Deep Brain Stimulation for Schizophrenia

DBS is now being explored as a potential schizophrenia treatment, particularly in cases where patients are resistant to conventional therapies.

Mechanism of Action

In schizophrenia, DBS aims to regulate abnormal neural circuits associated with psychotic symptoms. Targeted areas include:

- **Subgenual Anterior Cingulate Cortex (SACC):** Involved in mood regulation; overactivity is linked to depressive symptoms. - **Nucleus Accumbens (NAcc):** Plays a role in reward processing; dysregulation may contribute to negative symptoms. - **Substantia Nigra Pars Reticulata (SNr):** A component of the basal ganglia; its modulation has been investigated for its effects on psychotic symptoms.

DBS seeks to restore normal brain function and alleviate symptoms by stimulating these regions.

Clinical Evidence: Research into DBS for schizophrenia is still in its early stages, with studies primarily focusing on treatment-resistant cases. Notable findings include:

- **Johns Hopkins Medicine Study (2021):** Researchers reported that DBS targeting the SNr led to significant improvements in a patient with treatment-resistant paranoid schizophrenia, including the immediate cessation of chronic hallucinations.

- **Hospital Clínic Barcelona Study (2023):** A pilot study involving four patients with treatment-resistant schizophrenia and bipolar disorder found that DBS resulted in significant clinical improvements, including reductions in the Clinical Global Impression and Hamilton Depression Rating Scale scores.

These studies suggest that DBS may offer a promising alternative for patients with schizophrenia who do not respond to traditional treatments.

Challenges and Considerations: Despite its potential, several challenges remain:

- **Heterogeneity of Response:** Not all patients experience significant benefits, and some may encounter adverse effects. - **Optimal Target Identification:** Determining the most effective brain regions for stimulation requires further research. - **Long-Term Effects:** The durability of DBS effects over time and its impact on cognitive functions need thorough evaluation.

Ongoing clinical trials and research are essential to address these issues and establish DBS as a standard treatment for schizophrenia.

Conclusion: DBS represents a promising frontier in the treatment of schizophrenia, particularly for those with treatment-resistant forms. While early studies indicate potential benefits, comprehensive research is necessary to understand its efficacy, safety, and long-term outcomes fully.

Gill BJA, Khan FA, McKhann GM. You're Not Hallucinating: Potential New Targets for Schizophrenia Treatment. Neurosurgery. 2018 Dec 27. doi: 10.1093/neuros/nyy628. [Epub ahead of print] PubMed PMID: 30590758 [1].

Neumaier et al., reported the results and outcomes of different procedures in patients with schizophrenia including the selective leucotomy, mesoloviotomy, and anterior callosotomy. They concluded that none of these procedures were associated with favorable outcomes and improved clinical function in those with schizophrenia [2].

Taghipour and Ghaffarpasand, postulated that anterior corpus callosotomy would be beneficial in controlling the auditory and visual hallucinations in those with schizophrenia refractory to the highest medical therapy. This procedure would interfere with transmission and conduction of aberrant stimulations produced by the right brain (language areas) to the left brain and thus being perceived and obeyed. Although limited previous experiences have reported no clinical outcome, larger studies are required for the outcome [3].

Mikell et al, focused on an important pathological circuit involving the associative striatum, anterior hippocampus, and ventral striatum, and discuss the possibility of targeting these nodes for therapeutic neuromodulation with DBS. Finally, the authors examined ethical considerations in the treatment of these vulnerable patients. The functional anatomy of neural circuits relevant to schizophrenia remains of great interest to neurosurgeons and psychiatrists and lends itself to the development of specific targets for neuromodulation. Ongoing progress in the understanding of these structures will be critical to the development of potential neurosurgical treatments of schizophrenia [4].

Bikovsky et al, use the poly I:C rat model of schizophrenia to study the effects of medial prefrontal cortex (mPFC) and nucleus accumbens (Nacc) DBS on two behavioral schizophrenia-like deficits, i.e. sensorimotor gating, as reflected by disrupted prepulse inhibition (PPI), and attentional selectivity, as reflected by disrupted latent inhibition (LI). In addition, the neurocircuitry influenced by DBS was studied using FDG PET. We found that mPFC- and Nacc-DBS alleviated PPI and LI abnormalities in poly I:C offspring, whereas Nacc- but not mPFC-DBS disrupted PPI and LI in saline offspring. In saline offspring, mPFC-DBS increased metabolism in the parietal cortex, striatum, ventral hippocampus and Nacc, while reducing it in the brainstem, cerebellum, hypothalamus and periaqueductal gray. Nacc-DBS, on the other hand, increased activity in the ventral hippocampus and olfactory bulb and reduced it in the septal area, brainstem, periaqueductal gray and hypothalamus. In poly I:C offspring changes in metabolism following mPFC-DBS were similar to those recorded in saline offspring, except for a reduced activity in the brainstem and hypothalamus. In contrast, Nacc-DBS did not induce any statistical changes in brain metabolism in poly I:C offspring. Our study shows that mPFC- or Nacc-DBS delivered to the adult progeny of poly I:C treated dams improves deficits in PPI and LI. Despite common behavioral responses, stimulation in the two targets induced different metabolic effects [5].

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