitter, which possesses an inhibitory effect on the target neurons. Acetylcholine is another important neurotransmitter and is regularly used by both external inputs to the striatum and by a group of striatal neurons. Although the total number of cholinergic neurons is the smallest in all brain neurons, one of the major acetylcholine concentration regions is the striatum [4, 17].

Striatum (**Figures 3** and **4**) is currently considered to be the largest region of the basal ganglia that arise from numerous large and small bundles of nerve fibers [18]. The histological organization of the striatum is considered very complex. The great populations of striatal neurons

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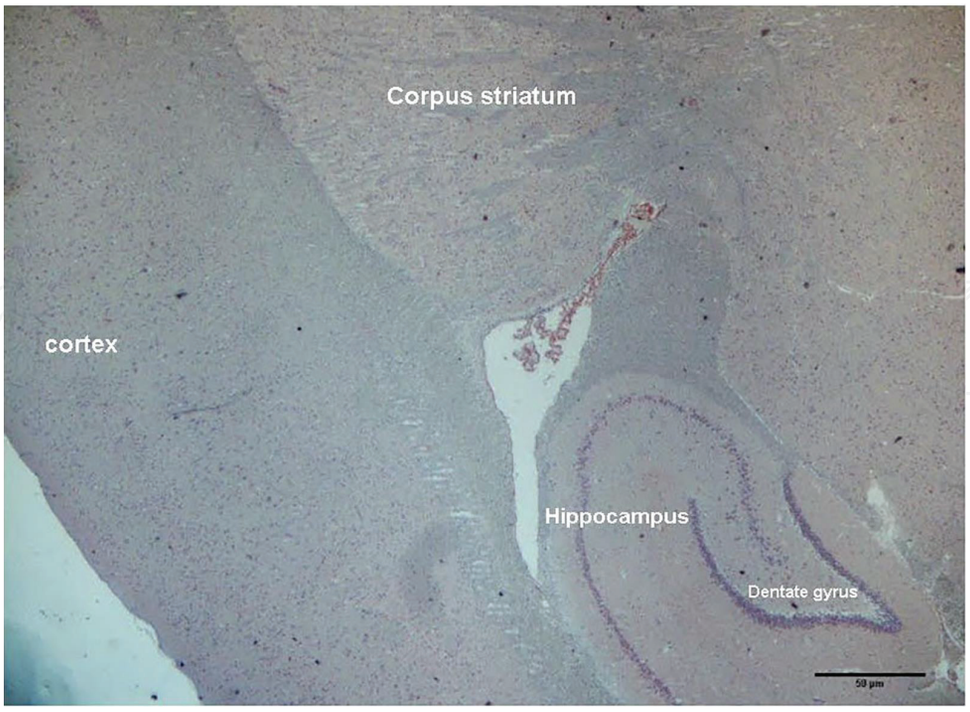

Figure 3. Corpus striatum in the sagittal section stained with caspase 3 immunostaining. Magnification, ×2 (with courtesy to Esra ASLAN MD).

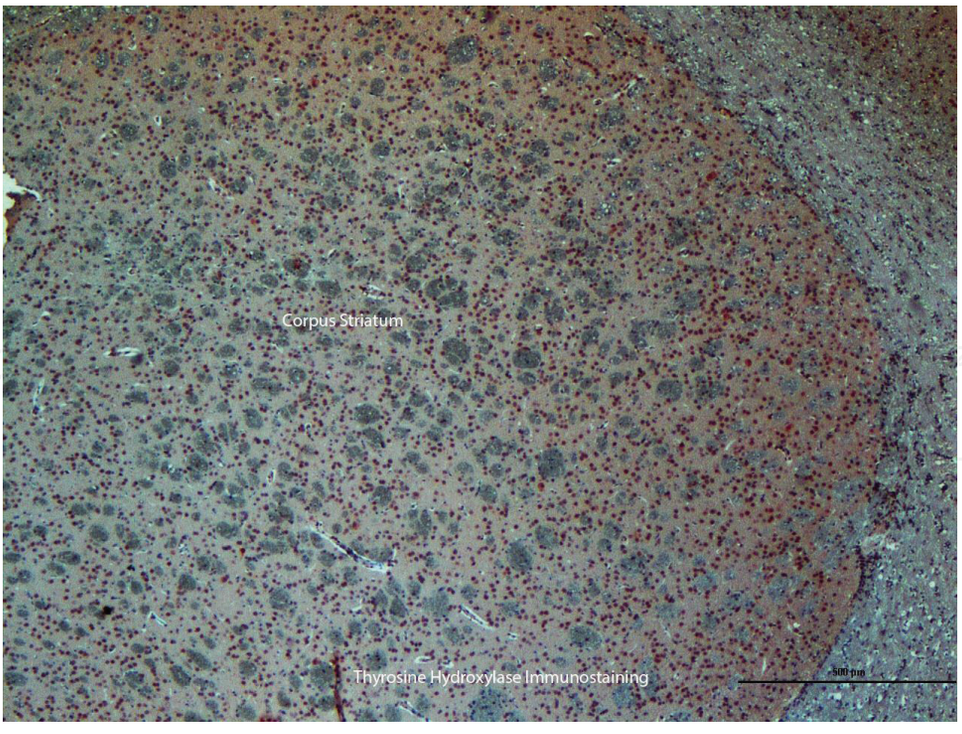

Figure 4. Corpus striatum in the coronal section with thyrosine hydroxylase immunostaining. Magnification, ×10. (with courtesy to Esra ASLAN, MD, Afyon Kocatepe University).

are medium spiny neurons, which are GABAergic cells with small bodies, densely covered dendritic spines that receive input from the cortex and the thalamus. The cholinergic neuron population in striatum comprises of the cholinergic neurons with smooth dendrites [2].

The pallidum consists of both the globus pallidus and the ventral pallidum. The globus pallidus can be divided functionally into the internal and external segments. Histologically, both segments have primarily GABAergic neurons [19]. While external segments receive inputs mainly from the striatum and pass through the subthalamic nucleus, the internal segment receives input from direct and indirect pathways. Pallidal neurons functions basically via de-inhibition, a mechanism in which there are inhibitory effects on the target [2].

The substantia nigra is a mesencephalic gray matter portion of the basal ganglia, which is divided into two parts: pars compacta and pars reticulate. Although pars compacta produces dopamine, which plays a major role as a regulator neurotransmitter in the striatal pathway, the pars reticulate has inhibitory effects on the thalamus [19].

The subthalamic nucleus is a diencephalic gray matter portion of the basal ganglia and produces glutamate, which is an excitatory neurotransmitter in the ganglia. This nucleus, while receiving inhibitory input from external part of the globus pallidus, also sends excitatory input to the internal part of the globus pallidus.

3. Basal ganglia-related pathological conditions

Clinically, many neurological diseases are characterized through the obvious pathology of the basal ganglia, and there are important findings that explain striatal neurodegeneration on the human brain. Some of these diseases are induced by bacterial and/or viral infections where the bacteria and/or virus introduces some genetic material and, as a consequence, either activated or downregulated some of the life's essential processes [20–26] or other diseases that are affected by the cytokine regulation in association with neurodegenerative diseases like TGF-β [27] or TNF-α [28] in addition to applications related to medical solutions like in dentistry [29]. Here, and as a consequence, affecting either the functionality or the neuronal structure or both of them can be seriously affected. Lately, more knowledge about the problems of the basal ganglia patients with neurodegenerative, vascular, metabolic, inflammatory, immunologic, allergic, congenital, traumatic, endocrine, malignant, and neurophyschiatric diseases became available [30–32]. A comprehensive understanding of the striatal projection loss while receiving striatal input/output on the neurons will contribute to the available knowledge related to the pathogenesis of the neurological diseases. Surgical interference can also be one alternative for neuronal disease treatment as it is the case for Parkinson's disease, thiamine responsive basal ganglia disease or Wilson's disease, respectively, in addition to the vascular or tumor surgery within this area. The lesions of the basal ganglia can cause tremors, grimaces, and repetitive movements [4, 17]. At the same time, in different pathological processes, such as Kernicterus, Tourette syndrome, hemiballismus, obsessive-compulsive disorder, neonatal and lacunar infarction, Huntington's and Parkinson's diseases, basal ganglia neurons were affected. Again, in carbon monoxide poisoning, selective necrosis is caused in the globus palidus [3, 33].

4. Potential approaches for basal ganglia disease treatment

In order to limit or inhibit this type of disorders, gene therapeutic [34] based treatment modalities bear potential for the treatment of nervous system diseases or disorders, these include viral vector systems [35, 36], gene-based vaccines and immunotherapy [37, 38], plasmid DNA applications [39], cytokine targeting like TNF-α targeting [28], epigenetic targeting [40] and anti nervous system degenerative diseases treatment by molecular regulators RNAi applications [41]. Several studies on basal ganglia supported by data aligned to age- and/or gender-dependent relation of intelligence with volumes of the nuclei were presented recently [42, 43], still limited results were known regarding the potential influence of age- and sexual distinctive diseases on the subcortical nuclei [44]. The basal ganglia (BG), which play a major role in selecting and shaping motor and cognitive behaviors, are significant for connection among forebrain nuclei [9].

Surgically, in some neurologic diseases, using deep brain stimulation (DBS), which is an implanted electrical device modulate for distinct targets at the brain, resulted in the symptomatic improvement of movement disorder, especially [45, 46] in both hyper- and hypokinetic movement disorders of the basal ganglia deep brain stimulation (DBS) that is considered highly effective. The clinical benefit of DBS is based on the experience with prior surgical ablative therapies for the disorders of these regions, and, in part, used by neurosurgeons decades ago. The most commonly DBS-treated conditions were and are Parkinson's disease and dystonia, which are treated by electrical or radiofrequency lesioning of that region before DBS [46–53]. The duration and temperature are important for both procedures. Applying electrical current the functions that were partially or totally lost due to nervous system disease or injury can be restored [54].

In stereotaxic surgery, some entry points described by the authors for nucleus accumbens [55] were as follows: 7–9 mm below the anterior commissure-posterior commissure (AC-PC) line, 19–23 mm prior to the midpoint, and 4–10 mm lateral to the median line. The original target is the core of the nucleus accumbens. For deep brain stimulation applications as refractory major depression, Tourette syndrome and obsessive-compulsive disorders the stereotactic coordinates were as follows: 4–4.5 mm ventral to the AC-PC plane, 1.5–2.5 mm anterior to the anterior border of the AC, and 6.5–8 mm lateral to the midline [56, 57].

In treating obsessive-compulsive disorders with accompanying major depression, Aouizerate et al. reported their experience in DBS targeting as the tips of the electrodes were situated 3.0 mm below the AC-PC line, 8.9 mm lateral to the AC-PC line, and 36.5 mm anterior to the PC on the right side, and 1.7 mm below and 7.6 mm lateral to the AC-PC line and 31.4 mm anterior to the PC on the left side [58].

The subthalamic nucleus (STN) of advanced Parkinson's disease patients undergoing deep brain stimulation application is a prominent target for treatment. In many patients, to identify significant target, microelectrode recording (MER) is used. Moran in a previous work showed that trajectories served as a training set and found the error in predicting the STN entry to be (mean ± SD) 0.18 ± 0.84, and 0.50 ± 0.59 mm for the STN exit point, which yields a 0.30 ± 0.28 mm deviation from the expert's target center by using MER [59]. In the correlation analysis, there was a negative correlation between right substancia nigra (SN) volume and unified Parkinson disease rating scale (UPDRS) score ($r = -0.466$, $p = 0.038$) and there was a tendency but not a significant correlation between the left SN volume and UPDRS score ($r = -0.443$, $p = 0.050$).

In a previous approach, it was shown that subjects suffering from Parkinson's disease showed a significant asymmetry between both the left and right SN, nucleus caudatus, and nucleus lentiformis volumes ($p = 0.001$, $p < 0.001$, $p = 0.044$), with taking into account that the control subjects also showed a significant asymmetry between the volumes of left and right SN, nucleus caudatus, and nucleus lentiformis ($p < 0.001$, $p = 0.003$, $p < 0.001$, respectively). Mean volume values for SN, nucleus caudatus, and nucleus lentiformis are shown in **Table 1** [60].

Further, in the same approach, the group was examined after subgrouping according to gender into male and female subgroups, as seen in **Table 2**.

In addition, during our experience using stereological methods on the basal ganglia volumetry on the right-handed patients with the Parkinson's disease, we found that the left basal ganglia structure was smaller than left ones. However, when we compared them with the control cases, only substantia nigra possessed a smaller volume. Also, evaluation of the basal ganglia and substantia nigra volume in Parkinson's disease (PD) patients revealed a significant atrophy in SN in comparison to the healthy age-matched control subjects. However, significant atrophy in nucleus lentiformis and nucleus caudatus was not found during the study. Basal ganglia and the SN are the regions with predominantly pathological changes in PD [61]. There are studies in the literature that examine the volumetric differences in basal ganglia and SN anatomy in PD; however, there is no study to our knowledge in the literature that evaluates the asymmetrical volume changes by using the stereological technique [62, 63]. Cavalieri's principle of stereological approaches through point counting is accomplished by overlying each selected section using a regular grid of test points that is randomly positioned [64]. The Cavalieri theorem of systematic sampling combined with point counting proved to be a reliable, simple, inexpensive, and efficient method for volume estimation in MRI [65], and this stereological approach can provide valuable information during the morphological changes evaluated during Parkinson's disease development.

Surgical procedures applied for this purpose can be variable. Gallina et al. [66] provided details of the surgical procedure for both caudate and putaminal tracks through a single frontal entry point for six patients, and for the following 10 procedures and they used two completely distinct routes, with two separate entry points, each for the nucleus caudatus and putamen, respectively.

	Parkinson patients	**Controls**	***P* value**
	Mean ± SD	**Mean ± SD**	
SN left	0.67 ± 0.16	0.78 ± 0.13	0.026
SN right	0.75 ± 0.17	0.92 ± 0.18	0.005
NC left	4.49 ± 0.50	4.42 ± 0.24	0.602
NC right	4.47 ± 0.54	4.60 ± 0.21	0.632
NL left	5.29 ± 0.57	5.25 ± 0.53	0.832
NL right	5.40 ± 0.54	5.52 ± 0.52	0.473

Table 1. Standard volumes of the substantia nigra, nucleus caudatus, and nucleus lentiformis and a group of Parkinson's disease patients compared to subjects of a healthy control group [59].

	Parkinson disease			**Control**		
	Mean ± SD			**Mean ± SD**		
	Left side	**Right side**	***P value***	**Left side**	**Right side**	***P value***
Male						
Substancia nigra	*n* = 13	*n* = 13	0.005	*n* = 10	*n* = 10	0.001
	0.69 ± 0.14	0.75 ± 0.16		0.77 ± 0.15	0.91 ± 0.16	
Nucleus caudatus	*n* = 13	*n* = 13	0.007	*n* = 10	*n* = 10	0.001
	4.56 ± 0.51	4.72 ± 0.60		4.40 ± 0.23	4.58 ± 0.25	
Nucleus lentiformis	*n* = 13	*n* = 13	0.515	*n* = 10	*n* = 10	0.001
	5.29±0.65	5.37 ± 0.57		5.24 ± 0.54	5.56 ± 0.44	
Female						
Substancia nigra	*n* = 7	*n* = 7	0.020	*n* = 10	*n* = 10	0.008
	0.63 ± 0.20	0.75 ± 0.2		0.77 ± 0.15	0.91 ± 0.16	
Nucleus caudatus	*n* = 7	*n* = 7	0.014	*n* = 10	*n* = 10	0.039
	4.36 ± 0.5	4.57 ± 0.45		4.40 ± 0.23	4.58 ± 0.25	
Nucleus lentiformis	*n* = 7	*n* = 7	0.092	*n* = 10	*n* = 10	0.001
	5.28 ± 0.43	5.45 ± 0.52		5.24 ± 0.54	5.56 ± 0.44	

Table 2. Substancia nigra, nucleus caudatus, and nucleus lentiformis volumes in male and female groups of Parkinson disease patients [60].

In surgical processes, surgeons use a stereotactic frame that helps to ensure optimal positioning of desired targets, or frameless stereotactic systems [67] or, alternatively, neuronavigation or electrophysiological mapping of the brain for lesioning-related basal ganglia and for obtaining the main target in a three-dimensional manner in addition to protect the surrounding neural tissue [53, 55, 57, 68, 69].

5. Conclusion

Extensive knowledge on the morphological basis of diseases of the basal ganglia along with motor, behavioral, and cognitive symptoms may significantly contribute to the optimization of both the diagnosis (especially anatomical and histological) and later treatment of the patients, especially patients suffering from neurodegenerative, vascular, metabolic, inflammatory, immunologic, allergic, congenital, traumatic, endocrine, malignant, and neurophyschiatric diseases, in order to at least delay the breakout or the pathogenic degenerative process related to the their disease and/or improve the life quality of the patients. Experimental set-ups dealing with this level of problems can provide us the necessary information for the treatment modalities applied in human therapy. Gene therapeutic approaches can be a future effective alternative for these classes of disease treatment.

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