DO ALL NEUROSTIMULATORY TREATMENTS HAVE SIMILAR EFFICACY: NO

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Neurostimulation for epilepsy includes a wide variety of techniques (1). Two, vagal nerve stimulation (VNS), and more recently the implanted responsive neurostimulator (RNS), are approved (In the US but not Europe). Several others, including a variety of deep brain stimulation (DBS) approaches, transcranial magnetic stimulation (TMS) and trigeminal nerve stimulation, are experimental. VNS has been shown to be effective for adults with focal and secondary generalized seizures, but not for children or for other seizure types. The two largest randomized studies compared high frequency to low frequency stimulation, with reductions in seizure frequency of 25-28% for the high, and 6-15% for the low frequency stimulation groups (2,3). In a one year open-label extension study, median seizure reduction was 45% (4).

One hundred ninety one subjects with medically intractable partial onset seizures were studied in a randomized in a multicenter double-blinded RNS controlled trial. Either one or two foci were implanted, and 1 month after implant randomized 1:1 to active or sham stimulation. After the fifth postimplant month, all subjects received responsive stimulation in an open label period with 2 years of total postimplant follow-up (5). Seizures were reduced -37.9% in the active and -17.3% in the sham group. During the extended open label period the median percent reduction was 44% at 1 year and 53% at 2 years.

In a multicenter trial 110 patients had anterior thalamic nucleus stimulation (6). The median reduction in seizures was 38.8% for the treatment group versus 22.8% for the sham control group, and in the last month of the three month trial 40% versus 14% (6). Temporal lobe seizures showed the best response; patients with extra=temporal foci showed no difference in response between active and sham stimulation. Interestingly, both groups showed a 20% decline in seizures during the one month recovery period before stimulation was turned on, perhaps due either to a placebo effect, or reversion to the mean in patients who may have been experiencing particularly frequent or severe seizures before entering a clinical trial involving a surgical procedure.

Several small trials of cerebellar stimulation have shown varying results, due in part to differing study design and statistical vagaries (7,8). Hippocampal stimulation has also been reported to reduce seizures by up to 100% in small groups of patients (8).

Several studies have evaluated rTMS) as a therapeutic modality. This approach has the advantage of simplicity, relatively low cost, and lack even of the surgery needed for VNS. One study showed a non-significant 16% greater reduction in active than sham-stimulated patients with mesial temporal foci (9). A significant reduction in seizures of about 50% (there was no change in the sham group) was found in patients with malformations of cortical development who had five days of one Hz, lasting several weeks after treatment (10). Seizure reductions of 80% were found in patients with mainly extra-temporal foci when rTMS at 90% of motor threshold was compared to ineffective stimulation at 20% motor threshold (11).

Trigeminal nerve stimulation has assessed in a double-blind randomized active-control trial that enrolled 50 patients with 2 or more focal or secondary generalized seizures per month, using active treatment at 120 hertz with a control at two Hertz. The mean reduction in seizure frequency was 16% for the 120 Hz group and 10.5% for the two Hz group (12). The 50% responder rate has 30% versus 21%. Neither of these differences was significant. However, as with other stimulation modalities, there was a trend toward better response in the 120 Hz group with longer treatment duration.

The true efficacy of brain stimulation procedures in intractable epilepsy is unknown. For example, limited available data suggests that hippocampal stimulation might be most effective for focal seizures originating in that structure. Clinical experience with RNS and DBS is still limited; in addition to the known surgical complications of invasive procedures, unexpected adverse events may appear. Depression occurred more frequently in DBS than during sham stimulation in the anterior thalamic trial (6). In contrast rTMS, and possibly VNS have anti-depressive effects. Just as for antiepileptic drugs, considerations in addition to efficacy, including side effects, convenience, and unfortunately expense will influence the choice of stimulation therapy as controlled clinical trial data emerge.

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