

## Rapid Communication

# Multifractal Analysis of Heart Rate Variability in Subjects Affected from Dysfunction of Autonomic Nervous System in Anxiety and Depression and Treated by Transcutaneous Vagus Nerve Stimulation

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## Introduction

Heart Rate Variability (HRV) is used to quantify activity of the Autonomic Nervous System. Cardiac rhythm is modulated by the two components of (ANS), the sympathetic and parasympathetic systems. Sympathetic dominance happens during stressful conditions and psychological and psychiatric disorders, whereas the vagal modulation induces normal heart rate dynamics and the correct its intrinsic variability. Consequently, Heart Rate Variability analysis (HRV) enables the study of autonomic influence as well as the effects of a number of psychological and psychiatric disorders. From a clinical point of view, the treatment of such mentioned psychological disorders requires often the continued use of drugs quite often coupled to psychotherapy. The use of alternative clinical approach is of importance especially in the several cases in which patients evidence conditions having pharmacologically resistance. A new non-invasive neurostimulating procedure, called transcutaneous Vagus Nerve Stimulation (tVNS) has been developed. The details of the applications are reported in [1].

First the subject applies a topical cream that has been designed to induce relax by counteracting adrenaline. The proprietary formula is only available in the NuCalm system and includes structured, nutrient-sourced building blocks that rapidly create a natural relaxation response. The treatment continues by applying tVNS and

## Abstract

A diminishing or disrupting fractal/multifractal structure of HRV is consistently reported as related to a serious ANS dysfunction that of course we study in several psychological and psychiatric disorders. We observed a net improvement in the multifractal HRV structure of such subjects during the transcutaneous Vagus Nerve Stimulation.

**Keywords:** Depression; Anxiety; Stress; Transcutaneous vagus nerve stimulation; Neuromodulation; Heart rate variability; Multifractals

noise-dampening headphones with binaural beats used to bring brain to synchronize at proper frequency bands in the interval (12Hz -4Hz). The whole treatment uses light-blocking eye masks with the obvious meaning to reduce perceptive effects enhancing alpha and related relaxing bands. Since it is intuitive that the use of a such combined procedure may produce only positive treatment effects, there is to agree on the evident benefit to use the mentioned cream as well as to add brain entrainment synchronizing in the frequency bands (4-12 Hz), it remains the basic interest to study the tVNS device from one hand under its technical profile and when applied to subjects having the above mentioned psychological disorders. We performed our studies by using the tVNS NuCalm device on subjects affected from anxiety or depressions. The study was performed on subjects having a serious ANS dysfunction as evidenced by our HRV analysis and examining the effect on the ANS of the Nu-Calm treatment for thirty minutes. During and after the tVNS treatment, the considered subjects evidenced a net improvement in ANS as indicated by multifractal analysis of HRV.

## Materials and Methods

The multifractal structure of the device is reported in [1]. Soon after we proceeded examining 20 subjects affected from anxiety and 20 subjects affected from depression. We examined subjects all having ages between 25 and 45. All the subjects gave their written

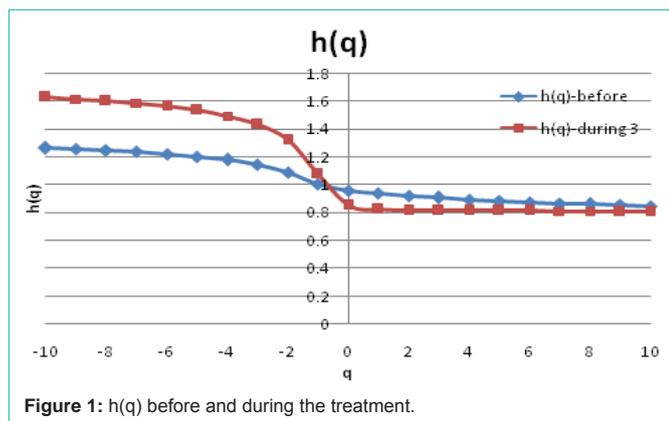


Figure 1: h(q) before and during the treatment.

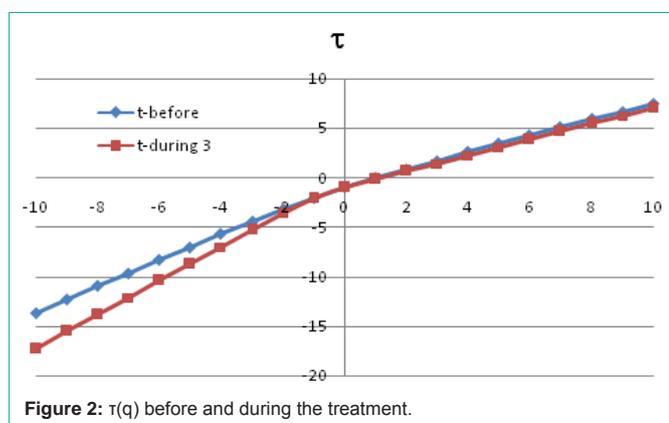


Figure 2: τ(q) before and during the treatment.

informed consent. According to the 1996 Task Force Standards of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, we selected the subjects excluding a priori those affected from well established other pathologies as we fixed in detail in [2]. To test the subjects each potential participant was given a non-structured interview following the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM). Participants selected for the study showed symptomatology of anxiety or depression. Those selected were divided into two groups and administered tests to evaluate the level of their anxiety and depression symptoms. The scales used to measure their scores were, respectively, the Hamilton Anxiety Scale (HAM-A) and the Hamilton Depression Scale (HAM-D). Both such tests were administered and showed medium scores, with HAM-A at 42 and HAM-D at 18. In this manner we selected a group of subjects whose scores representing a sample symptomatology both for anxiety and for depression. The obtained tachograms were recorded by finger Plethysmography (PG) and each time were compared to those obtained by ECG, accounting for Pulse Wave Transit Time (PWTT)

The t-VNS device was used applying gel electrode patches near the right and left ear lobes, and setting the current value at 0.1 mA. The PG recording of five minutes was performed without tVNS. Then the PG recording was extended for 30 minutes with the subject under stimulation. This scheme enabled us to estimate HRV before and during the tVNS.

## Results

The data were subsequently analyzed by the MF-DFA-1-D.

Here we have the results (Figure 1-4).

The results of the multifractal analysis are as it follows:

$$\Delta\alpha = \alpha_{\max} - \alpha_{\min} = 0.506 \pm 0.06$$

before the treatment and

$$\Delta\alpha = \alpha_{\max} - \alpha_{\min} = 0.919 \pm 0.102$$

during the treatment.

$$\Delta f = f(\alpha_{\max}) - f(\alpha_{\min}) = 0.231 \pm 0.027$$

before the treatment and

$$\Delta f = f(\alpha_{\max}) - f(\alpha_{\min}) = 0.774 \pm 0.090$$

during the treatment.

## Discussion

For a detailed discussion on fractals and multifractals see the [1]. The salient feature that relates the finality of our paper is that in recent years multifractal structure has been identified in heart rate dynamics and HRV that are actually the basic objects of the present paper [3-5].

The approach is that the pathology usually reduces or can disrupt this multifractal dynamics resulting in the alteration of its fractal properties. The MFDFA-1-D method that we have used, was first conceived by Kantelhardt et al [4].

## Conclusion

The conclusion is that in the clinical context HRV multifractal analysis assumes large importance since a diminishing or disrupting

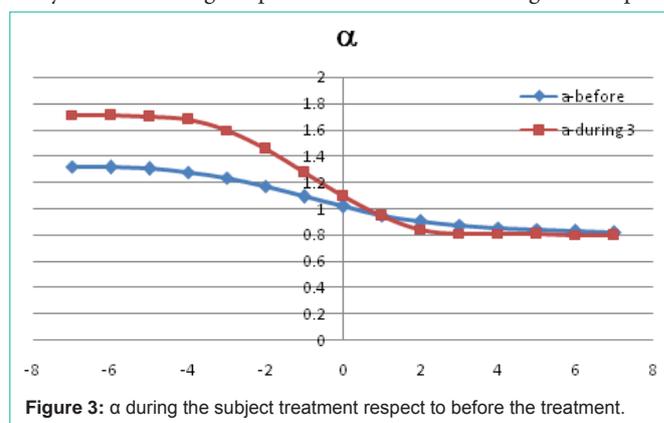


Figure 3: α during the subject treatment respect to before the treatment.

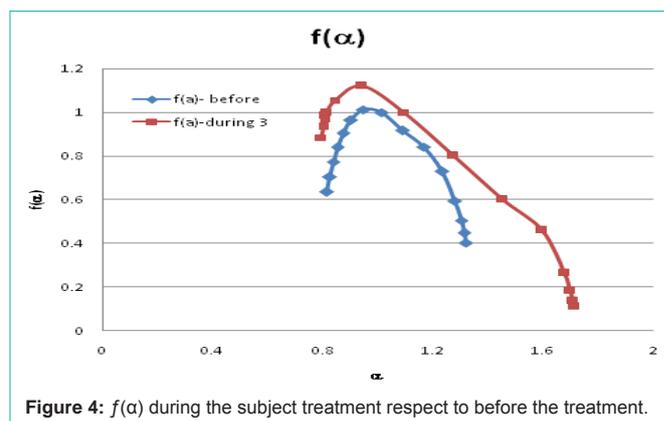


Figure 4: f(α) during the subject treatment respect to before the treatment.

multifractal HRV regime, is consistently reported as related to a serious ANS dysfunction. This is to say that different factors influence HRV scale-free dynamics, and in such context, the potential contribution of the Central Nervous System (CNS) cannot be ignored. On the other hand the Sympathetic (SNS) and Parasympathetic (PNS) branches of the Autonomic Nervous System (ANS) realize a complex interaction between SNS and PNS that requires advanced investigation. The results given in (Figures 1-4) indicate that we had a net improvement for  $h(q)$ ,  $\alpha$  and  $f(\alpha)$  during the subject treatment respect to before the treatment. This happens particularly in the regions of small fluctuations ( $q < 0$ ). The values of  $\Delta\alpha$  and  $\Delta f$  clearly indicate that the tVNS treatment induced a net improvement in the HRV of such subjects.

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