



Letter to the Editor

Response to “Vagus nerve stimulation: Urgent need for the critical reappraisal of clinical effectiveness”

We have read with interest a recent editorial written by Dr. Hoppe¹ about our article “Long-term results of vagal nerve stimulation for adults with medication-resistant epilepsy who have been on unchanged antiepileptic medication”,² and we are surprised about his comments and conclusions. We would like to add some data that we hope will help clarify some of his considerations, which we do not consider accurate. Our paper was the first prospective study performed on adults which analysed the net effect of VNS, since medication was held constant during the assessment period.

First, we would like to explain some data presented in our paper and mentioned in Dr. Hoppe's review, which were not correctly understood. Dr. Hoppe mentions that vagal nerve stimulation was ineffective in 26% of our cases.¹ This constitutes a misinterpretation of our data.² This percentage includes patients whose improvement has been less than 50%, but not zero. It is important to consider that some patients achieving a less than 50% reduction in their seizure frequency may experience an improvement in the severity and duration of their seizures, in their mood, degree of alertness and ability to cooperate with their caregivers, as quantified in other series.³

We are surprised about Dr. Hoppe's assumption that a 50–100% sustained reduction in the patients' seizure frequency does not represent substantial relief. We would also note that Dr. Hoppe mentions that no patient had a complete and sustained response. This is incorrect, as reflected in the article: one patient was rendered seizure-free by VNS therapy.²

Dr. Hoppe discussed in his editorial that proportion of patients experiencing side effects was 51%, not considering that most side effects were transient. Moreover, side effects that were considered moderate or severe disappeared when the VNS system was inactivated or explanted, and no patient had any permanent sequelae. He did not mention that drug therapy for epilepsy also involves significant side effects, which may be as disabling as those associated with VNS.

We would like to inform Dr. Hoppe that patients treated with VNS are able to undergo MRI at 1.5 Tesla using a send-receive head coil, as long as the VNS is temporarily inactivated. According to the physician's manual, 3.0 Tesla MRI scans can also be carried out on VNS patients with certain precautions.^{4,5}

Dr. Hoppe states that an uncontrolled study cannot demonstrate causal effects. However, it is well known that causality can be established by different methods (“modus ponens, modus tollens”), and that different study designs provide complimentary evidence. Our study is the first prospective study analyzing the long-term outcome of VNS treatment in adults with medication-resistant epilepsy. As stated in the article, previous series have demonstrated that the outcome of patients with drug-resistant epilepsy under best medical treatment depends on patients'

clinical features and the definition of drug resistance. Our patients had a long disease duration (25 years), multiple previous treatments (all had tried at least five antiepileptic drugs previously), most had intellectual disability and generalized seizures.² All of these factors reduce the chances of achieving a remission of epilepsy remission with best medical management.⁶

Regarding the possibility of a “regression towards the mean” phenomenon, we should take account of the fact that our patients' pre-VNS mean seizure frequency was calculated on the basis of seizure frequencies registered over a period of at least one year before the implantation of VNS. A regression to the mean phenomenon also seems less likely given that these patients had already been treated medically for a long time prior to VNS insertion and had undergone several consistent assessments in different institutions over this time.

A number of studies have looked at the cost-effectiveness of VNS therapy. The most recent by Helmers demonstrated net cost savings for health care purchasers over 1.5 years from VNS implantation.⁷ Other studies have demonstrated a decrease of epilepsy-related direct medical costs in patients receiving VNS treatment rather than AED treatment alone, significant reductions in health care utilization, time spent on health-related activities, time lost from work with the use of VNS, and reduced hospitalization in patients treated with VNS. This can even occur in patients with a less than 25% seizure frequency reduction.^{7–10}

We are surprised that the author insists that best medical treatment might have been able to improve the patients' medical condition. In our series, best drug therapy had been tried for a mean of 25 years, and 81% of participants still had disabling seizures on a daily basis at the time of surgery.²

We thank you for the opportunity of presenting these additional explanations about our study.

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16 March 2013