

VNS therapy in epilepsy

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INDICATION of VNS

Refractory partial epilepsy with partial and/or secondary generalized seizures

Surgery is not indicated

Unsatisfactory effect of previous surgery

Patient does not agree with surgery ?

Refractory generalized epilepsies

(generalized tonic-clonic seizures, myoclonic seizures, absence, ..)

SYMPTOMATIC, IDIOPATHIC SYNDROMES

(LGS, JME, „absence“ epilepsies)

Paliative procedure in refractory epilepsies

**VNS can not replace resective surgery
where it is possible**

Experimental effect on EEG

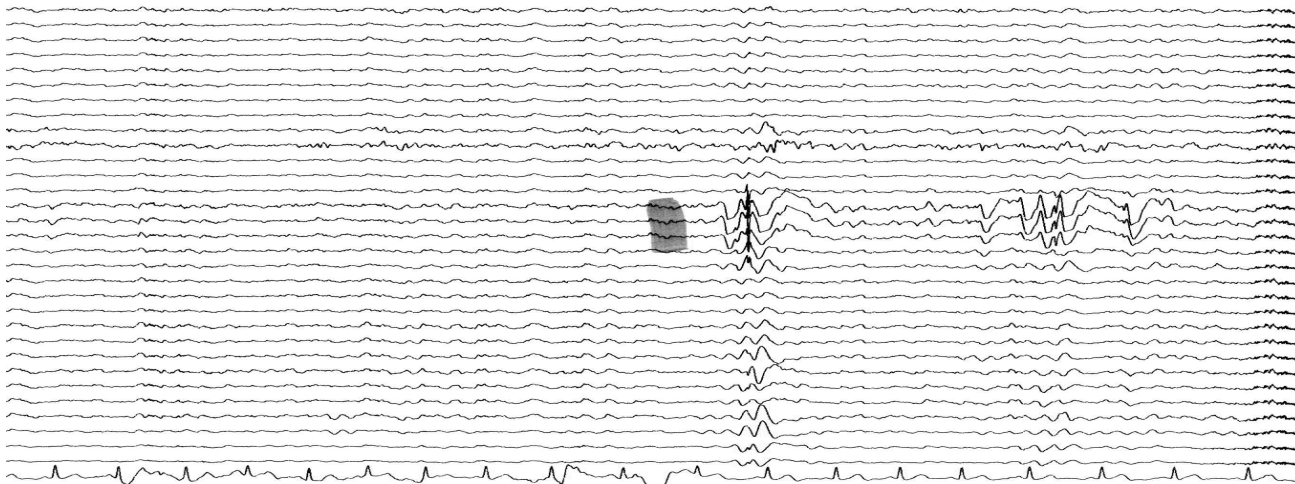
Synchronization or desynchronization of EEG activity according to the type of stimulation



Low frequency stimulation – synchronization

High frequency stimulation – desynchronization

Bailey et al. 1938; Zanchetti et al.; 1952 Chase et al.1967; McLachlan 1993;



VNS – mechanism of action

The mechanism of action has not yet been fully understood

Probable multiple mechanisms

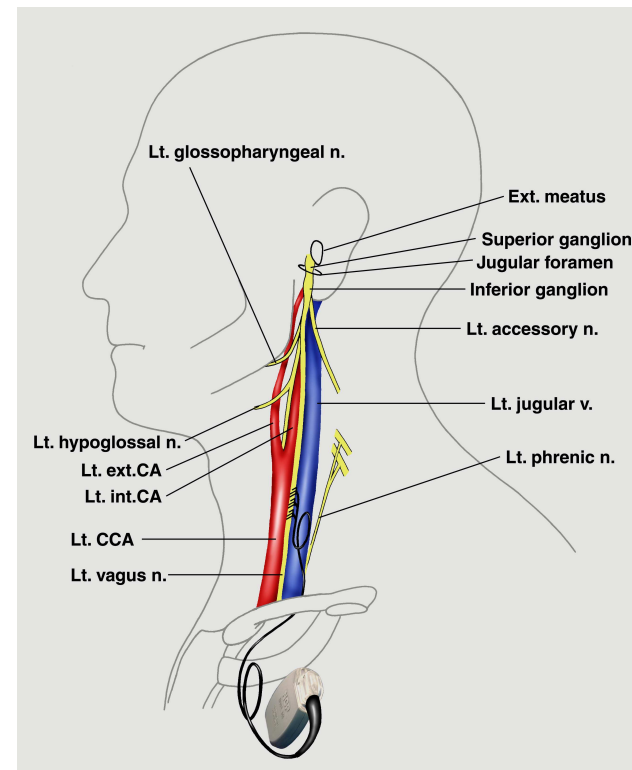
Left vagal nerve at its cervical portion

80% afferent fibers, mostly myelinated

20% efferent fibers, mostly unmyelinated
parasympathetic fibers

(left side mostly to ventricles,
right side mostly to atrial structures),

with myelinated fibers to vocal muscles



VNS – mechanism of action

SPECT, PET, fMRI studies – changes of perfusion in various cortical and subcortical structures – mainly thalamus

Significant bilateral changes in blood flow observed during VNS therapy

Increased blood flow in the thalamus has been shown to have significant correlation with long-term seizure control

Henry TR, et al. 1998, Henry TR, et al. 1999.
Narayanan et al. 2002,

VNS – mechanism of action CONCLUSION
– theoretical concept

Not fully understood

Specific changes in various **cortical and subcortical structures – SPECT and fMRI changes**

Influence on **thalamocortical pathways – decrease of synchrony of some cortical areas**

Influence on synaptic activity in **central parts of autonomic nervous system (hypothalamus, insular cortex)**

Influence on activity of **limbic structures (ncl. amygdalae, hippocampus, cingulate gyrus)**

VNS therapy implant procedure

Approximately 1 to 1.5 hour

General anesthesia is used (data about local anesthesia)

Chest/axillary border incision for pulse generator

Neck incision for lead

Generally inpatient procedure

Oral antibiotics 7-10 days

VNS – stimulation parameters

Parameter	Units	Range	<u>Typical</u>
Output Current	milliamps	0 - 3.5	<u>>1.0</u>
Signal Frequency	hertz	1 - 30	<u>20</u>
Pulse Width	microseconds	130 - 1000	<u>250</u>
Signal On-time	seconds	7 – 60s	<u>21-30</u>
Signal Off-time	seconds/minutes	14s-180 m	<u>3-5 minutes</u>

VNS stimulation parameters

Intraoperative NCP lead test

First electrical stimulation of vagal nerve

Necessary to check the transmission of the electrical signal from the electrode to the vagal nerve

Intraoperative onset of chronic stimulation

250 μ s, 20Hz, on/off time – 30seconds/3minutes

Basal output current  0.25mA

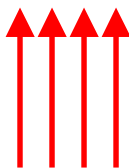
VNS stimulation parameters

A computer (P-PC)
Software
Wand communicate
transcutaneously to the
pulse generator



**Continual intermittent
stimulation**

0.25mA



Up to the clinical effect, usually to 1.0-1.75mA

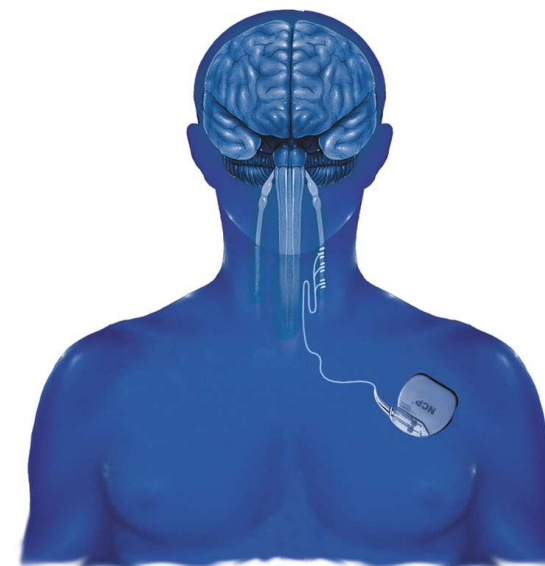
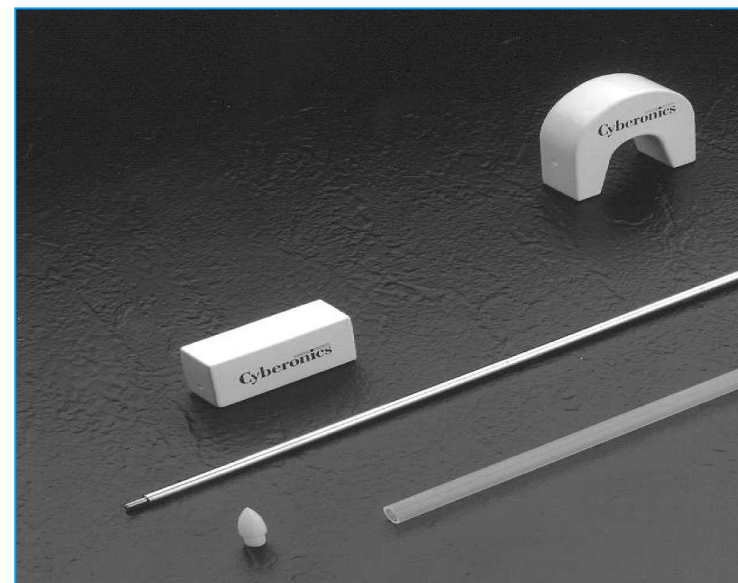
Programming visit – each 4-6 weeks

VNS anti-seizure effect

Effects of VNS

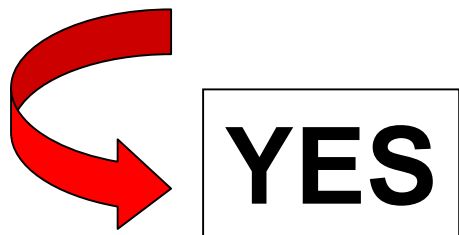
Chronic „anti-seizure“ effect (long-term neuromodulation by intermittent regular stimulation)

Acute „anti-seizure“ effect (effect of „on demand“ stimulation at the time of seizure onset)



VNS – reimplantation procedure

Decision point – improvement of quality of life???



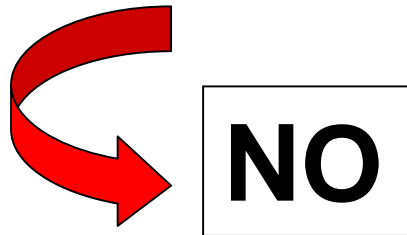
Typically performed under local anesthesia

30-45 minute procedure

Battery replacement only involves replacing the generator, not the lead

VNS – Removal of the NCP System Lead and Generator

Decision point – improvement of quality of life???



Typically performed general anesthesia

1.0-1.5 hours procedure

**3 patients in our center – without complication,
without the physical injury of vagal nerve**

VNS – bradycardia/asystole

Incidents of bradycardia followed by asystole (as of 01/00)

6 incidents out of 7,000 implants (1/1,167 implants or ~0.1%)

All events took place during the routine intraoperative NCP lead test

No asystolic events have occurred outside of the O.R.

Tatum, et al., *Neurology*, Volume 52, Number 6, p. 1267-1269, 1999

Asconape, et al., *Epilepsia*, Volume 40, Number 10, P.1452-1454, 1999

VNS – side effect during chronic treatment

Several side effects described (very low incidence)

Mostly intermittent hoarseness during the time of stimulation

In our series about half of patients

Habituation is almost always present

It is rarely the indication for the discontinuation of the VNS treatment



VNS – CONCLUSION

**VNS is PALIATIVE extracerebral surgery
procedure in REFRACTORY EPILEPSY
(focal and generalized)**

Worldwide used in both children and adults

Used in mentally disabled patients

VNS – CONCLUSION

Implantation and chronic stimulation are the safe procedures

„on demand“ stimulation is effective to interrupt the seizures in 1/3 of all patients

In general >50% of patients experience >50% seizure reduction

In general in 2/3 of patients VNS significantly improves their quality of life

VNS – CONCLUSION

Surgical complications are rare

Side effect of chronic stimulation are well tolerated and usually are not the indication for VNS discontinuation