Letter: Deep Brain Stimulation in Epilepsy: A Role for Modulation of the Mammillothalamic Tract in Seizure Control?

To the Editor:

The results of the article by Schaper et al,[1] "Deep Brain Stimulation in Epilepsy: A Role for Modulation of the Mammillothalamic Tract in Seizure Control?" published in *Neurosurgery*, September 1, 2020;87(3):602-610, validate that the junction between the anterior nucleus of the thalamus (ANT) and mammillothalamic tract (MThT) can be selected as an anatomic target in deep brain stimulation (DBS) of the ANT. Their work signifies important evidence not only for the treatment of epilepsy but also for better understanding of the functional anatomy of the brain. Their observation that active contacts of microelectrode lead placed close to the ANT-MThT junction were associated with increased seizure control led them suggest that co-stimulation of white matter tracts may play a fundamental role in the mechanism of seizure control by ANT-DBS and warrants further study. This junctional location is also where the main mammillary bundle splits into 2 components: MThT and mammillotegmental tract (MTgT). It should therefore be kept in mind that not only MThT projecting to ANT from the mammillary body, but also MTgT projecting to tegmental nuclei of the brainstem may have an influence in controlling the pursuit of the seizure.[2]

The MTgT is thought to take part in controlling visceral functions and transformation of spatial data by influencing the brain stem's autonomic nuclei.[2,3] In animal experiments, metabolic epilepsy trials have demonstrated hypometabolic behavior of cerebral glucose in the epileptic center and limbic system after status epilepticus.[2,3] The understanding of these metabolic cerebral alterations in epilepsy has given rise to the use of vagal nerve stimulation as a therapeutic choice.[2,3] Together with the dorsal longitudinal fasciculus and fasciculus retroflexus, the MTgT shows a significant function in the start of visceral impetus[2,4] and, therefore, has a close interrelationship with the autonomic nervous system. Thus, just as effective results are obtained in vagal nerve stimulation, the MTgT can contribute to the control of epileptic seizures in surgical treatment using DBS.

A further important consideration is that currently used treatments for epilepsy, whether medical or surgical, have adverse effects, including major cognitive deficits.[5,6] It is important to note that the MThT stimulation targeted in epilepsy therapy has shown a strong, beneficial effect on memory function.[2,7,8] Thus, its role in memory function may be another explanation for selecting the MThT as an epilepsy treatment target.[2,9] This favorable effect can also be given by the acts of MTgT. Anatomic findings suggest that tegmental afferent fibers have a crucial role in modifying the transport of information from hippocampal formation to the anterior thalamus.[2] An extrapolation from this anatomic information is that the fibers that project between the mammillary body and tegmental nuclei function as an input control center of hippocampal formation.[2,10,11] The descending projections through the MTgT from the mammillary body are excitatory, whereas ascending projections from the dorsal and ventral tegmental nuclei to the mammillary body are GABAergic.[2,11-13] Rhythmic oscillations in other parts of the brain are generated by these reciprocal excitatory-inhibitor circuits.[2,14]

In conclusion, because the target that was found to be more effective in the control of epilepsy in the study of Schaper et al[1] is adjacent to the region where the two efferents of the mammillary body branch, the roles of both MThT and of MTgT in the control of epilepsy in DBS merit consideration and investigation. Also, the selection of the target reported by Schaper et al[1] could probably have beneficial effects on memory function.

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