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Deep Brain Stimulation for Schizophrenia

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In this review article, Mikell et al. [1] discuss the hypothetical use of deep brain stimulation in the hippocampus or nucleus accumbens to treat schizophrenia. From a historical prospective there is a modest literature on the nucleus accumbens or 'septal area' by direct or indirect lesioning or stimulation. Hallucinations, delusions, depression, anxiety, aggression, obsessions and 'schizoaffective' disorders (generally referring to manic depression, but all of these terms used might be defined differently today) were reportedly helped by medial thalamotomy, amygdalotomy, hypothalamotomy, anterior cingulotomy, corpus callosotomy and multiple lesion combinations. Schizophrenia is a very diffuse disorder and the 'triple target' lesioning of Cox and Brown [2] was an attempt to include key areas believed to be affected. But in the most extensive review of this literature by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1977 [3], schizophrenia was the least likely disorder to improve. The hippocampus would be a totally novel target for schizophrenia. In this era, we should be striving for reestablishment of emotional control while preserving cognition and personality without blunting affect.

They start with the role of dopamine dysregulation which is believed to contribute to the pathogenesis of schizophrenia. They then go on to hypothesize that the hippocampus and nucleus accumbens are potential targets for deep brain stimulation in the treatment of this disease. While the authors should be commended for the intriguing discussion of the possibility of deep brain stimulation for this dreaded syndrome for which current treatments are still unsatisfactory, it should be regarded with caution. The neurophysiologic and neuroanatomic basis of schizophrenia has to this time not been well elucidated. While most agree that dopamine dysregulation plays an important part in the development of the positive symptoms of schizophrenia such as hallucinations and psychosis, it is probable that the neurotransmitter derangements are more wide-ranging than simply dopamine dysregulation. Current treatment of schizophrenia includes the use of atypical antipsychotics, which affect serotonin in addition to dopamine, in contrast to typical antipsychotics. This suggests that serotonin may play an important role as well [4]. In addition, recent studies have suggested that glutamate dysregulation may also have a critical responsibility in the pathogenesis of schizophrenia [5]. Also, recent studies have even suggested an autoimmune basis for the development of schizophrenia [6].

Most troubling, however, may be that schizophrenia is a group of syndromes in which the physiologic derangements differ rather than a solitary disease in and of itself [7]. Thus, stimulation of a target which only affects the dopamine system may only treat some of the symptoms of schizophrenia, likely the positive symptoms and do little for the 'negative and cognitive symptoms'. As the authors have alluded, this may still be a worthwhile goal. To be successful it is not imperative that all symptoms improve but that the patient's overall quality of life be enhanced. This may be achieved by diminishing the amount and number of drugs, and improving drug performance among others. At worst, however, partial treatment of schizophrenia by modulating the dopamine system may lead to unintended effects previously unanticipated. As such, this review article must be regarded as highly preliminary that requires more basic research before transition to clinical study. Multiple leads in numerous targets may be required to treat all the symptoms of schizophrenia [2]. Even with this in mind, however, the authors have presented a very interesting argument for the future role of deep brain stimulation in this disorder. Thus, it could represent a small step toward effective palliation of this disease. Undeniably, schizophrenia is a chronic life-altering disorder of the brain that merits vigorous investigation.

References

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