Hippocampal Transections for Epilepsy

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KEYWORDS

• Multiple hippocampal transection • Temporal lobe epilepsy • Long-term outcome • Verbal memory

KEY POINTS

- Multiple hippocampal transection (MHT), supplemented with multiple subpial transection (MST) and limited cortical resection, is a relatively safe procedure that affords excellent seizure control that is equal to or exceeds the results typically achieved with standard temporal lobectomy; in addition, verbal memory and stem cells are preserved.
- Intraoperative electrocorticography is of paramount importance in ensuring that all seizure foci are abolished. This is especially true for nonresective procedures like MST and MHT.
- This approach is best suited in patients who are not suitable candidates for standard temporal lobectomy due to failed Wada test, dominant temporal lobe epilepsy, or the absence of hippocampal sclerosis.

INTRODUCTION

Representing nearly 25% of all cases of epilepsy, of which an estimated 70% are referred for consideration of surgical intervention, temporal lobe epilepsy (TLE) represents the single most common type of seizure disorder.[1–3] Unfortunately, approximately 30% of patients with TLE fail to achieve satisfactory control of their seizures with antiepileptic medications. In addition, many of them suffer from side effects of antiepileptic drugs when an attempt is made to increase their dosage in order to reduce the frequency of seizures.[4–6] Surgical intervention offers these patients the possibility of seizure-freedom or near seizure-freedom with a reduced dependency on antiepileptic medication.[5]

Treatment of intractable TLE classically involves resection of the anterior part of the temporal lobe, including resection of the parahippocampal gyrus, amygdala, hippocampus, and the fimbria. This procedure is considered the gold standard in the treatment of TLE.[7] Resection of the hippocampus is performed because the hippocampus is involved in the generation and propagation of seizures, and there is a close association between hippocampal sclerosis and TLE.

However, resection of the hippocampus is undesirable because it is an integral part of the limbic system, has important connections with the entorhinal cortex, is the site for new memory formation, including auditory and visual organization, and is involved in memory retrieval. Furthermore, temporal lobe neocortex is essential for accurate perception and interpretation of social communication, recognizing familiar faces and facial emotions, interpreting voice, understanding a person's intentions and emotions from their body posture, gestures, and movements, and participation in precipitating emotional empathy.[8,9]

Therefore, complications of standard temporal lobectomy include impairment of social cognition, decline in verbal memory, general intelligence, emotional and vocational disturbances, psychosis, character disorders, depression, and linguistic dysfunctions.[9–19] Although the Wada test is

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routinely used to ascertain the dominant side for memory, Wada asymmetry (using mixed stimuli) fails to predict postoperative verbal memory.[12] Furthermore, there is a higher risk of memory dysfunction in those cases with minimal or no sclerosis, or those in whom the dominant hemisphere is involved.[14,15] Furthermore, the subventricular and subgranular zones of the hippocampus, which are the main source of neural progenitor cells,[20–23] are resected. These cells are critical in the ongoing repair process of the brain following trauma or ischemic injuries.[24–28]

In order to obviate the problems associated with temporal lobectomy and eliminate the need for brain tissue resection, several neuromodulator methods are presently under trial. They include deep brain stimulation, vagal nerve stimulation, and transcranial magnetic stimulation. Several targets in the brain, including the anterior thalamus, the centromedian nucleus of the thalamus, the subthalamic nucleus, and the hippocampus, have been used as targets for deep brain stimulation. Despite some encouraging initial results using these treatment modalities, their clinical value remains to be determined because none of them to date have produced results equal to anterior temporal lobectomy.[29] Other methods under investigation are selective stereotactic destruction of the hippocampus using radiofrequency current, ultrasound, LASER (light amplification by stimulated emission of radiation), and stereotactic radiation.[30] However, these methods do not address seizures originating from the extrahippocampal structures.[31–35] In addition, in these methods, neural stem cells within the hippocampus are destroyed.

Against this background, multiple hippocampal transection (MHT) is a procedure worth considering. MHT is a novel procedure[36–39] in which the longitudinal fibers responsible for seizure propagation are transected at several points along the length of the hippocampus (**Fig. 1**) without resecting the hippocampus. MHT preserves the hippocampus and the stem cells within it and decreases the probability of affecting the hippocampal functions. Furthermore, in order to disrupt seizure circuits in the extrahippocampal cortex, multiple subpial transection (MST) is performed. In addition, when MST fails to abolish epileptogenic activity, minimal cortical resection is performed.[39] In this article, the authors review this approach of treatment of intractable TLE.

PATIENT EVALUATION OVERVIEW

Patients presenting with treatment-refractory TLE typically have at least 1 to 3 seizures per week with many having more than one seizure per day. Routine preoperative evaluation includes video electroencephalography (EEG), magnetic resonance (MR) imaging, magnetoencephalography and PET scans, neuropsychological evaluation, Wada test, and EEG studies using depth and subdural electrodes. Patients are maintained off antiepileptic drugs (AED) 2 days before surgery. Anesthesia is induced using methohexital, and seizure-suppressing drugs (eg, benzodiazepine, propofol) are not used.

SURGICAL PROCEDURE

First, the temporal horn is opened through the middle temporal gyrus using the BrainLab Neuronavigation System (BrainLab AG, Feldkirchen, Germany). Subsequently, using the operative microscope, MHTs are performed at 4- to 5-mm intervals over the head, body, and proximal portions of the tail of the hippocampus. During the procedure, a small incision is made on the ventricular surface of the hippocampus through the alveus using a no. 11 blade scalpel (**Fig. 2**). The knife is inserted no more than a millimeter deep. Through this opening a blunt wire loop 3 or 5 mm in diameter is vertically inserted into the gray matter of the hippocampus to perform transection through the entire transverse diameter of the hippocampus. At the head and proximal part of the body of the hippocampus, the 5-mm-diameter loop is used. At the distal body and proximal tail, a 3-mm-diameter loop is used. The thickness of the hippocampus is measured on coronal MR images at different points, with the depth of insertion of the loop tailored to those distances. In addition, the resistance offered by the alveus on the other side is an indication to stop further insertion. The loop is also moved side to side inside the hippocampus within the limits of the alveus in order to ensure adequate transection within the alveus. The fimbria is left intact. Should the preoperative depth electrode recording show epileptogenic activity in the amygdala, it is excised through the temporal horn. Further details regarding this procedure have been described in previous publications.[37,39]

Next, MST is performed over the lateral and basal surfaces of the temporal lobe in and around areas that showed epileptogenic activity based on preoperative EEG studies. The area usually extends 5 to 7 cm posterior to the tip of the temporal lobe and includes the parahippocampal gyrus and the entorhinal cortex.

Following this, intraoperative electrocorticography (ECoG) is recorded for an hour with intracranial electrodes over the hippocampal and