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Investigation of the relationship between anxiety and heart rate variability in fibromyalgia: A new quantitative approach to evaluate anxiety level in fibromyalgia syndrome

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ABSTRACT

Background: Fibromyalgia syndrome (FMS) is identified by widespread musculoskeletal pain, sleep disturbance, nonrestorative sleep, fatigue, morning stiffness and anxiety. Anxiety is very common in Fibromyalgia and generally leads to a misdiagnosis. Self-rated Beck Anxiety Inventory (BAI) and doctor-rated Hamilton Anxiety Inventory (HAM-A) are frequently used by specialists to determine anxiety that accompanies fibromyalgia. However, these semi-quantitative anxiety tests are still subjective as the tests are scored using doctor-rated or self-rated scales.

Method: In this study, we investigated the relationship between heart rate variability (HRV) frequency subbands and anxiety tests. The study was conducted with 56 FMS patients and 34 healthy controls. BAI and HAM-A test scores were determined for each participant. ECG signals were then recruited and 71 HRV subbands were obtained from these ECG signals using Wavelet Packet Transform (WPT). The subbands and anxiety tests scores were analyzed and compared using multilayer perceptron neural networks (MLPNN).

Results: The results show that a HRV high frequency (HF) subband in the range of 0.15235 Hz to 0.40235 Hz, is correlated with BAI scores and another HRV HF subband, frequency range of 0.15235 Hz to 0.28907 Hz is correlated with HAM-A scores. The overall accuracy is 91.11% for HAM-A and 90% for BAI with MLPNN analysis.

Conclusion: Doctor-rated or self-rated anxiety tests should be supported with quantitative and more objective methods. Our results show that the HRV parameters will be able to support the anxiety tests in the clinical evaluation of fibromyalgia. In other words, HRV parameters can potentially be used as an auxiliary diagnostic method in conjunction with anxiety tests.

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1. Introduction

Fibromyalgia Syndrome (FMS) is a disorder characterized by widespread musculoskeletal pain accompanied by fatigue, sleep disturbance, anxiety and mood issues [1]. Paresthesia, cognitive difficulties, dizziness, weakness and a subjective feeling of swelling are also frequent symptoms of the disease. Another important characteristic feature of FMS is that of altering the sympathetic/parasympathetic balance immediately and completely. On the other hand, anxiety, which generally leads to a misdiagnosis, is very common in fibromyalgia and has been found to be related to the severity of pain in symptoms of FMS [2].

In many clinics, the Beck Anxiety Inventory (BAI) and Hamilton Anxiety (HAM-A) tests are both frequently used to determine anxiety level that accompanies fibromyalgia as well as to determine anxiety level in physiological and psychological disturbances. These are the most popular indicators currently used to evaluate the anxiety [3]. The BAI was developed by Beck and his colleagues in 1988 for determining the severity of anxiety [4]. Respondents indicate how much they have been affected by each symptom over the past week. It is composed of 21 questions and the responses are rated on a 4-point scale [5]. Each response is assigned a score ranging from zero (not at all bothered) to three (severely bothered), with a possible range of total scores from zero to 63. The value of the total score determines the person's anxiety level, with high scores indicating high anxiety levels. The HAM-A test is a psychological questionnaire originally published by Max Hamilton in 1959. It is a test composed of 14 questions, each with 5 possible responses, designed to rate anxiety severity [6–8]. It has a possible range of total scores from zero to 56. Total scores indicate the severity of the symptoms. Higher scores on both the BAI and HAM-A are found in patients with FMS than in the normal population.

The BAI is a self-rated test and simpler in comparison to HAM-A. The HAM-A is doctor rated test and it is scored during quite detailed interviews. Both are not gold standard tests, but they are also not unreliable. Validity and reliability studies of the BAI and HAM-A tests in Turkey were conducted by Ulusoy et al. in 1988 [9] and Yazıcı et al., respectively. [10]. However, both BAI [11] and HAM-A [6,12,13] tests are still questionable because of their subjectivity and do not represent gold standards. Therefore, these tests should be supported with quantitative and more objective methods in the clinical evaluation of fibromyalgia. Moreover, even though fibromyalgia has many symptoms, there is no specific physical examination finding or laboratory test to diagnose a patient with FMS so far. Actually, there are many different assessments available to diagnose the FMS; however, their reliabilities need to be improved. So, none of the current tests is definitive.

Heart Rate Variability (HRV) is an efficient tool for the assessment of autonomic balance in the human body [14,15]. On the other hand, psychological disturbances like anxiety are known to be closely related to disturbances of autonomic balance. This suggests that autonomic balance indicators, which are quantitative and more objective, may be used instead of BAI and HAM-A tests or may be used as an auxiliary diagnostic method in conjunction with these anxiety tests. Additionally, the reliability of these doctor- and self-rated tests may be evaluated with autonomic balance indicators. Due to the reasons mentioned above, it may be possible to determine if there is a correlation between HRV analysis and the BAI and HAM-A tests. Additionally, such a correlation could occur more noticeably in FMS patients.

HRV signals are analyzed using different signal processing methods such as time analysis, frequency analysis and nonlinear methods [16]. But, a possible correlation may be better observed in subband analysis, unlike the standard HRV method. Time-frequency analysis of HRV signals can be analyzed using wavelet analysis, which is a more efficient method of feature extraction at low frequencies [17,18]. We could not find any information examining this approach in the literature in the evaluation of anxiety level that accompanies fibromyalgia and FMS.

We used a Multi-Layer Perceptron Neural Network (MLPNN) for the analysis of relationship between anxiety that accompanies fibromyalgia and -HRV variables [19]. MLPNN is the popular feed forward artificial neural network model that has been playing a central role in applications of neural networks [20]. A back-propagation training algorithm is frequently used to train a MLPNN [21–23]. Levenberg–Marquardt (LM) backpropagation algorithm, the fastest backpropagation algorithm method, has been widely used for MLPNN training [24,25]. A MLPNN consists of more than one layer of nodes in a directed graph. Each one fully connected to the next layer. Each node works as a processing element with a nonlinear activation function other than the input nodes. Multi-Layer Perceptron (MLP) benefits from a supervised learning technique for the training part of the network [26,27].

In this study, we examined the relationship between semi-quantitative anxiety tests and HRV variables. We aimed to support anxiety tests with an electrophysiological signal according to identify the anxiety accompanying fibromyalgia syndrome using a more objective and quantitative measure. In other words, the main purpose of this study is the quantification or digitizing of the verbal anxiety test to measure the anxiety level more objectively. Because, the accuracy of the self-reported answers given by the patient's and specialist with current psychology is still questioned. Therefore, it needs to be confirmed by quantitative tests such an electrophysiological signal. For this purpose HRV signal is preferred. Because, HRV signals have shown potential as a quantitative test because both HRV signal and anxiety are associated with the autonomic nervous system. Therefore, we propose that HRV signal monitoring may present a new electrophysiological signal based auxiliary test support to the anxiety test to measure the patient's anxiety level in FMS. Thus, an electrophysiological signal may supplant the anxiety tests as a means of assessing anxiety levels.

We extracted the important characteristic features of HRV signal to understand the relationship between the anxiety tests and the electrophysiological signals by using Wavelet Packet Transform (WPT) which is more effective for HRV signals [15,17]. Therefore, the basebands are decomposed into subbands, these subbands are applied to the Multilayer Perceptron Neural Network (MLPNN) inputs, and it is evaluated with output values that contain BAI and HAM-A scores.

2. Materials and methods

2.1. Subjects

We received approval from the Suleyman Demirel University Clinical Research Ethics Committee for this study. The patients, included in the study following ethical committee approval, were selected from the patients who were applied to Suleyman Demirel University, Faculty of Medicine, Physical Therapy and Rehabilitation Department. Patient group ($n=56$) was formed patients diagnosed with FMS for the first time by specialists according to the 1990 American College of Rheumatology (ACR) criteria [28] and the other clinical assessments. A control group ($n=34$) of the study was formed by healthy volunteers who had visited the outpatient clinics of the same hospital for routine check-ups or were hospital employees; this control group was paired with the patient groups with respect to age and gender. The number of controls admitted to the clinic for check-up, was relatively lower than the number of patients. So, numbers of controls are limited