Epilepsy Behav. 2011 Jan;20(1):57-63. Epub 2010 Dec 8.

Vagus nerve stimulation in 436 consecutive patients with treatment-resistant epilepsy: Long-term outcomes and predictors of response.

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Abstract

OBJECTIVE: The goal of this study was to assess the efficacy and safety of vagus nerve stimulation in a consecutive series of adults and children with treatment-resistant epilepsy (TRE).

METHODS: In this retrospective review of a prospectively created database of 436 consecutive patients who underwent vagus nerve stimulator implantation for TRE between November 1997 and April 2008, there were 220 (50.5%) females and 216 (49.5%) males ranging in age from 1 to 76years at the time of implantation (mean: 29.0±16.5). Thirty-three patients (7.6%) in the primary implantation group had inadequate follow-up (<3months from implantation) and three patients had early device removal because of infection and were excluded from seizure control outcome analyses.

RESULTS: Duration of vagus nerve stimulation treatment varied from 10days to 11years (mean: 4.94years). Mean seizure frequency significantly improved following implantation (mean reduction: 55.8%, P<0.0001). Seizure control ≥90% was achieved in 90 patients (22.5%), ≥75% seizure control in 162 patients (40.5%), ≥50% improvement in 255 patients (63.75%), and <50% improvement in 145 patients (36.25%). Permanent injury to the vagus nerve occurred in 2.8% of patients.

CONCLUSION: Vagus nerve stimulation is a safe and effective palliative treatment option for focal and generalized TRE in adults and children. When used in conjunction with a multidisciplinary and multimodality treatment regimen including aggressive antiepileptic drug regimens and epilepsy surgery when appropriate, more than 60% of patients with TRE experienced at least a 50% reduction in seizure burden. Good results were seen in patients with non-U.S. Food and Drug Administration-approved indications. Prospective, randomized trials are needed for patients with generalized epilepsies and for younger children to potentially expand the number of patients who may benefit from this palliative treatment.

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Childs Nerv Syst. 2010 Nov;26(11):1495-504. Epub 2010 Apr 1.

Epilepsy secondary to tuberous sclerosis: lessons learned and current challenges.

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Abstract

BACKGROUND: In tuberous sclerosis complex (TSC), a substantially increased risk of developing epilepsy is present as a result of a disruption of a TSC gene expression in the brain and secondary abnormal cellular differentiation, migration, and proliferation. Dysregulated excitation probably has its roots in the disruption of GABAergic interneuron development. There is an age-dependent electroclinical expression of seizures, and epilepsy is often quite severe and unremitting. DISCUSSION: The majority of patients (>60%) who are candidates for surgery remain seizure-free after tuberectomy. During the recent years technical advances in the localization of the epileptogenic zone during the recent years have lead to a 63% of Engel class I status after surgery compared with a previous 52%. In medically refractory patients not suitable for surgery, vagus nerve stimulation has proved efficacy in significantly reducing seizure frequency in more than 50% of cases. New evidence suggests that mTOR inhibitors may be helpful in the management of intractable epilepsy for individuals with TSC.

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Vagus nerve stimulation in refractory epilepsy: effects on pro- and anti-inflammatory cytokines in peripheral blood.

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Abstract

OBJECTIVE: The vagus nerve has important immunological functions that may be relevant for its anticonvulsive action. We postulate that this anticonvulsive action is activated by a shift in the immune system resulting in a reduction of neurotoxic and an increase of neuroprotective tryptophan metabolites.

METHODS: Eleven patients with refractory epilepsy and 11 controls matched for age and gender were included in this study. The primary outcome measure was a 50% seizure reduction. Other variables were pro-inflammatory cytokines IL-6 and TNF-α, anti-inflammatory cytokine IL-10, cortisol, and the tryptophan metabolites 3-hydroxykynurenine (3-OH-KYN), kynurenic acid (KYNA), kynurenine, serotonin (5-HT) and 5-hydroxyindol acetic acid (5-HIAA). Blood samples were scheduled during baseline, and in week 28 of add-on treatment.

RESULTS: IL-6 levels were higher in the responders than in the control group, and decreased after vagus nerve stimulation (VNS), whereas IL-10 was low and increased after VNS. In nonresponders, VNS resulted in an increase of IL-6 plasma levels and in a decrease of IL-10. Cortisol concentrations are higher in the epilepsy group than in the control group. After VNS, these concentrations decreased. The concentrations of the tryptophan metabolites were lower in the epilepsy group than in the control group. The KYNA ratios are defined as the ratio of neuroprotective KYNA versus neurotoxic 3-OH-KYN and KYNA versus neurotoxic kynurenine: these ratios were lower in epilepsy patients than in controls, and they both moderately increased after VNS.

CONCLUSION: The outcome of this preliminary study indicates that VNS causes a rebalancing of the immune system. This results in: (1) a reduction of neurotoxic and an increase of neuroprotective kynurenine metabolites and (2) in the normalization of cortisol levels.

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Newer anticonvulsant medications in pediatric neurology.

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Abstract

OPINION STATEMENT: Antiepileptic drugs (AEDs) are the mainstay of treatment for recurrent seizures. Uncontrolled seizures may cause medical, developmental, and psychological disturbances. The medical practitioner should thus strive to eliminate or minimize seizures. Treatment advances in epilepsy include 1) identification of the basic mechanisms of epilepsy and action of AEDs, 2) the introduction of new AEDs, and 3) the use of neurostimulation, including vagus nerve stimulation. Treatment with AEDs involves balancing each AED's efficacy against its side effects. In some patients, effective AEDs must be discontinued because of intolerable side effects. Although all AEDs have a proven efficacy, the choice of AEDs should be based on better efficacy for individual seizure types or epilepsy syndromes. Side effects also differ from drug to drug and must be taken into account. This article focuses on studies and expert opinion consensus to guide the choice of AEDs.

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Anti-inflammatory effect of vagus nerve stimulation in a rat model of inflammatory bowel disease.

Meregnani J, Clarençon D, Vivier M, Peinnequin A, Mouret C, Sinniger V, Picq C, Job A, Canini F, Jacquier-Sarlin M, Bonaz B.

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Abstract

Vagus nerve stimulation of afferents is used as an adjunctive treatment for drug-resistant epilepsy and depression. In addition, anti-inflammatory properties of vagus nerve stimulation have been reported in various experimental models of inflammation but not in colitis. These effects are thought to be mediated via peripheral release of acetylcholine from the vagus and subsequent activation of macrophages. Our aim was to evaluate in rats the anti-inflammatory effects of chronic vagus nerve stimulation on colonic inflammation. Colitis was induced by intracolonic instillation of trinitrobenzene sulfonic acid. Vagus nerve stimulation (left cervical) was performed in freely moving animals 3h per day for five consecutive days. Assessment of colonic inflammation was obtained using physiological (e.g. body weight, temperature and locomotor activity) parameters, macroscopical (area of lesions), histological, and biological parameters (e.g. myeloperoxidase activity, cytokine and cytokine-related mRNAs), both at the level of the damaged colon and the colon immediately above. A global multivariate index of colitis was then generated for a better characterization of colonic inflammation. Vagus nerve stimulation reduced the degree of body weight loss and inflammatory markers as observed above the lesion by histological score and myeloperoxidase quantification. This anti-inflammatory effect was also demonstrated by the improvement of the multivariate index of colitis. These data argue for an anti-inflammatory role of vagus nerve stimulation chronically performed in freely moving rats with colitis and provide potential therapeutic applications for patients with inflammatory bowel diseases.

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Operative and technical complications of vagus nerve stimulator implantation.

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Abstract

BACKGROUND: The treatment of refractory epilepsy by vagus nerve stimulation (VNS) is a well-established therapy option for patients not suitable for epilepsy surgery and therapy refractory depressions.

OBJECTIVE: To analyze surgical and technical complications after implantation of left-sided VNS in patients with therapy-refractory epilepsy and depression.

METHODS: One hundred five patients receiving a VNS or VNS-related operations (n = 118) from 1999 to 2008 were investigated retrospectively.

RESULTS: At the time of operation, 84 patients were younger than 18 years, with a mean age of 10.5 years. Twenty (19%) patients had technical problems or complications. In 6 (5.7%) patients these problems were caused by the operation. The device was removed in 8 cases. The range of surgically and technically induced complications included electrode fractures, early and late onset of deep wound infections, transient vocal cord palsy, cardiac arrhythmia under test stimulation, electrode malfunction, and posttraumatic dysfunction of the stimulator.

CONCLUSION: VNS therapy is combined with a wide spread of possible complications. Technical problems are to be expected, including electrode fracture, dislocation, and generator malfunction. The major complication in younger patients is the electrode fracture, which might be induced by growth during adolescence. Surgically induced complications of VNS implantation are comparably low. Cardiac symptoms and recurrent nerve palsy need to be taken into consideration.

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Magnetoencephalography in epilepsy patients carrying a vagus nerve stimulator.

Carrette E, De Tiège X, De Beeck MO, De Herdt V, Meurs A, Legros B, Raedt R, Deblaere K, Van Roost D, Bourguignon M, Goldman S, Boon P, Van Bogaert P, Vonck K.

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Abstract

Due to technical constraints, magnetoencephalography (MEG) is challenging in vagus nerve stimulation (VNS) patients. This study evaluates (1) the feasibility of MEG in VNS

patients and (2) the added value of MEG in their presurgical evaluation (PE). Ten VNS patients were studied by MEG using the spatiotemporal signal space separation (tSSS) method. Equivalent current dipoles (ECD) were classified "clustered"/"scattered". It was evaluated whether MEG (1) confirmed localisation of the hypothesized epileptogenic zone (HEZ), (2) improved delineation of the HEZ, or (3) identified 1 out of multiple HEZs. Finally it was evaluated whether adding MEG to the PE improved patient management by changing or supporting the hypothesis. In 7/10 patients, tSSS allowed to obtain interpretable MEG data, with interictal epileptiform discharges in 6/7. ECD clustered within 1 lobe in 4/6; confirming the localisation of the HEZ in 2/4 and improving delineation of the HEZ in 2/4. When ECD clustered within 2 lobes (1/6) or were scattered (1/6), MEG could not identify 1 out of multiple HEZs. In 2 patients, MEG changed management to invasive video-EEG monitoring (IVEM) and resective surgery (RS). In 4 patients, MEG further supported the management; IVEM in 2/4 and unsuitability for RS in 2/4. So far IVEM, performed in 2, resulted into RS. This study demonstrates the feasibility of MEG in VNS patients. MEG changed management in 20% and further supported the proposed management in 40% illustrating the clinical value of MEG in the PE of VNS patients.

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Mania following vagus nerve stimulation: A case report and review of the literature.

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Abstract

Vagus nerve stimulation (VNS) is an increasingly used therapy for patients with treatment-refractory epilepsy and depression. Hypomanic and manic symptoms are a rare but recognized adverse effect of VNS treatment. Here we describe a case in which VNS treatment in a patient with epilepsy and unipolar depression was associated with the rapid development of manic symptoms. The patient's manic symptoms resolved with temporary discontinuation of the VNS current, and the patient was eventually able to resume VNS treatment with good effect and without further manic symptoms. Mania is a rare but serious side effect of VNS; however, in this case and in the majority of reported cases of VNS-associated mania, symptoms resolve and VNS can be safely administered.

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Long-term outcome of vagus nerve stimulation therapy after failed epilepsy surgery.

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Abstract

OBJECTIVE: Adequate control of intractable epilepsy continues to be a challenge. Little is known about the role of VNS therapy in intractable epilepsy in patients who failed to respond to surgical management. The objective of the present study is to determine the efficacy of vagus nerve stimulation therapy in patients with intractable epilepsy who have failed surgical and medical therapy.

METHODS: All the patients who had persistent seizures after cranial surgery who subsequently underwent vagus nerve stimulator (VNS) placement at our institution from 1998 to 2008 were included in the study. Thirty-seven consecutive patients were enrolled and followed for the outcome measures of seizure burden, anti-epileptic drug (AED) burden and quality of life (QoL). Minimum follow-up was 18 months.

RESULTS: Overall, 24 (64.9%), 9 (24.3%), 4 (10.8%) patients reported less than 30%, between 30% and 60% and greater than 60% reduction in seizure frequency after VNS placement, respectively at a mean of 5 years follow-up period. Post-VNS anti-epileptic requirement exhibited a decreasing trend. 17 patients (45.9%) report an improvement in QoL (better or much better).

CONCLUSION: VNS therapy in patients who have failed medical and surgical therapies only provides marginal improvement in seizure control but has greater likelihood to improve subjective QoL issues. In addition, VNS has the potential to reduce AED burden without adversely impacting seizure management. Given the low surgical risk of VNS placement, vagus nerve stimulation as a therapeutic modality should be individualized to achieve best clinical response and fewest side effects.

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Efficacy of vagus nerve stimulation for refractory epilepsy among patient subgroups: A re-analysis using the Engel classification.

Wheeler M, De Herdt V, Vonck K, Gilbert K, Manem S, Mackenzie T, Jobst B, Roberts D, Williamson P, Van Roost D, Boon P, Thadani V.

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Abstract

Optimal candidates for VNS as a treatment for refractory epilepsy have not been identified. In this retrospective two-center study, we used the Engel classification for evaluating seizure outcome, and tried to identify predictive factors for outcome by means of subgroup analysis. The medical records of patients who have been treated with VNS for at least one year at Dartmouth-Hitchcock Medical Center and Ghent University Hospital were evaluated. Seizure frequency outcome was assessed using the Engel classification for the study population as a whole, and for patient subgroups with regard to mental functioning, seizure type, predisposing factors for developing epilepsy, age at time of VNS implantation and epilepsy duration. 189 patients (102M/87F) were included in the study (mean FU: 41 months). 6% had a class I outcome (seizure-free), 13% a class II outcome (almost seizure-free), 49% a class III outcome (worthwhile improvement) and 32% had a class IV outcome (no improvement). When patients were divided into specific subgroups, a statistically significant better outcome was found patients with normal mental functioning (p=0.029). In our series, results for VNS are clearly inferior to resective surgery, but comparable to other treatment modalities for refractory epilepsy. With combined class I and II outcomes around 20%, and another 50% of patients having worthwhile improvement, VNS is a viable alternative when resective surgery is not feasible.

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