THE EFFECTS OF VNS NEUROSTIMULATION ON THE VISUAL EVOKED POTENTIAL

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PURPOSE

Vagus nerve stimulation (VNS) is one currently used adjunctive neurostimulation therapy for refractive epilepsy. The purpose of this study was to determine the effects of neurostimulation on cortical lateral interactions manifest in the steady-state VEP. A further aim was to compare these effects with those found previously with adjunctive gabapentin treatment in which VEP indices of cortical lateral interactions were reversibly changed.

METHODS

PATIENTS - Six chronic VNS patients (3M, 3F; avg. age: 34.8 yrs).

Inclusion Criteria
- VNS treatment > 1 year
- Stable AED therapy > 1 month
- VA corrected to 20/40 or better OU

Exclusion Criteria
- Photosensitive seizures
- Ophthalmological disease that might affect VEPs
- Seizures within 24 hrs prior to VEP testing

CONTROLS - 21 age-matched normal subjects (15M, 6F; avg. age: 32.9 years).

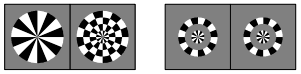
Chronic VNS Patient Characteristics

Patient	Sex	Age	Seizure Onset Age (yrs)	Etiology	Seizure Type(s)	Last Seizure Prior to VEPs	AEDs/Dosages	VNS Device Settings: Duration VNS Therapy	Current (mA)	On/Off Cycle	Frequency (Hz)	Pulse Width (μsec)
Pt 1	M	51	34	Cryptogenic (LRE)	CPS	4 years	Topamax 100 mg/d	7 years	2.5	30 sec / 48 sec	30	500
Pt 2	F	31	2.5	Symptomatic (CP)	CPS	1+ years	Tegretol 1600 mg/d	6 years	0.5	30 sec / 48 sec	30	500
Pt 3	F	46	40	Symptomatic (abscess)	CPS	1.5 years	Topamax 400 mg/d Dilantin 400 mg/d	5 years	0.25	7 sec / 12 sec*	30	500
Pt 4	M	31	4	Cryptogenic (LRE)	CPS + SG	2 months	Keppra 3000 mg/d Tegretol 1200 mg/d	3.5 years	1.5	30 sec / 108 sec	30	500
Pt 5	M	27	infancy	Symptomatic (infarct)	CPS + SG	1+ years	Keppra 4000 mg/d Zonegran 500 mg/d	6.5 years	1	7 sec / 66 sec	30	750
Pt 6	F	23	14	Idiopathic	PGTC Myoclonic	1+ years	Depakote 1000 mg/d Trileptal 600 mg/d	4.5 years	0.75	7 sec / 12 sec*	20	500

*off-cycle changed to 48 sec for Pt 3 & 108 sec for Pt 6 to allow for VEP testing

STIMULI
Stimuli consisted of conventional contrast-reversal checkerboards and the radial windmill/dartboard pattern shown on the right. Modulation rate: 4.19 Hz., Contrast: 0.30. Binocular viewing at 1 m. Field size: 8.8 x 8.8 deg.

Windmill/Dartboard Stimuli



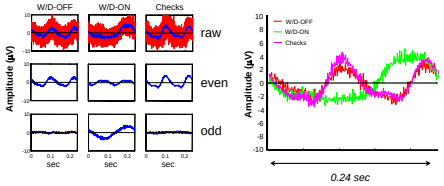
The modulated regions are identical in the W/D-ON and W/D-OFF configurations, but the static region is present only in the W/D-ON configuration. Thus, interactions between these regions may result in differences between the VEP waveforms that the two stimuli elicit.

PROCEDURE
For the patients, single channel (Oz-Cz; grd: mastoid) steady-state VEPs were recorded with the VNS stimulator on (STIM-ON) and off (STIM-OFF) in recording sessions separated by approximately one hour. The order of the recording sessions was counterbalanced across patients. Two surface electrodes were placed over the sternocleidomastoid muscle near the surgical scar, to detect the activity of the VNS stimulator. In the STIM-ON condition, trials (duration: 30 sec) were initiated when the stimulator cycled off as evidenced in the neck recordings or in the EEG tracing. A total of 3 minutes (6 trials) of responses to each stimulus were collected for STIM-ON and STIM-OFF. Each 30 sec trial was divided into 10 sec epochs. We excluded all epochs in which there were artifacts or in which the device cycled on.

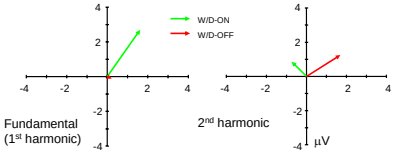
Procedures for controls were identical, except that only one set of 6 trials for each stimulus was collected, and no neck electrodes were placed.

ANALYSIS & RESULTS

CONTROL SUBJECT



Raw VEP waveforms from each valid epoch were averaged and Fourier analyzed to obtain even and odd harmonic response components (above). Fourier components can be represented as vectors, whose magnitude indicates amplitude and whose direction indicates phase (below).



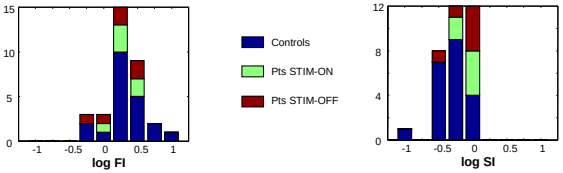
We observed two differences between the VEP waveforms elicited by W/D-ON and W/D-OFF stimuli, as measured by their Fourier components. The fundamental response is absent in W/D-OFF (since it is a contrast-reversing pattern, like a checkerboard), but present in W/D-ON. Its normalized size is quantified by a "Facilitation Index." The second harmonic response is attenuated in the W/D-ON configuration compared to the W/D-OFF configuration, as quantified by a "Suppression Index." These indices reflect lateral interactions between nearby neurons in visual cortex.

Facilitation Index

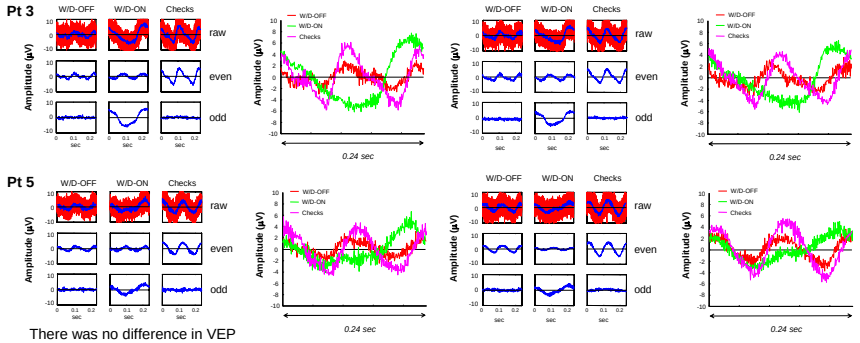
$$FI = \frac{\text{fundamental (W/D-ON)}}{\text{2nd harmonic (W/D-ON)}}$$

Suppression Index

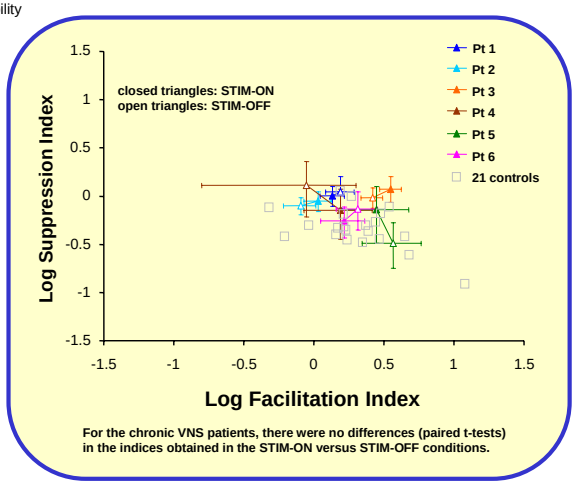
$$SI = \frac{\text{2nd harmonic (W/D-ON)}}{\text{2nd harmonic (W/D-OFF)}}$$



CHRONIC VNS PATIENTS



There was no difference in VEP waveforms or waveform variability obtained during STIM-ON and STIM-OFF sessions (above).



For the chronic VNS patients, there were no differences (paired t-tests) in the indices obtained in the STIM-ON versus STIM-OFF conditions.

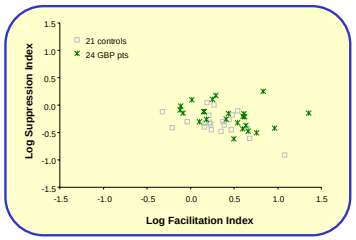
SUMMARY & CONCLUSIONS

- **Steady-state VEPs can be reliably recorded during the off-cycling of VNS neurostimulation, and responses were not significantly different from responses obtained when the stimulator is turned off for an hour.**
- **Compared to normal controls, both patient groups showed no difference in the facilitation index, but significantly less lateral suppression.**
- **With appropriate stimuli, the steady-state VEP is a noninvasive measure of the status of cortical interactions.**

Summary of Group Means

	log FI	log SI
21 Controls	.31 +/- .31	-.33 +/- .21
6 VNS Pts: STIM-ON	.26 +/- .20	-.07 +/- .11
STIM-OFF	.21 +/- .28	-.09 +/- .21
24 GBP Pts	.43 +/- .36	-.20 +/- .22

For both patient groups, the FI did not differ from that of controls. However there is significantly ($p < .05$) less suppression than in controls.



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http://www-users.med.cornell.edu/~jdvicto/vps.html