THE EFFECT OFVAGUS NERVE STIMULATION ON THE ELECTROENCEPHALOGRAPHIC SIGNAL

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An original stimulation-recording system was assembled for the study of the brain response to the non-invasive stimulation of vagus nerve aiming to increase the attention and concentration. We applied continuous 5 Hz biphasic impulses and bursts of 5 Hz impulses. The increase of the attention index and the reduction in the meditative tendency were found after that. The complexity of the brain system was analyzed using the correlation dimension and the Lyapunov exponent, highlighting the differences between the resting state and the two types of vagus nerve stimulation.

Key words: vagus nerve, electrical impulses, brain focus, chaotic dynamical trend.

1. Introduction

Recent advancements in neuromodulation highlighted the potential of non-invasive vagus nerve stimulation in alleviating the acute and chronic pain syndromes, certain heart activity parameters, anxiety and the average brain focus. Therapies such as functional electrical stimulation use electrical impulses to generate muscle contractions and restore function, while transcutaneous electrical nerve stimulation and interferential currents help manage pain by interfering with pain signals. Transcutaneous auricular vagus nerve stimulation (taVNS) is a non-invasive neuromodulation technique that applies electrical impulses to the vagus nerve auricular branch. It was shown that taVNS has reduced the seizure frequency [1], demonstrating therapeutic outcomes previously attributed only to implanted VNS devices. Likewise it was shown the improvement in memory performance [2], in the ability to select appropriate responses to a given task [3], in vocabulary acquisition rates [4], in attentional regulation [5].

In this paper, we present a practical application of taVNS based on an original scheme, as a tool for obtaining direct insight into the complexity of the neural system's response to electrical stimulation of the state of concentration and attention. Electroencephalographic signals before and after taVNS were analyzed with computational tests provided by the commercially available CDA software (Chaos Data Analyzer), to highlight nonlinear dynamic trends for different types of

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taVNS. This study was conceived as a presentation of a proposed method for highlighting the effects of taVNS application on some cognitive parameters, namely the attention index and the meditation index applied to the author himself. The process of analyzing the captured encephalographic signal is based on the NeuroSky software as other authors have done for the study of pain [6], the article being a demonstrative one preceding a future case study. In addition, we analyzed the complexity of the neural system by applying several nonlinear dynamics tests on the EEG signal on the same signals and all can be also a demonstrative lesson for students in Medical Physics.

2. Experimental

2.1. The neural stimulation system

The stimulation and measurement system is composed of the stimulating signal source, a single channel remote encephalograph and related software (Fig. 1):

Fig. 1. The stimulation and the measurement system

The novelty of the electronic device lies in the fact that the stimulatory electrical impulses are biphasic, close to those generated by neurons, that is, action potentials in relation to the refractory period.

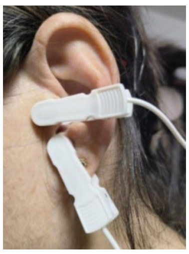


Fig. 2. Ear clips electrodes attached to the tragus and cymba conchae of the right ear, for taVNS [7]

Fig. 3. The Neurosky Mindwave device connected to the lobe of the left ear [8]

The biphasic electric impulses, with a duty cycle of 200 microseconds are obtained by using a STM32 microcontroller programmed in C/C++ language. Their frequency can be manually adjusted between 2 and 50 Hz with 1 Hz step, while the intensity can also be adjusted from 10% to 100% up to a slight perception threshold, with 10% step. The device can function either connected to a 9V…12V and 200 mA power supply or, better, to a 9V rechargeable battery in order to remove the 50 Hz artifacts.

The device connection with the ear lobes is presented in Fig. 2. In order to stimulate the auricular branch of the vagus nerve, there were attached two ear clips electrodes coming from the device which delivers adjustable low frequencies electric impulses, to the tragus and cymba conchae of the right ear (Fig. 2). Also, the headset with the NeuroSky Mindwave device which captures the raw EEG signal and transmits it to the laptop via the RF USB Dongle was placed on the forehead, with the clip connected to the lobe of the left ear (Fig. 3).

2.2. Measurements

The taVNS effects on the brain activity were recorded using a single-channel remote encephalograph [9] type “NeuroSky Mindwave” able to capture the raw EEG signal with 512 data/sec [10] and to display brain wave intensities and calculate the Meditation Index and the Attention Index using its own eSense algorithm displaying results on a relative scale of 0 to 100.

Although NeuroSky has not published the exact formula for calculating the 2 indices, it can be found that [11]: (i) Attention Index correlates most strongly with beta activity (alert, focused) and inversely with delta/theta (drowsiness); (ii) Meditation index correlates with alpha and theta activity (relaxed, calm) and inversely with high beta (mental effort, stress). Each index is scaled into a range 0–100, with ~40–60 being “baseline,” below 40 “low,” and above 60 “high.” All the measurements were performed on the author in the idea that the resulting article should be a demonstrative one preceding a future case study. In addition, we analyzed the complexity of the neural system by applying several nonlinear dynamics tests on the EEG signals and all can constitute also a demonstrative lesson for students in Medical Physics.

The same stimulation intensity was adjusted to perceptual threshold level. The average values of three repeated measurements (3% StDev) under well-defined conditions, such as a bright and quiet experimental environment, ensuring high comfort and the same musical background are considered.

2.3. Theoretical background

The characterization of complex systems dynamics, such as the neural system, can be done on the basis of the theory of hidden determinism or chaos theory, thanks to the advanced mathematical approaches developed in the last half century to satisfy the need for understanding biological systems and not only. The state space, as an appropriate framework for the applications of computational analysis, could be reconstructed on the basis of Taken's theory [12]. The attractor is a specific subset of phase space toward which trajectories converge over time, defined by the system variables, taken as the *n* position coordinates ($x_1, x_2, x_3, \ldots, x_i, x_{i+1}, \ldots, x_n$) and the corresponding *n* velocity coordinates ($x_1', x_2', x_3', \ldots, x_i', x_{i+1}', \ldots, x_n'$). Takens's theorem demonstrated that a multidimensional state space can be accurately reconstructed from a single observed variable *x(t),* using delay coordinates, i.e. *x(t)* and *x(t-m),* where *m* is the chosen delay, thus preserving key properties such as attractor structure and allowing the analysis of chaotic systems from a single type of measurement. For two evolutions of the system from close initial positions d_0 and $d_0+\delta d_0$ in a state space, two trajectories of the system can be considered as parametric functions of time being given by specific laws of evolution of the system according to some equations or systems of equations. Their rapid, exponential divergence occurs for complex, chaotic systems and is measured by Lyapunov exponent [13] which is a positive number while their convergence corresponds to stable – non chaotic systems with Lyapunov exponent negative or zeroed:

$$LE = \lim_{\substack{t \to \infty \\ \delta d_0 \to 0}} \left(\frac{1}{t}\right) ln\left(\frac{\delta d(t)}{\delta d_0}\right) \quad (1).$$

Rosenstein [14] developed an algorithm for calculating the largest Lyapunov exponent, appreciated as most robust approach for analyzing noisy biomedical or biological datasets. He defined the Lyapunov exponent, λ, for a dynamical system with the relation (2):

$$d(t) = d_0\, exp(\lambda t) \quad (2)$$

where *d(t)* is the mean Euclidean distance between two neighboring trajectories at the time moment *t* and d_0 is the initial separation between them at the starting moment. The correlation dimension is a measure of the complexity of a chaotic system giving the fractal dimension of its attractor. It can be calculated using the Grassberger-Procaccia algorithm [15]:

$$C(r) = \lim_{N \to \infty} \left(\frac{1}{N^2}\right) \sum_{i,j=1}^{N} \theta\left(\mathrm{r} - \lceil \mathrm{X_i} - \mathrm{X_j} \rceil\right) \quad (3),$$

where θ is the Heaviside step function: $\theta(x)=1$, for $x>0$, and $\theta(x)=0$, for $x<0$, $Xi\text{-}Xj$ is the separation distance between two points on the attractor, *i and j*. The Embedding dimension (*ED*) is the dimension of the state space, i.e. the number of states that are monitored at a particular moment in time [16]. Among the studies that reported successful analysis of biological systems with the theory of complex systems we mention those focused on chaos behavior in lung airways [17], complexity trends in perinatal growth [18], fractals in membrane changes in normal and pathological tissues [19]. The complexity of the EEG signal [20] has been studied by many authors in search of a new computational tool to describe the neural system and, ultimately, to gain access to the hidden causes of some pathological conditions. Some have focused on fractal dimension for the epileptic disorders [21], or in the encephalopathy [22], or in certain emotional states [23]. Similarly, the Lyapunov exponent was taken into account in the analysis of the complex EEG signal for patients with schizophrenia [24], or in superficial and deep anesthesia [25].

We next report the results of taVNS effect on attention indicator categories according to [26] and then some results of nonlinear dynamic analysis for single-channel EEG recordings with these semiquantitative tests to reveal the complexity of the neural system response to vagus nerve stimulation. The commercially available Chaos Data Analyzed software package was used.

2.4. The results of the brain waves measurement for various stimulation sessions

The reference point for the measurements was the normal active state, without a specific focus of activity. According to the readings of the BrainWave Visualizer software downloaded from the Neurosky website, the average meditation index was about 91 while the attention index around 34 which means less attention, this is normal since the meditation state requires a reduced state of alertness or attention.

The taVNS measurements were performed in two experimental designs: (i) stimulation with 5 Hz continuous electrical impulses for 20 minutes; (ii) stimulation for 20 minutes with 5 Hz trains of impulses (1 sec pause between each two trains of impulses), with respect to the reference point.

In Fig. 4 it is shown that for 5 Hz continuous taVNS the brainwave intensities decreased compared to the reference state (no taVNS), but in different amounts, leading to an increase in the attention index of 82 while for the reference state it was 34.

This result was obtained via the proprietary computational algorithm, eSense (NeuroSky). After 5 Hz burst stimulation, because along with the decrease in high alpha waves, there was a high increase in beta, gamma, delta and theta waves (two-three times) (Fig. 4), a higher attention index was obtained, A.I.=97 (high focus), and a lower index of meditation (calmness), M.I. of 48 (Fig. 5).

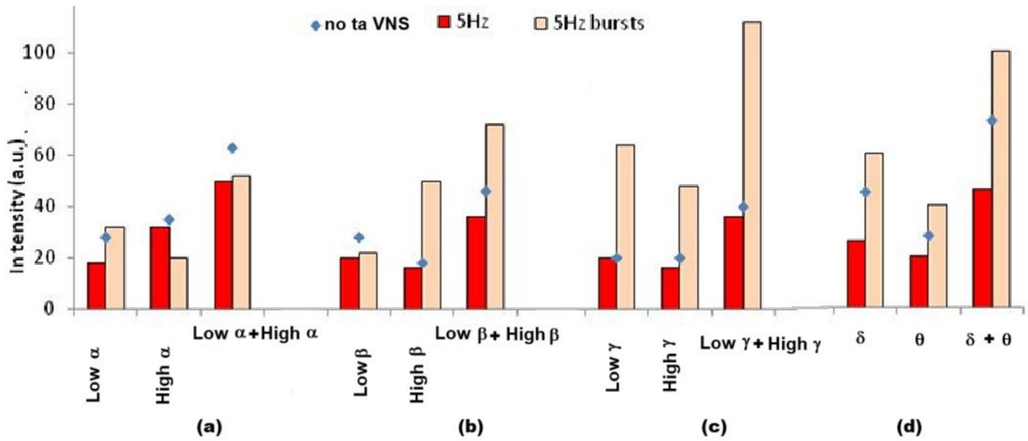


Fig.4. The brain wave intensities: (a) the alpha waves; (b) the beta waves; (c) the gamma waves; (d) the delta and theta waves

The attention index is the expression of active concentration (focus), while the meditation index provides the capacity for passive observation (calmness).

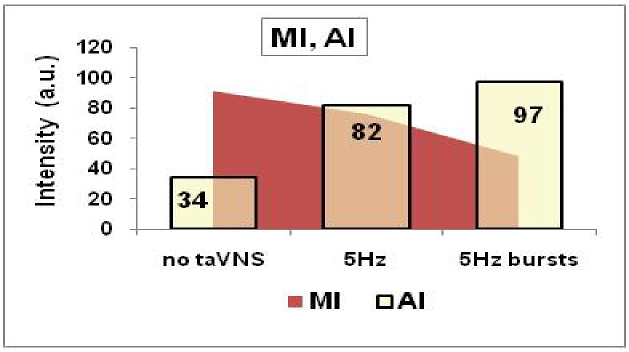


Fig. 5.The effect of taVNS on Meditation Index and Attention Index

The attention and meditation indexes are not direct band ratios; they are computed by a proprietary algorithm inside the ThinkGear chip. NeuroSky has not published the exact formula. However, according to the official support article described in [12], attention correlates most strongly with beta activity (alert, focused) and inversely with delta/theta (drowsiness) while meditation correlates with alpha and theta activity (relaxed, calm) and inversely with high beta (mental effort, stress). According to MindWave User Guide [27] each index is scaled into a range 0–100, with ~40–60 being “baseline,” below 40 “low,” and above 60 “high.”

The authors of [28] used NeuroSky to measure meditation/attention and describe using EEG bands, especially beta and alpha, in the context of educational measurement, in [29] a related research project using NeuroSky sensors focused on the recording of attention and meditation levels while students learn: good correlation was demonstrated between NeuroSky attention data and (d2) standard neuropsychologic attention test [30].

The validity of the adequacy of the recording and analysis system used is supported by various bibliographical references, of which we mention a few:

Sabio *et al*., (2024) [31] demonstrated that the second most widely used EEG device for research is the NeuroSky MindWave, while Johnstone *et al.* [32] found very little difference in signal quality between a NeuroSky MindWave and a Nuamps Neuroscan, implying its validity as a capture and analysis system.

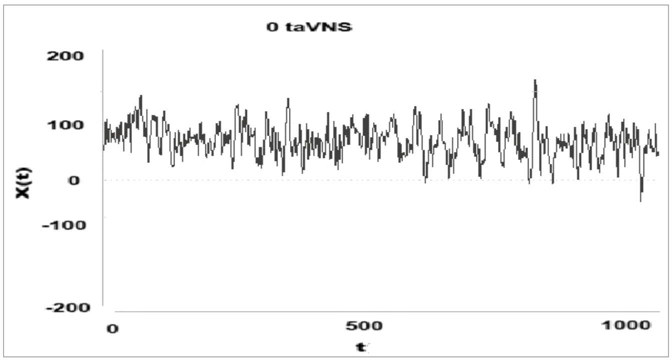
Rogers *et al.* [33] found that the NeuroSky MindWave EEG device can help predict functional outcomes after stroke and used it to determine EEG patterns associated with transient ischemic attack [34] and to distinct EEG profiles for patients who had suffered a transient ischemic attack or ischemic stroke [35].

Rieiro *et al.* [36] compared the NeuroSky MindWave to a medical-grade ambulatory device with gold electrodes and found remarkable agreement between the signals, with the NeuroSky providing stable recordings for both short and long periods of time. Azunny *et al.* [37] used NeuroSky MindWave to study the relationship between states of attention and meditation, demonstrating that meditation improves attention and working memory.

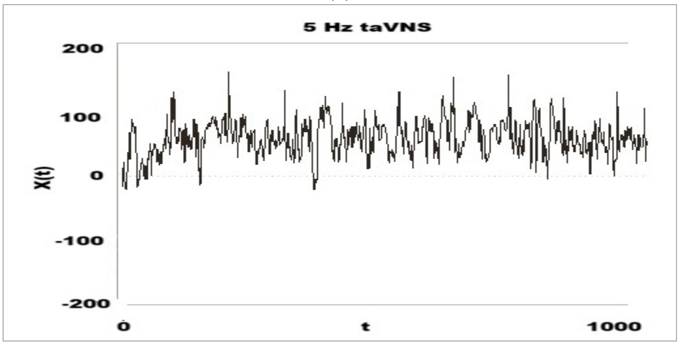
3. The computational analysis results

We present the graphical representation of EEG recorded data (Fig. 6a–c) and the associated attractors in Fig.7a–c.

Comparing the presented EEG signals only allows qualitative observation of their general shape, which seems to show an accentuation of the amplitudes of EEG signal variations after the application of taVNS, without any distinct periodicity or irregularity appearing. EEG recordings to observe the effects of taVNS on attention and some parameters of nonlinear brain wave dynamics were performed under normal conditions, but the influence of some disturbing environmental factors, which could have appeared as signal distortions, was not identified. Delimiting the size of the data series was necessary to enable the application of CDA algorithms. The EEG signals corresponding to taVNS treatment were recorded after 20 min of brain stimulation.



(a)



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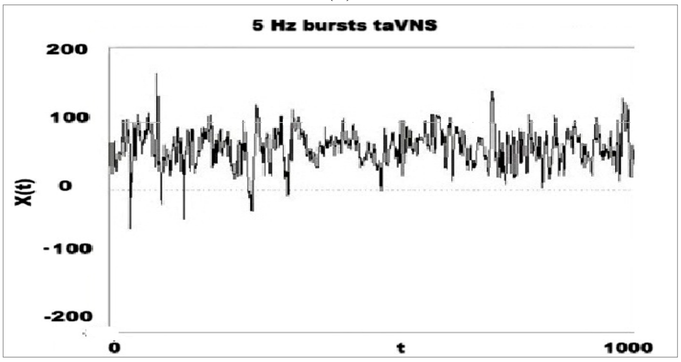
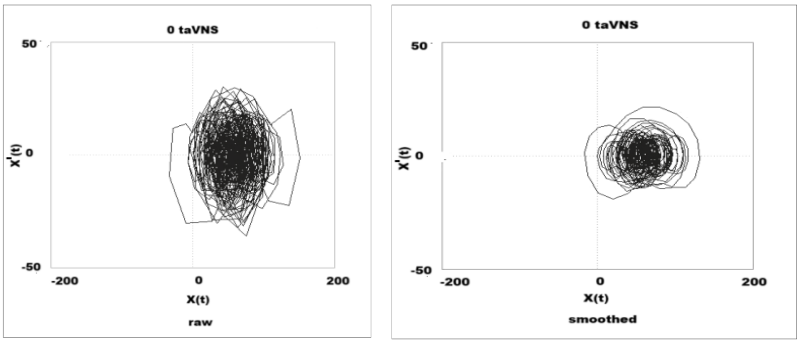


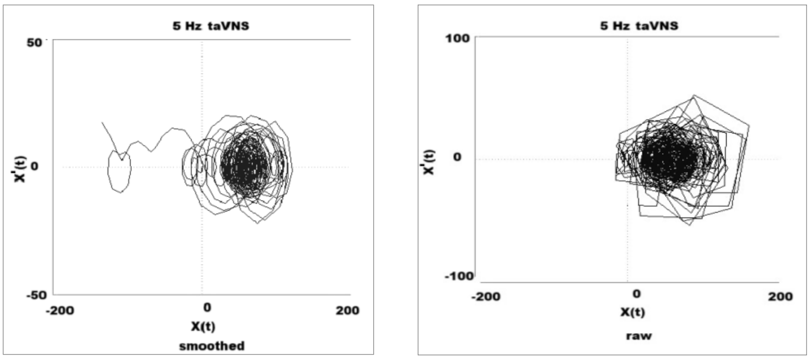
(c)

Fig. 6. The EEG data series for: (a) no taVNS stimulation; (b) taVNS continuous 5 Hz; (c) 5 Hz bursts taVNS

They can be shortly described as having typical form, of irregular variations, with no distinct periodicity which is the main challenge in computational approach but we do not overlook the fact that remote encephalographic recordings may exhibit artifacts due to either environmental noise or to involuntary blinking or interference with the ECG signal, and even the baseline may be affected.



(a)



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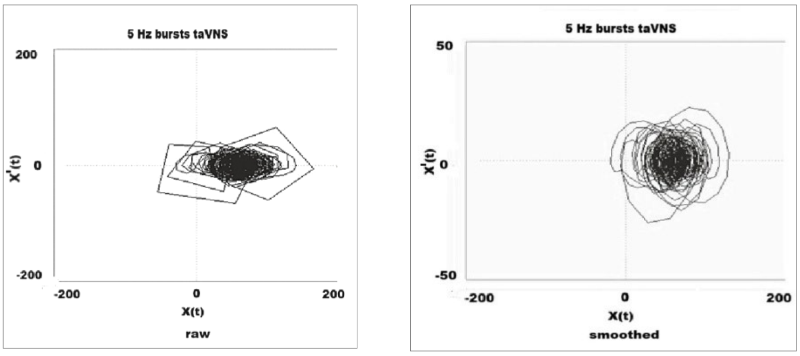


(c)

Fig. 7. The EEG attractors for: (a) no taVNS; (b) 5 Hz continuous taVNS; (c) 5 Hz bursts taVNS

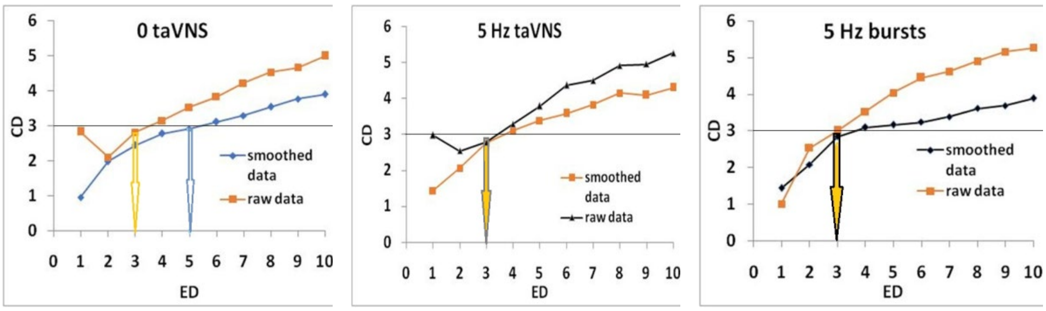
We worked with no signal pre-processing and thus the base line appeared shifted [38]. It can be seen that the attractors are placed in smaller value ranges after smoothing the data. In the absence of taVNS, the value range is not significantly reduced (Fig. 7a), but after 5 Hz stimulation (Fig. 7b) the attractor can be placed between the values of -50 and +50 after smoothing, compared to -100 and +100 for the raw data. After 5 Hz burst stimulation the attractor range is narrowed by smoothing from -200 and +200 to -50 and +50 (Fig. 7c).

To get a semiquantitative insight in the neural system dynamics we present the results of the fractal dimension estimation by means of *CD* – the correlation dimension (Figs. 8 a – c) for raw as well as for smoothed data (every value being replaced with the average between itself and the two neighbor data).

Numerical smoothing of the data series was done by replacing each value with the average between it and its nearest neighbors. The procedure is practiced to reduce the recording noise inherent to any recording but can also diminish some variations/fluctuations intrinsic to the investigated system. Numerical smoothing was applied to study whether the responses to nonlinear dynamics tests are modified in the sense of highlighting clearer influences of taVNS on the EEG signal.

According to theoretical background [15] for a reliable *CD* value of the correlation dimension of an attractor related to a data series, certain relationship must be met with the number of data, *N*. This is: $N \sim 10^{CD}$. For example, for $N=10^4$ the reliable *CD* is up to 4 while for $N=10^3$ the reliable *CD* should be no more than 3. And, according to the methodology related to CDA, if a saturation value of the *CD(ED)* graph can be identified, then the corresponding *CD* is also an expression of the fractal dimension of the strange attractor of the system.

In the case of our data series taken into analysis (*N*=1000) we look for *CD* with value ≤ 3, which is obtained in the absence of taVNS (reference state) for *ED* ≤ 3 for the primary data and *ED*≤ 5 for the smoothed ones (Fig. 8 a). Also for taVNS (Fig. 8 b, c) *CD* ≤ 3 is corresponding to *ED*≤ 3.



(a) (b) (c)

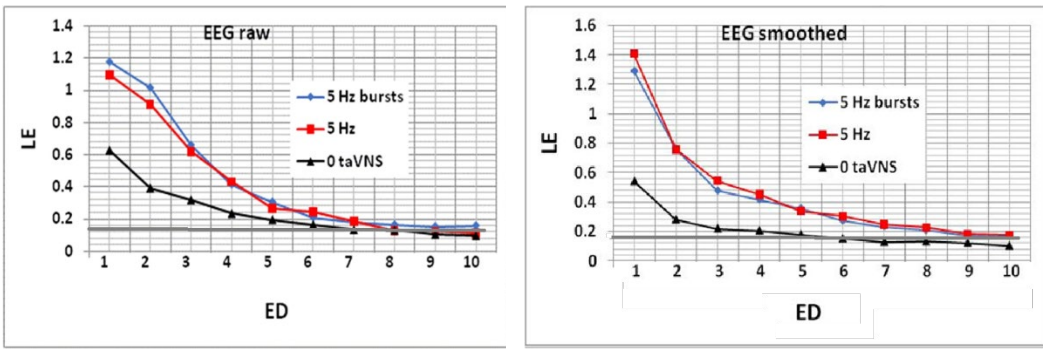
Fig. 8. The correlation dimension (CD) versus the embedding dimension (ED) for the EEG signal: (a) no taVNS stimulation; (b) taVNS continuous 5 Hz: (c) taVNS 5 Hz bursts

In the absence of saturation there could be no equivalence between this reliable *CD* and the true fractal dimension of the system.

The EEG signal having a remarkable complexity, at this point of the presented analysis we can only say that the hidden determinism behind the nonlinear dynamics of the recordings made by us cannot be but partially revealed by means of a single applied computational test.

In Fig. 9 a–c the results of Lyapunov exponent obtained for the studied data series can be seen. The *LE* exponent decreases with increasing *ED* (Fig. 9), as in the case of noisy or small-sized data series, but, according to the theory [39], it tends to stabilize for *ED* ≥ the actual size of the attractor. In [40], the decrease of *LE* for *ED* between 1 and 10 was demonstrated for the movement of atmospheric air masses in the case of a cyclone, the decrease reaching a value of *ED* considered representative for the respective system analyzed.

We analyzed the Lyapunov exponent looking for saturation tendency and for its values for *ED* at which *CD* satisfies Procaccia's condition [15]. The stabilization of *LE* is observed at approximately the same value of 0.18 for both the raw and smoothed data (Fig. 9) in all analyzed cases. For *ED*=3 that fulfills the Procaccia's condition (*CD*=3) in the raw data in the absence of taVNS, the Lyapunov exponent (Fig. 9) has the value 0.318 and for the smoothed signal, for *ED*=5 (for which *CD*=3), *LE* is equal to 0.181 which is along the saturation level.



(a) (b)

Fig. 9. The Lyapunov exponent (*LE*) versus the embedding dimension (ED) for the analyzed EEG data: (a) raw data; (b) smoothed data; the grey line marks the level of values saturation

For 5 Hz continuous taVNS, for *ED*=3 (corresponding to *CD*=3) we have the Lyapunov exponent of 0.62 and 0.545 (Fig. 9) for the raw and smoothed signal, respectively, which denotes that the complexity of the system has increased because the divergence of the trajectory is higher before saturation, for the application of taVNS.

Also, for 5 Hz bursts of stimuli, the Lyapunov exponent is 0.658 for the raw EEG data and 0.478 for the smoothed ones (Fig. 9 c), corresponding to *ED*=3 that satisfies Procaccia's condition for *CD*, according to the data series size of 1000.

Thus, the application of taVNS leads to the highlighting of the value *CD*=3 as being in a first approximation the reliable value of the system attractor size for raw data but also for the smoothed ones, as well as for the raw data corresponding to the reference state with no taVNS and the value of 0.18 giving a representative *LE*.

4. Conclusions

We presented a demonstration of the influence of non-invasively applied electrical stimuli on brain waves. The stimulation system, designed for trans-auricular application to the local endings of the vagus nerve and used in combination with a remote single channel EEG device, wirelessly captured the brain response, which was analyzed with the NeuroSky system, showing the influence of taVNS on attention and calmness. The attention indicator, derived from the intensities of alpha, beta, gamma, delta and theta waves, showed increased values for both 5 Hz biphasic stimuli applied continuously and as bursts, demonstrating the potential of the taVNS method to improve the state of active concentration. Through computational analysis of EEG signals based on the calculation algorithms in the CDA software, it was shown that the reliable correlation dimension is 3, for values of the embedding dimension below 3.

The Lyapunov exponent presented progressive decreases starting from significantly higher values in the case of taVNS application than for the reference state (no taVNS) with stabilization at the same plateau, of a positive value of approximately 0.18, which shows the sensitivity to the initial conditions, specific to the complex character, of the nonlinear, chaotic dynamics of the brain wave patterns. The demonstration can be the basis of a practical laboratory lesson for neuroscience students through the simplicity and accessibility of applied physics concepts related to the influence of electrical stimuli on brain wave paths. New studies are planned to analyze each type of brain waves and to establish the optimal stimulation parameters and the long-term efficacy of this non-invasive system as a promising therapeutic approach.

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