INTRODUCTION

Inherited basal ganglia disorders are the most devastating brain malfunction affecting children ***(Aldridge and Berridge, 2002)***.

The basal ganglia are composed of parallel, reentrant cortico-subcortical circuits, originating from cortical areas, and terminating in their respective area of origin in the frontal lobe, after traversing the basal ganglia and thalamus ***(Mahlon and Thomas, 2007)***.

The basal ganglia comprise a group of subcortical nuclei (clusters of neurons) at the base of the forebrain. Anatomically, the basal ganglia's motor circuit includes the dorsal striatum (caudate nucleus and putamen), the substantia nigra pars reticulata and pars compacta, the globus pallidus internus and externus, and the subthalamic nucleus. Whereas the limbic circuit consists of ventral striatum (nucleus accumbens and olfactory tubercle), ventral pallidum, and ventral tegmentum. The limbic circuit is responsible for processing information about motivation and emotion ***(Parr-Brownlie and Reynolds, 2017)*.**

The cortico-basal ganglia circuits are important for chunking isolated movements into precise and robust action sequences that permit the achievement of particular goals. During sequence learning, many neurons in the basal ganglia

develop sequence-related activity - related to the initiation, execution, and termination of sequences - suggesting that action sequences are processed as action units. Cortico-striatal plasticity is critical for the crystallization of action sequences, and for the development of sequence-related neural activity. These findings have implications for understanding the symptoms associated with movement and psychiatric disorders ***(Jin and Costa, 2015).***

Basal ganglia disorders are considered as circuit disorder, which result from neuronal activity pathological disturbances throughout specific cortico-subcortical loops ***(Mahlon and Thomas, 2007)***.

The basal ganglia are highly metabolically active, which leads to their symmetrical affection in metabolic abnormalities and neurodegenerative diseases ***(Hedge et al., 2011)***.

Systemic or metabolic causes of basal ganglia lesions are strongly suggested if the abnormalities are bilateral, symmetrical and diffuse, involving the lentiform and caudate nuclei. On the other hand, infections or neoplasms present with asymmetrical, focal or discrete lesions affecting only part of the basal ganglia ***(Hedge et al., 2011).***

Advanced techniques in radiodiagnosis are now capable of detecting unsuspected but readily apparent abnormalities, and may be the first to indicate the correct diagnosis, by taking

all relevant clinical and laboratory information into consideration. MR imaging features do not only include restricted diffusion and the presence of hemorrhage, but may also include abnormalities affecting other brain parts such as the cerebral cortex, brainstem, and white matter. The differential diagnosis can be markedly narrowed by using confirmatory neuroimaging investigations, especially diffusion-weighted imaging, MR angiography, MR venography, and MR spectroscopy, during the same examination ***(Hedge et al., 2011).***

Symptoms of basal ganglia disorders may include dystonia, choreo-asthetosis, hemi-ballisum. Dystonia is characterized by sustained muscle contraction, causing abnormal postures, twisting and repetitive movements; it's due to spontaneous activity of neurons from the internal or external globus pallidus ***(Philip et al., 2005)***.

Chorea is non-rhythmic, jerky, involuntary, semi-purposeful, non-suppressible movements in distal muscles and face; while asthetosis is non-rhythmic, slow, sinuous, more in distal muscles, may alternate with proximal limb postures. They result from impaired inhibition of thalamocortical neurons by basal ganglia. Excess dopaminergic activity may be the mechanism. Hemi-ballisum is unilateral, non-rhythmic, rapid, flinging movements of proximal limb ***(Hector, 2015)***.

From the foregoing review we suppose that early diagnosis of treatable inherited basal ganglia diseases will help in early management, which could be lifesaving and reversible in many cases.

AIM OF THE WORK

Our aim is to:

Study the clinico-radiological correlation in inherited basal ganglia diseases by using the new neuroradiological modality in diagnosing the disease and comparing it with the clinical findings, thus starting appropriate treatment for children with inherited basal ganglia diseases especially reversible ones.

BASAL GANGLIA

Background:

Basal ganglia refer to a group of subcortical nuclei responsible primarily for motor control, as well as other roles such as motor learning, executive functions, behaviors and emotions. The classical basal ganglia model shows how information flows through the basal ganglia back to the cortex through two pathways with opposing effects for the proper execution of movement. Disruption of the basal ganglia network forms the basis for several movement disorders ***(Lanciego et al., 2012).***

The term basal ganglia in the strictest sense refers to nuclei embedded deep in the brain hemispheres (striatum or caudate-putamen and globus pallidus), whereas related nuclei consist of structures located in the diencephalon (subthalamic nucleus), mesencephalon (substantia nigra), and pons (pedunculopontine nucleus), as shown in figure (1).

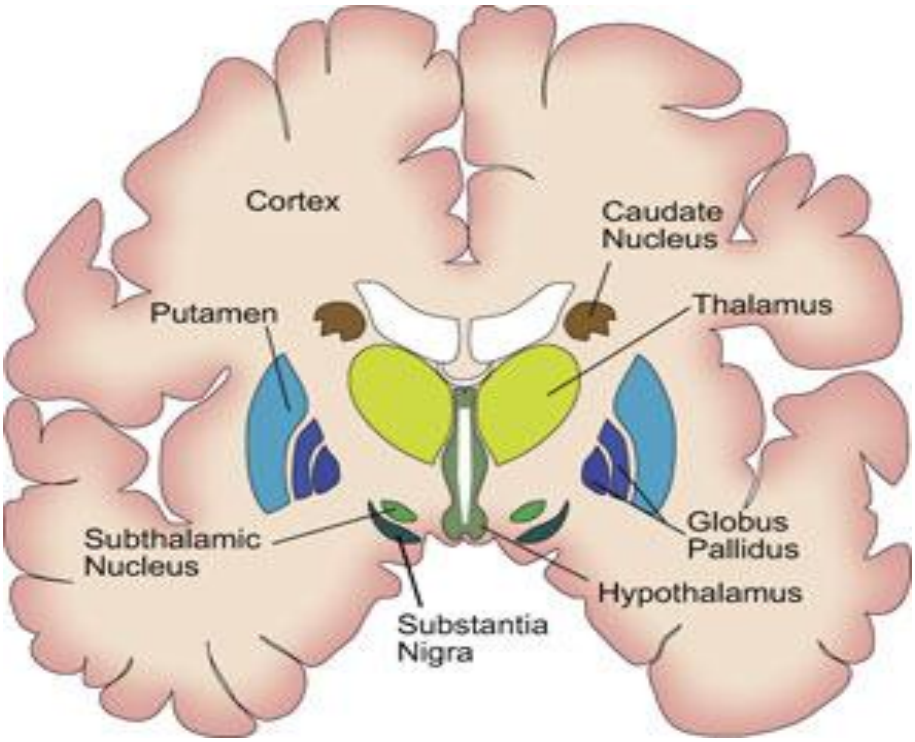

Figure (1): Basal Ganglia Axial view ***(Alzheimer's Association, 2013).***

Structure (Basal ganglia nuclei):

Basal ganglia are subcortical nuclei that are located in the telencephalon, diencephalon, and midbrain ***(Steward, 2012)***, as shown in figure (2).

Corpus Striatum:

The caudate and the putamen form the major input structure known as the corpus striatum. The caudate is a large C shaped nucleus that is connected to the putamen by grey matter bridges that pass through the internal capsule. The corpus striatum is a GABA-ergic nucleus that has direct control over

the globus pallidus, and the substantia nigra pars reticulata ***(Naidich et al., 2012).***

Globus Pallidus:

This nucleus is divided into two nuclei: the globus pallidus pars externa, and the globus pallidus pars interna. These are both GABA-ergic nuclei. The globus pallidus pars externa innervates the subthalamic and the globus pallidus pars interna innervates the thalamus ***(Buchanan et al., 2015).***

Substantia Nigra:

It is divided into the substantia nigra pars reticulate and the substantia nigra pars compacta. The substantia nigra pars compacta is superior to the substantia nigra pars reticulata. The substantia nigra pars compacta is the only dopaminergic in the basal ganglia and both excites and inhibits different pathways in the basal ganglia by innervating the corpus striatum. The substantia nigra pars reticulata is GABA-ergic and innervates the thalamus ***(Carpenter, 2013).***

Subthalamic Nucleus:

It is located inferior to the internal capsule and superior to the substantia nigra. It is a glutamatergic and innervates the globus pallidus pars interna and the substantia nigra pars reticulata ***(Ammari et al., 2010).***

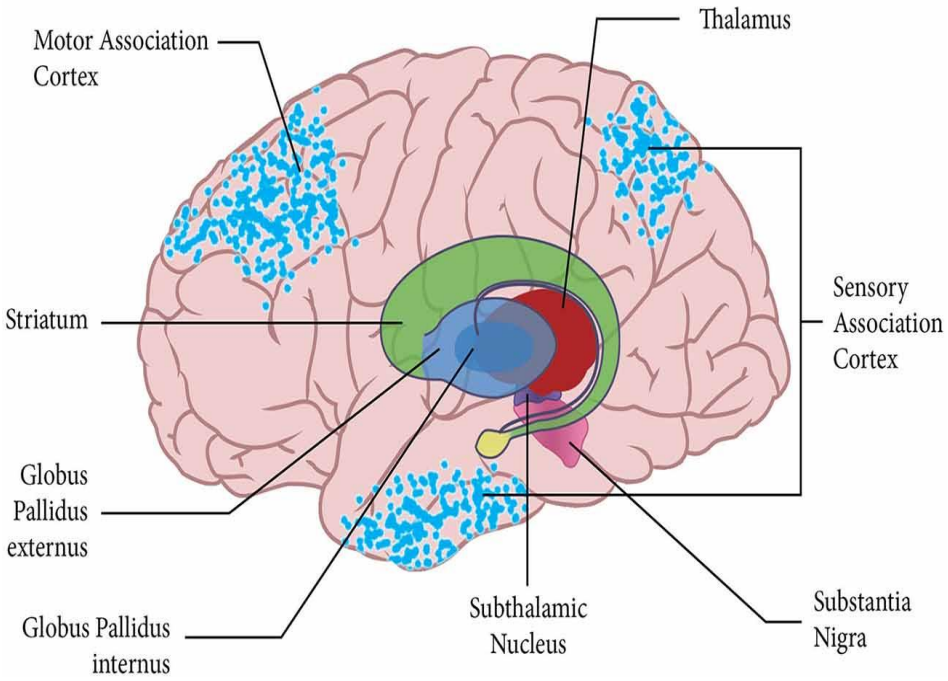

Figure (2): Sagittal view**.**

The figure shows the cortical surface with an overlay of the basal ganglia and thalamus. The blue dots on the cortical surface represent the neuronal activity for a notional emulation. This emulation is abstract, and the active neural networks instantiating the emulation are in higher-level motor and sensory association areas of the brain ***(Colder, 2015).***

Basal Ganglia Pathways:

The major motor pathway is the corticostriatal pathway. This pathway is responsible for the control of movement. It is divided into two pathways: the direct and indirect pathways. The direct pathway is responsible for allowing movement. The indirect pathway, on the other hand, suppresses movement. This means that the indirect pathway is the common pathway to suppress sporadic and unwanted movement ***(Calabresi et al., 2014).***

The three major neurotransmitters that innervate the basal ganglion are γ-aminobutyric acid (GABA), glutamic acid, and dopamine. γ-Aminobutyric acid has an inhibitory effect on the nuclei. In contrast glutamic acid is an amino acid that has an excitatory effect. Dopamine has the ability to excite and inhibit different pathways in the basal ganglia ***(Sesack and Grace, 2010).***

Direct Pathway:

The substantia nigra pars compacta produces dopamine which excites the D1 pathway exciting the direct tract, and inhibits the D2 tract thus inhibiting the indirect tract. This is to allow the motor signal to go through so the motor cortices can generate body movement because the indirect pathway is constantly suppressing movement ***(Eagle et al., 2011).***

The corpus striatum innervates the globus pallidus pars interna and the substantia nigra pars reticulata, involving the synaptic transmission of GABA, both then send GABA as an inhibitory signal to the thalamus. The globus pallidus pars interna and the substantia nigra pars reticulata are inhibited so the innervation of the thalamic nuclei is disinhibited. Thus the thalamus can excite the cortex and can generate movement. Since the dopamine inhibits the indirect pathway, the globus pallidus pars externa inhibits the subthalamic nuclei to prevent the excitation of the globus pallidus pars interna and the substantia nigra pars reticulata ***(Calabresi et al., 2014)***, as shown in figure (3 “A”).

Indirect Pathway:

Without the dopaminergic input from the substantia nigra pars compacta, the information passes through the indirect pathway. The corpus striatum innervates the globus pallidus pars externa with GABA which projects to the subthalamic nuclei by a GABA-ergic synaptic connection. Since the globus pallidus pars externa is inhibited, this disinhibits the subthalamic nuclei. The subthalamic nuclei project to the globus pallidus pars interna and the substantia nigra pars reticulata by a glutamatergic synapse that excites the globus pallidus pars interna and the substantia nigra pars reticulata. The excitation of the globus pallidus pars interna and the substantia nigra pars reticulata produces GABA that inhibits the thalamus. This prevents the generation of the movement ***(Tanimura et al., 2010)***, as shown in figure (3 "B").

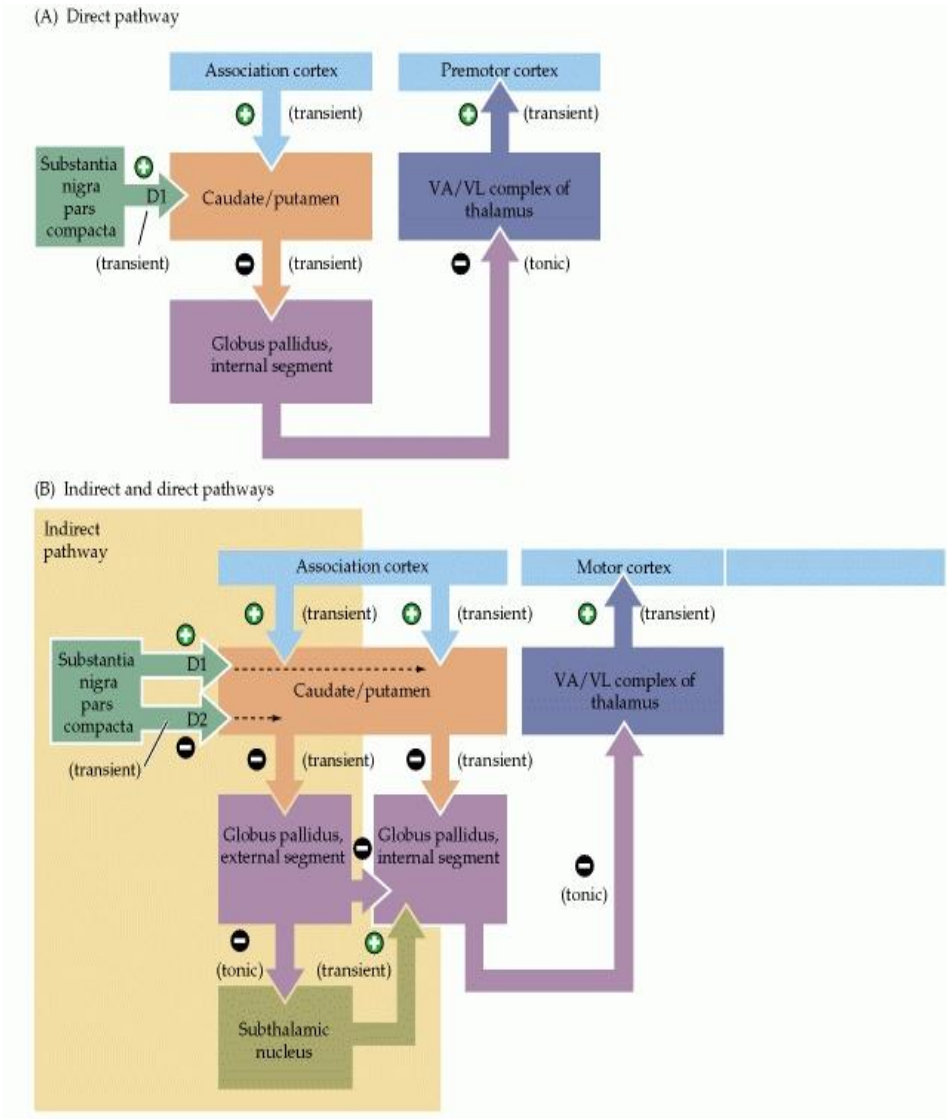

Figure (3): The "direct pathway" [Fig. A] of the basal ganglia acts to release the motor neurons from tonic inhibition. The "indirect pathway" [Fig. B], on the other hand, serves to increase tonic inhibition. The neurons from the external segment of the globus pallidus then project to the subthalamic nucleus. The subthalamic nucleus, receiving both excitatory input from the cortex and inhibitory input from the external segment of the globus pallidus, then projects to the internal segment of the globus pallidus, which in turn makes any changes that need to be made to the "direct pathway" ***(Purves et al., 2001).***

Function:

The cortico-basal ganglia circuits are important for chunking isolated movements into precise and robust action sequences that permit the achievement of particular goals. During sequence learning, many neurons in the basal ganglia develop sequence-related activity - related to the initiation, execution, and termination of sequences - suggesting that action sequences are processed as action units. Cortico-striatal plasticity is critical for the crystallization of action sequences, and for the development of sequence-related neural activity. These findings have implications for understanding the symptoms associated with movement and psychiatric disorders ***(Jin and Costa, 2015).***

There is increasing evidence that cortico-basal ganglia circuits, including the mesencephalic dopamine system, play a critical role in generating, shaping, and executing action sequences ***(Tecuapetla et al., 2014).***

The basis of the model resides in the striatopallidal connections via the direct and the indirect projections, which have an opposite functional effect on basal ganglia output ***(Stocco et al., 2010).***

The basal ganglia are functionally subdivided into motor, associative, and limbic/emotional domains based on their relationship with relevant cortical projection areas and the engagement of these regions. Thus, in addition to the well-known role of the basal ganglia in motor control, there is now a

better appreciation for other functions such as attention and time estimation, implicit learning and habit formation, and reward-related behavior and emotions, all of which are associated with the activation of cortical loops that connect with the CN, the anterior putamen, or the ventral putamen ***(Foerde and Shohamy, 2011).***

The basal ganglia network may be viewed as multiple parallel loops and re-entering circuits whereby motor, associative, and limbic territories are engaged mainly in the control of movement, behavior, and emotions. This is likely to be sustained by the same basic architectural and functional organization, differentially applied to: (1) selection and facilitation of pre-frontal-striatopallidal activity during the performance and acquisition of new activities and tasks (goal-directed system); (2) reinforcement learning to create habitual responses automatically performed by the motor circuit (habit system); and (3) stopping an ongoing activity and switching to a new one if necessary, which is mainly mediated by the inferior frontal cortex/STN-cortical circuit. Abnormalities in these domains and functions lead to movement disorders such as parkinsonism and dyskinesias, obsessive compulsive disorders, and alterations of mood (i.e., apathy, euphoria) ***(Lanciego et al., 2012).***

BASAL GANGLIA DISORDERS

Lesions of the lenticular nucleus (putamen and globus pallidus) and the subthalamic nucleus (STN) were associated with parkinsonian signs, dystonia, and hemiballismus ***(Mehanna and Jankovic, 2013).***

Movement disorders comprise a variety of motor problems, not all of which are associated with dysfunction of the basal ganglia. Those that have a clearly established pathological basis and are caused by pathophysiological mechanisms directly involving the basal ganglia are the following: (1) the parkinsonian syndrome composed of rigidity, akinesia/bradykinesia, and resting tremor; (2) dystonia characterized by prolonged muscle spasms and abnormal postures; and (3) chorea-ballism, in which fragments of movements flow irregularly from one body segment to another, to cause a dance-like appearance. When the amplitude of the movement is very large, the term *ballism* is applied ***(Wichmann and Dostrovsky, 2011).***

The Parkinsonian Syndrome:

The best known cause and example of the parkinsonian syndrome is Parkinson's disease, which is a neurodegenerative disorder that affects about 1.5% of the global population over 65 years of age. It is mainly characterized by poverty of spontaneous movements (hypokinesia) and slowness of voluntary movement (bradykinesia), as well as increased