

EFFECTS OF VAGUS NERVE STIMULATION ON HEART RATE VARIABILITY IN CHILDREN WITH EPILEPSY

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OBJECTIVES

- Vagus nerve stimulation (VNS) is a non-pharmacologic antiepileptic therapy for patients with refractory epilepsy who are not candidates for resective surgery or who have had resective surgery with unsatisfactory results.
- Although some studies have shown that VNS treatment is safe, well tolerated and effective in seizure reduction, there are only a few reports concerning effects of VNS on cardiac autonomy.
- The aim of this study was to investigate the effects of VNS on heart rate variability (HRV) in patients with refractory epilepsy.

METHODS

- Twenty patients (mean age 11.7 ± 4.2 years) with refractory epilepsy were evaluated in terms of interictal heart rate variability with 24-hour ECG recordings before, after 6 and 12 months of VNS treatment for each patient.
- We analyzed heart rate, pulse interval, frequency-dependent parameters including total power, low-frequency (LF), high-frequency (HF), LF/HF ratio, time-dependent parameters including SDNN, SDNN index, SDANN, RMMSD, PNN50 and triangular index.
- HRV at both daytime and night were separately investigated for diurnal rhythm. The results were compared to age and gender matched healthy controls.

HRV parameters in patients and controls

HRV parameters	Before VNS	6 month	12 month	Controls	P1 B-C	P2 6-C	P3 12-C	P4 B-6	P5 B-12	P6 6-12
Minimum HR	58 ± 10	54 ± 9	55 ± 7	48 ± 4	<0,001	<0,01	<0,001	0,2	0,2	0,7
Maximum HR	152 ± 23	155 ± 17	155 ± 20	168 ± 16	<0,05	<0,05	<0,05	0,9	0,5	0,9
Mean HR	95 ± 12	90 ± 9	92 ± 8	83 ± 7	<0,001	<0,05	<0,001	<0,05	0,1	0,3
Pulse interval	94 ± 23	100 ± 15	100 ± 20	120 ± 17	<0,001	<0,01	<0,001	0,4	0,3	0,8
Total power	1637 ± 1149	2331 ± 1074	2027 ± 823	5199 ± 2124	<0,001	<0,001	<0,001	<0,01	<0,05	<0,05
LF	345 ± 250	505 ± 263	421 ± 179	1030 ± 336	<0,001	<0,001	<0,001	<0,01	0,1	<0,05
HF	259 ± 206	388 ± 243	332 ± 187	629 ± 266	<0,001	<0,01	<0,001	<0,001	0,1	0,1
LF/HF ratio	1,85 ± 1,26	1,58 ± 0,79	1,47 ± 0,61	1,77 ± 0,62	0,8	0,4	0,1	0,2	0,2	0,5
Triangular index	24 ± 10	31 ± 9	30 ± 10	46 ± 13	<0,001	<0,001	<0,001	<0,01	<0,05	0,9
SDNN	93 ± 30	111 ± 24	111 ± 29	151 ± 36	<0,001	<0,001	<0,001	<0,01	<0,05	0,6
SDNN index	41 ± 15	49 ± 13	46 ± 10	73 ± 15	<0,001	<0,001	<0,001	<0,05	0,2	0,1
SDANN	83 ± 31	100 ± 24	100 ± 29	131 ± 36	<0,001	<0,01	<0,01	<0,01	<0,05	0,6
RMMSD	29 ± 15	38 ± 18	33 ± 11	49 ± 15	<0,001	<0,05	<0,001	<0,05	0,2	0,1
PNN50	10 ± 10	15 ± 12	11 ± 8	22 ± 9	<0,001	<0,05	<0,001	<0,05	0,4	0,1
Daytime total power	1428 ± 986	2103 ± 1048	1798 ± 786	4715 ± 2092	<0,001	<0,001	<0,001	<0,01	<0,01	0,1
Daytime LF	295 ± 211	444 ± 222	387 ± 141	890 ± 298	<0,001	<0,001	<0,001	<0,01	<0,05	0,2
Daytime HF	189 ± 187	287 ± 179	232 ± 136	470 ± 242	<0,001	<0,05	<0,001	<0,01	0,3	0,2
Daytime LF/HF ratio	2,36 ± 1,55	1,8 ± 0,76	1,88 ± 0,62	2,16 ± 0,84	0,6	<0,05	0,2	0,1	0,2	0,6
Daytime SDNN	77 ± 25	97 ± 21	96 ± 29	127 ± 33	<0,001	<0,01	<0,01	<0,01	<0,01	0,8
Daytime RMMSD	25 ± 12	33 ± 14	28 ± 9	42 ± 14	<0,001	<0,05	<0,001	<0,01	0,1	0,1
Daytime PNN50	7 ± 7	11 ± 9	8 ± 6	18 ± 9	<0,001	<0,05	<0,001	<0,05	0,5	0,1
Night total power	1975 ± 1535	2680 ± 1234	2329 ± 1090	6014 ± 2727	<0,001	<0,001	<0,001	<0,05	0,3	0,1
Night LF	428 ± 372	579 ± 335	477 ± 276	1311 ± 602	<0,001	<0,001	<0,001	<0,05	0,6	0,1
Night HF	387 ± 306	544 ± 385	505 ± 320	918 ± 387	<0,001	<0,01	<0,001	<0,05	0,1	0,5
Night LF/HF ratio	1,55 ± 1,21	1,46 ± 0,99	1,22 ± 0,74	1,56 ± 0,71	0,9	0,7	0,2	0,6	0,3	0,2
Night SDNN	68 ± 28	80 ± 24	78 ± 24	115 ± 24	<0,001	<0,001	<0,001	0,1	0,1	0,9
Night RMMSD	37 ± 21	46 ± 23	41 ± 16	64 ± 21	<0,001	<0,05	<0,001	<0,05	0,4	0,3
Night PNN50	16 ± 16	22 ± 17	19 ± 13	36 ± 12	<0,001	<0,01	<0,001	0,1	0,4	0,3

P1: Before VNS - control group P2: after 6 month VNS - control group, P3: after 12 month VNS - control group, P4: Before VNS - after 6 month VNS, P5: Before VNS - after 12 month VNS, P6: after 6 month VNS - after 12 month VNS

RESULTS

- The minimum and mean HR were increased, pulse interval was narrowed in patients before treatment compared to control group ($p < 0.05$).
- HRV was also depressed in patients before treatment in all frequency and time-dependent parameters compared to control group ($p < 0.05$).
- It was observed that, cardiac autonomic system is under the effect of sympathetic system especially at daytime, when the increased LF/HF ratio was taken in to account, in patients before treatment ($p < 0.05$).
- However, these differences between pre and post VNS implantation were seen especially at 6 months of treatment ($p < 0.05$) and there were no significant additional changes at 12 months of treatment.
- Even so, these parameters were still significantly different at 12 months of treatment than control group ($p < 0.05$).
- There was also significant seizure reduction (almost 50%) after VNS treatment ($p < 0.05$).

CONCLUSIONS

- A significant improvement was observed in all HRV parameters after VNS therapy.
- Interestingly, maximum improvement was seen at 6 months of treatment and then no further improvement was observed.
- It can be explained by tolerability or adaptation of the autonomic system to the treatment.