Hippocampal stimulation in medically intractable mesial temporal lobe epilepsy may be effective in reducing seizure frequency in patients for a period of up to 18 months

Clinical Scenario: A 55 year-old man has had temporal lobe epilepsy for 20 years and has failed treatment with multiple antiepileptic medications. He has on average 20 complex partial seizures per month. He does not have mesial temporal sclerosis on MRI. He is not considering surgery. Video EEG and electrode depth recording has confirmed a left mesial temporal lobe (MTL) focus.

Clinical Question: What is the safety, efficacy, and long term seizure control in patients with MTL epilepsy treated with hippocampal stimulation?

Search Strategy: Medline was used to search for articles by combining “epilepsy, Temporal lobe/th [therapy]” with hippocampal stimulation which mapped to “electric stimulation/ or hippocampus”. This yielded 51 articles; when English language and humans were used as limits yielded 35 articles. Three articles were relevant. The first article by Boon et al. (2007) was an open pilot study and two of the 12 consecutive patients with refractory MTL seizures underwent resective surgery. The other study by Tellez-Zenteno et al. (2006) used an individual patient randomized-controlled trial design (N of 1), but only included 4 patients. It was felt that the study by Velasco et al. (2007) was the best evidence having the largest published study using a double-blinded protocol.

Clinical Bottom Lines:

1. A seizure reduction of 79% (p<0.0005) occurred in all patients with electrical stimulation of the hippocampus. In patients without mesial temporal sclerosis (MTS) compared to those with MTS, seizure reduction appeared earlier (at 1 mo vs. 8 mo) and to a greater extent (95%, p<0.0005 vs. 69%, p<0.05 at 18 months).

2. There was a significant rate of complication consisting of skin erosion resulting in infection requiring removal of the stimulation device in 3 out of 9 participants (33%).

The evidence:

Velasco et al. (2007) evaluated the safety, efficacy of hippocampal electrical stimulation and long-term follow-up in nine non-consecutive patients with medically refractory mesial temporal lobe epilepsy. All patients had complex partial seizures with 7/9 also having secondary generalized tonic-clonic seizures. Patients were selected from a larger group of patients who underwent bilateral hippocampal electrode implantation for diagnostic purposes. The study group consisted of 9 patients (6 male, 3 female) between the ages 14-43. Average number of seizures per month was 28 (15-70) measured within 3 month period. Five had normal MRIs and
remaining 4 had mesial temporal sclerosis. Three patients had bilateral foci and 6 had a unilateral focus of MTL seizure activity. Patients were randomized to a double blind stimulation protocol: five of the patients had an initial 1 month “off” period and the remaining 4 initiated stimulation immediately after implantation. Patients were evaluated at baseline (3 months prior to electrode implantation) and subsequently every 3 months up to 84 months (mean-37 months). Every 3 months up to 18 months patients were evaluated with EEG, neuropsychological testing, neurophysiological testing, seizure frequency and complications. No changes were made to antiepileptic therapy. For the purpose of the study all participants were evaluated up to month 18 for main outcome measures (seizure frequency and neuropsychological performance) in addition to 3 months of baseline. Complications were reported regardless of duration of follow-up.

Results

<table>
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<tr>
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<th>Mean Seizure frequency per month at baseline</th>
<th>Mean Seizure frequency per month at 18 months</th>
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<tbody>
<tr>
<td><strong>Combined Group</strong></td>
<td>28 [15-70]</td>
<td>6 [0-23] (significant from month 2); p&lt;0.0005 from month 6</td>
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<tr>
<td><strong>Normal MRI (n=5)</strong></td>
<td>37 [15-50]</td>
<td>0.2 [0-1] (significant from month 1); p&lt;0.0005 from month 3</td>
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<tr>
<td><strong>MTS (n=4)</strong></td>
<td>39 [23-70]</td>
<td>12 [6-23] (significant from month 8) P&lt; 0.05</td>
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</table>

* seizure count regardless of on or off group assignment was reduced in both groups. Statistical analyses could not be performed because of a small number of observations

** 3/9 patients had skin erosion with infection requiring removal of hardware at 24 months

*** no deterioration in memory deficit following implantation. Trend at 18 months for improvement in all tests, but small numbers did not permit statistical analyses

Comments:
1. There was an attempt at double blinding, but patients were aware of allocation.
2. Patient selection was non consecutive, inclusion and exclusion criteria were not clearly defined, and the characteristics of the patients in the two groups were not specified.
3. One month follow up was not sufficient to see effect of hippocampal stimulation in the MTS group.
4. Statistical comparisons could not be made for the efficacy of hippocampal stimulation within the various subgroups (bilateral vs. left vs. right implantation) or on neuropsychological changes over time by group because of the small sample size of the study.
5. No confidence intervals or effect sizes were calculated.
6. It is unclear what the neuropsychological cut-offs (i.e. Standard deviation on tests) were used for degree of memory impairment.
7. A complete follow-up in all patients of 18 months (18-84) was short.
8. Limited information was given on patient’s antiepileptic medications and whether they were changed during the baseline period.

References


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