

# Basal ganglia and movement disorders argumentative essay examples

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It was originally thought that basal ganglia were responsible for voluntary motor movements, and movement disorders were associated with pathological changes in the basal ganglia. However, it was found that the basal ganglia are associated with different cortexes with distinctive circuits, which are called loops, so a pathological transformation of tissue can manifest as a psychological or motor disorder, depending on the loop affected. The cortico-basal ganglia-thalamocortical loop is a one-way circuit that allows the basal ganglia to receive input from the cortex and send output via the thalamus back to different regions of the cortex. Pathological changes in this loop are associated with various movement disorders, which can now be treated with deep brain stimulation, but it is not yet possible to accurately predict whether the outcome will be positive or result in severe complications.

## **Background**

The basal ganglia are a group of four nuclei called the striatum, globus pallidus, substantia nigra, and subthalamic nucleus. The striatum is further divided into caudate nucleus, ventral striatum, and putamen. Its main function is receiving input from the brain stem, thalamus, and cerebral cortex while sending output to the globus pallidus and substantia nigra. The subthalamic nucleus is also connected to the globus pallidus and substantia nigra, and its glutaminergic cells are the only excitatory projections within the basal ganglia.

The globus pallidus and substantia nigra are the two output nuclei in the basal ganglia, and their role is to tonically inhibit target nuclei in the brain stem and thalamus. The input they receive is sent by the striatum via direct

and indirect pathways. The indirect pathways pass through the external pallidal segment of the globules pallidus and are received by the subthalamic nucleus. The indirect pathway uses the  $\gamma$ -aminobutyric acid (GABA) neurotransmitter in that section of the pathway. The rest of the indirect pathway runs from the subthalamic nucleus to the output nuclei and uses excitatory glutaminergic projection. The indirect pathway inhibits the thalamocortical neurons, which means the indirect pathway is used to inhibit movement.

At high frequencies, globus pallidus and substantia nigra discharge tonically. The direct pathway is activated by excitatory inputs, and it runs from the striatum to the pallidum. When activated, the direct pathway momentarily inhibits tonical discharge in the pallidum, which activates the cortex and thalamus. The role of the direct pathway is to disinhibit the thalamus and increase thalamocortical activity. Although the basal ganglia are key components of voluntary movement performance, they do not have direct connections with the spinal cord in terms of input or output. Instead, they receive input from the cerebral cortex, and the output is sent to the brain stem. The thalamus mediates the output to the motor, prefrontal, and premotor cortices, so the direct pathway is responsible for disinhibiting the thalamus and facilitating voluntary movement.

It was thought that the basal ganglia are responsible exclusively voluntary movement performance because pathological changes in the basal ganglia was observed in movement disorders, but anatomical research proved that basal ganglia have several connections with different systems, which are organized in discrete loops (Middleton and Strick, 2000). Therefore, if a loop

associated with the motor areas is damaged, it will result in movement disorders while damage to the loops associated with non-motor areas will result in cognitive disorders (Middleton and Strick, 2000).

The cortico-basal ganglia-thalamocortical loop is related to movement, and its functional model is used to explain motor disorders (Silkis, 2001). In this circuit, the precentral motor areas send signals that activate the putamen in the striatum that inhibits the motor neurons of the internal segment of globus pallidus and substantia nigra pars reticulata, which results in utilizing the direct pathway. Other striatal segments inhibit the external segment of the globus pallidus, resulting in inhibiting the excitatory projections of the subthalamic nucleus and the internal segment of globules pallidus, which is characteristic for the indirect pathway. Depending on the pathway used, the striatal neurons will facilitate transmission with D1 dopamine receptors in the direct pathway and reduce transmission with the D2 dopamine receptors in the indirect pathway.

The information received by the basal ganglia from the cortex cannot be sent directly back to the cortex because the cortico-basal ganglia-thalamocortical loop is a one-way circuit. Instead the output must be sent to the thalamus, which acts as a mediator between the basal ganglia and the cortex. However, the thalamic relay nuclei pathways involved in mediating information between the basal ganglia and the cortex are not passive.

Although they are a critical link responsible for transmitting basal ganglia output to frontal cortical areas, thalamocortical circuits can modulate and regulate cortical activity by projecting to different cortical layers (McFarland and Haber, 2002). Thalamocortical projections cannot affect the entire cortex

directly, but sending output to different cortical layers can affect different subpopulations of cortical neurons and their output.

Pathological modifications in the cortico-basal ganglia-thalamocortical loop are associated with various movement disorders. For example, studies investigating Parkinson's disease found that the dopamine deficit in the basal ganglia leads to modifications in cortical input and decreases the inhibition of output from the basal ganglia, which leads to akinesia (Silkis, 2001). In Huntington's disease, the increase of D1 dopamine receptors in the striatum results in signal transduction modifications, which diminish the indirect pathway of the cortico-basal ganglia-thalamocortical loop and cause choreiform movements (Silkis, 2001). Because movement disorders are neurodegenerative, deep brain stimulation can be used to alleviate symptoms, but it cannot completely cure any movement disorder.

## **Deep Brain Stimulation**

Deep brain stimulation (DBS) is a treatment in which a brain pacemaker used to send impulses that will alter brain activity in the targeted regions. The brain pacemaker consists of three parts. The implanted pulse generator is the part responsible for sending electrical pulses that interfere with neural activity. The extension transmits those pulses to the lead, which is placed in the target area in the brain that needs to be modified.

DBS is used for treating any disorder characterized by involuntary movements and tremor. The diagnosis will determine where the lead needs to be implanted. DBS was proven successful in treating Parkinson's disease, essential tremor, and dystonia (Mink et al., 2006), but the implications of

DBS in the Tourette syndrome and Huntington's disease are still experimental opinions (Duits et al., 2012)

## **Essential Tremor**

A systematic review by Flora et al. (2010) found that DBS is a safe and effective treatment for essential tremor. The analysis of 430 cases showed that potential side-effects are mild and can be regulated by calibrating the implanted pulse generator while all studies showed improvements in patients after DBS when the results were compared with their baseline scores. It is generally agreed that the ventral intermediate nucleus of the thalamus should be targeted for treating essential tremor, and the treatment proved effective and safe even in long-term follow-ups (Zhang et al., 2009).

## **Tourette's Syndrome**

Patients with Tourette's syndrome display a variety of motor and vocal tics, such as involuntary movements and involuntary sounds produced by contractions in the diaphragm or oropharynx. Although there are potential benefits to regulating those symptoms with DBS, the inclusion criteria for patients with Tourette syndrome need to be strict because comorbid disorders (e. g. somatoform disorder and psychological disorders) can be contraindications for DBS (Duits et al., 2012). A detailed baseline analysis of the patients' medical history and comorbid symptoms is also required because it determines the placement of the lead (Mink et al., 2006).

Although the correlation between Tourette's syndrome and pathological abnormalities in the basal ganglia have been established, it is not yet clear which parts of the basal ganglia or their thalamocortical connections with the

cortex are exclusively responsible for the tics. Previous research analyzed the impact of DBS on the centro-median-parafascicular complex of the thalamus, the internal segment of globus pallidus, and the anterior limb of the internal capsule, but there is no specific data that confirms the preference of one location over the other (as cited in Mink et al., 2006). A case study on a single patient showed that high-frequency bilateral thalamic and pallidal stimulation was found effective in restoring social functions, but psychological issues remained consistent after treatment (Houeto et al., 2005). Other types of stimulations proved ineffective or dangerous because of their side-effects, so rigorous inclusion criteria are recommended for considering DBS for patients with Tourette's syndrome.

## **Parkinson's Disease**

Parkinson's disease is characterized by instability, bradykinesia, tremor, and rigidity, which are caused by neurodegeneration. Although DBS is approved for treating Parkinson's disease, it is not a complete cure and is used only to improve motor function and quality of life in patients with advanced Parkinson's disease. The globus pallidus interna and subthalamic nucleus are both acceptable targets in DBS for Parkinson's without significant differences in treatment efficacy (Follett et al., 2010). However, high-frequency stimulation in Parkinson's disease patients is useful only for alleviating symptoms of instability, bradykinesia, tremor, and rigidity. It cannot resolve dementia and cognitive deficits, which may increase if the patient is exposed to the DBS procedure (Benabid et al., 2009).

## **Huntington's Disease**

The outcomes of DBS in Huntington's disease are contradictory. While long-term studies showed significant improvements in chorea and consistency in other symptoms, short-term studies showed a reduction in chorea with worsening in cognitive functions, gait, and balance (Zeef et al., 2011).

However, a key limitation to treating Huntington's disease with DBS is the inability to determine whether the outcomes are related to stimulation or disease progression. The main research target in DBS case reports is the globus pallidus interna, but globus pallidus externa, the subthalamic nucleus, and the substantia nigra pars compacta are other potential targets recommended for research. Without consistent evidence regarding treatment outcomes and neural targets, DBS for Huntington's disease remains experimental.

## **Dystonia**

The efficacy of DBS in dystonia depends on the type of dystonia. According to Andrews et al. (2010), primary forms of dystonia, some sub-types of heredo-degenerative dystonia, tardive dystonia, and myoclonus dystonia can be significantly improved by DBS while outcomes for patients with secondary forms of dystonia and certain sub-types of heredo-degenerative dystonia are less predictable and effective. The most common target area for DBS in dystonia is the globus pallidus interna. Although DBS momentarily affects functions in Parkinson's disease, effects of DBS for dystonia treatment may show only after several months, but they are more permanent because most

patients retain normal function even after the DBS is turned off (Ruge et al., 2011).

## Potential Complications

Various neuropsychiatric side-effects have been recorded in patients undergoing DBS. Although DBS was proven superior to medication interventions alone in managing Parkinson's disease, Deuschl et al. (2006) found that 12.8 percent of the patients in the DBS treatment group showed adverse events while only 3.8 percent of them reported adverse events in the medication only group. Some patients in the DBS group died because of suicide, cerebral hematoma, and pneumonia, but other serious adverse events were mainly related to falls, infections of stimulator sites, and mobility decline. Other complications were associated with Parkinson's disease progression.

A study by Weaver et al. (2009) found that motor functioning improved by 12.3 points in the DBS group while the control group improved by only 1.7 points. Nevertheless, the DBS group reported more instances of falls, dystonia, depression, and gait disturbances than the control group, and those events persisted even after six months, which suggests that DBS side-effects can potentially be permanent.

According to Burn and Tröster (2004), hypersexuality, depression, mania, euphoria, and mirth are the most common side-effects reported, but only few permanent issues have been documented. Some examples of common permanent issues include working memory and executive function alterations. Although permanent side-effects are rare, rigorous inclusion

criteria are required to prevent unnecessary complications in patients whose condition can be managed with medication.

## **Conclusion**

DBS in the basal ganglia or thalamus can interfere with brain activity and modify the pathological changes in the cortico-basal ganglia-thalamocortical loop. However, the outcomes are different for each type of movement disorder. In dystonia, it may take time for patients to see improvement, but they will more likely remain permanent. In Parkinson's disease and essential tremor, the patients will experience immediate improvements, but further calibrations of the implanted pulse generator may be necessary to maintain results. However, because DBS is not a cure for most movement disorders, it should only be used as a method for improving the quality of life rather than replacing medication therapy. Further research is needed for Huntington's disease and Tourette's syndrome to determine which areas need to be targeted for stimulation and to improve inclusion criteria for preventing adverse events in patients with comorbid disorders.

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