



## Investigating the effect of sympathetic skin response parameters on the psychological test scores in patients with fibromyalgia syndrome by using anns

Murat YILDIZ<sup>1\*</sup>, Özhan ÖZKAN<sup>1</sup>, Etem KÖKLÜKAYA<sup>1</sup>

<sup>1</sup>Sakarya Üniversitesi, Mühendislik Fakültesi, Elektrik Elektronik Mühendisliği, Sakarya

*09.09.2012 Geliş/Received, 04.02.2013 Kabul/Accepted*

### ÖZET

Bu çalışmada, Süleyman Demirel Üniversitesi, Tıp Fakültesi, Fiziksel Tıp ve Rehabilitasyon Bölümü'nde seçilen hasta ve sağlıklı deneklere Görsel Analog Ağrı Skalası, Verbal Ağrı Skalası, Beck Depresyon Envanteri, Beck Anksiyete Envanteri, Hamilton Depresyon Değerlendirme Skalası ve Hamilton Anksiyete Değerlendirme Skalası gibi psikolojik testler uygulandı ve skorları kaydedildi. Sempatik deri cevabı (SSR) ölçümlerinin yapılabilmesi için aynı bölüme bir ölçüm sistemi kuruldu. SSR ölçümleri yapıldı ve kaydedildi. Kaydedilen SSR verilerinden gecikme süresi, maksimum genlik ve iki uyartım arası geçen süre gibi parametreler, Matlab yazılımı kullanılarak hesaplandı. Analizde SSR parametre değerleri psikolojik test skorlarına eklendi ve yapay sinir ağıları kullanılarak fibromiyalji sendromu (FMS)'na ilişkin teşhis doğruluk yüzdeleri hesaplandı. Elde edilen benzetim sonuçları SSR'nin seçilen parametreleri ile FMS'nin ilişkili olduğunu ve SSR'nin FMS'de bir teşhis metodu olarak kullanılabileceğini göstermiştir.

**Anahtar Kelimeler:** Sempatik deri cevabı, fibromiyalji sendromu, YSA, fibromiyaljide psikolojik testler

## Fibromiyalji hastalarında sempatik deri cevabı parametrelerinin psikolojik test skorlarına etkisinin ysa kullanılarak incelenmesi

### ABSTRACT

In this study, psychological tests such as Visual Analogue Pain Scale, Verbal Pain Scale, Beck Depression Inventory, Beck Anxiety Inventory, Hamilton Depression Rating Scale and Hamilton Anxiety Scale were applied to the selected healthy subjects and patients with Fibromyalgia Syndrome (FMS) in Suleyman Demirel University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation and the scores were recorded. A measurement system was established in the same department of the university to measure the sympathetic skin response (SSR) from the subjects. The SSR was measured and recorded. The parameters such as latency time, maximum amplitude and the elapsed time were calculated by using Matlab software from the recorded SSR data. SSR parameters were added to the scores and diagnosis accuracy percentages of the FMS calculated by using artificial neural networks. Obtained results from the simulations showed that the specified parameters of the SSR and FMS were concerned and these parameters can be used as a diagnostic method in FMS.

**Keywords:** Sympathetic skin response, fibromyalgia syndrome, ANN, psychological tests in fibromyalgia

\* Sorumlu Yazar / Corresponding Author

## 1. INTRODUCTION

Fibromyalgia syndrome (FMS) whose symptoms are appeared as widespread body pains and fatigue is a chronic disease of the musculoskeletal system [1]. The most characteristic feature is widespread muscle pain. In this disease, beside complaints such as weakness, fatigue, disinclination and sleep disorders, there are important disease signs such as muscle function disorders, central nervous system disorders and the neuroendocrine system changes, immunological disorders and psychological factors [2,3]. The disease complaints increase with the seasonal changes, especially with cold weather. Patients with these complaints, because of the pain which can not be determined the origin, resort to various branches doctors and the various treatments are applied to these patients. However, because of the accurate diagnosis of the disease can not be done, specific treatment methods can not be applied to FMS. The complaints of pain usually ignored with pain relief medications. This method reduces the symptoms for certain time, but after a while the symptoms appear again.

FMS is a widespread disease generally seen in women. Cause of the disease is not fully known yet, but the autonomic nervous system is significantly affected by the disease [4]. Specific diagnosis of disease is only consists of found pain zones and applied psychological tests to the patient. However, FMS, associated with components of several parameters. One of the most important of these parameters is Sympathetic Skin Response (SSR) [5].

SSR is an electrophysiological method used in evaluation sympathetic sudomotor fibers function by using the skin resistance change. SSR is an instantaneous and nonpersistent change given by the internal and/or external stimulus in the electrical potential of the skin of palm and sole [5]. Studies shows that latency time obtained from SSR data of patients with FMS has been affected dysfunction in the autonomic nervous system [5,6]. FMS also significantly affects the autonomic nervous system, a relationship between the SSR and FMS is clear. Therefore, the use of SSR is very important in the classification of FMS. In addition, the subsequent studies in patients with the first symptoms of the disease - of boundary values -, even prior to the onset of serious clinical signs the relationships between autonomic nervous system dysfunction and SSR can be detected.

## 2. SYMPATHETIC SKIN RESPONSE

SSR which a part of electrical impedance of the body is defined by arising spontaneously depending on the body's internal dynamics or by means of a stimulus is applied externally to the body as a reflex that can occur

temporary electrical potential difference in the skin [5]. Although the SSR parameters that affect in the human body is unknown exactly in many studies, investigation the sympathetic nervous system function of SSR may be a non-invasive approach have been proposed [6-8]. Measurements of SSR is easy, but they are not be safe enough for diagnostic applications when valid procedures are taken into account and autonomic and sudomotor function disorders in particular are not found an absolute accuracy relationship between the obtained clinical findings and the measurements of SSR [7, 8]. Though SSR can be obtained easily and non-invasive, many problems are available in application because of variation in parameters such as latency time, maximum amplitude, the elapsed time. As a result of clinical trials the wave forms of the many parameters in the SSR content were found.

In some of the studies, it has been determined that changes were occurred in the SSR values in diseases that are affected the autonomic nervous system [8]. As a result of these investigations, it was concluded that obtained measurement values could be brought more clearly by using soft-computing techniques [6,9,10].

## 3. USED PARAMETERS IN SIMULATIONS

The SSR parameters such as latency time (LT), maximum amplitude (MAXG), elapsed time (TT) and psychological tests such as visual analogue pain scale (VAS), verbal pain scale (VRS), Beck depression scale (BDI), Beck anxiety scale (BAI), Hamilton depression rating scale (Ham-D) and Hamilton anxiety scale (HARS) are used as parameters in FMS classification. Brief descriptions of these parameters are given below. Obtained these SSR parameters and psychological test scores were used in classification as a feature.

### 3.1. SSR Parameters

**Latency time (LT):** Latency time is used to mean any delay from the start of the stimulus artifact to the first deflexion of SSR as shown in figure 1. Latency time also has the most significant results in SSR waveform analysis and interpretation.

**Maximum amplitude (MAXG):** The maximum amplitude value obtained from the SSR measurement is taken as maximum potential changes between two sequential stimulations.

**Elapsed time (TT):** It is the time between two sequential stimulations that applied to measure SSR.

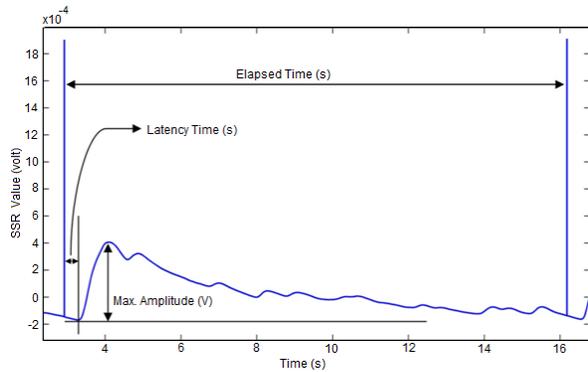


Figure 1: Sample SSR waveform

### 3.2. Psychological Test Scores

Visual Analogue Pain Scale (VAS) score: Widely used to assess the severity of pain, “0” value if no pain, “10” indicating that unbearable pain the value of 10 cm with the intensity scale is used [11].

Verbal pain scale (VRS) score: Widely used to assess the severity of pain, 0: no pain, 1: mild pain, 2: moderate pain, 3: severe pain, 4: unbearable pain. A likert-type scale is also used [12].

Beck Depression Inventory (BDI) score: It is an inventory measured the emotional, physical, cognitive and motivational symptoms in depression. It is assessed by a Likert-type scale and consists of 21 questions. Sum of the scores obtained from the answers of questions gives the Beck depression inventory score. Total score ranges from 0-63. The complains are evaluated as 0-13 points no depression, 14-24 points mild depressive symptoms, higher than 25 points intensive depressive symptoms [13].

Beck Anxiety Inventory (BAI) score: An inventory measures symptoms in the anxiety. It is evaluated by a Likert-type scale and consists of 21 questions. Sum of the scores obtained from the answers of questions gives the Beck Anxiety Inventory score. Total score ranges from 0-63. The higher the total score shows the higher person's anxiety level [14].

Hamilton Anxiety Rating Scale (HARS): It is a test consists of 14 question and interrogated mental and physical symptoms. A total score is obtained between 0-56 points with 5 item Likert-type scale [15].

Hamilton Depression Rating Scale (Ham-D) score: One of the scales is commonly used to determine the severity of depressive symptoms. In the evaluation of 17 questions version of the test the interviewer assesses the patient by using the structured interview guide and obtain

a score from 0-53 points. According to the obtained total score is graded as <13: mild, 13-17: normal, > 17: severe depression [16].

## 4. MATERIALS AND METHODS

Database used in this study were recorded in Suleyman Demirel University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation. Database was consisted of psychological test scores and SSR measurements that were measured from 29 healthy subjects and 57 patients who were diagnosed with FMS according to the 1990 ACR criteria [17]. When measurements are taken, it has been noted that the subjects are lying on his/her back and in comfortable as possible. The ambient of taken measurement is far from the noise and electromagnetic environment. Before the SSR measurements were obtained, some parameters of the subjects which are more effective on SSR (height, weight, age) were chosen between the specific limits [18]. In the study, the measurements were taken of care to stay the subjects' age, height and weight within these limits. The boundaries of subjects and the mean of these features are given in Table 1.

Table 1: Physical characteristics of subjects for patients and controls

|          | Number | Age  | Weight | Height |
|----------|--------|------|--------|--------|
| Patients | 57     | 45.5 | 72.3   | 161.1  |
| Controls | 29     | 42.8 | 69.6   | 158.3  |

Specified parameters of SSR were recorded from subjects by using the measurement system consisted of AD Instruments ML870/P PowerLab8/30, AD Instruments PowerLab ML116 GSR Amplifier, AD Instruments MLT116P GSR finger electrodes and stimulator within 12m2 indoor area. Grounding of the system was restructured to eliminate the noise factor. Records were transferred to the computer via Lab Chart Pro software.

For stimulation, 20µA of current was passed through the FMS patients and healthy subjects by electrodes, temporary potential changes as the response of this current on the skin were measured and recorded. Data analysis was performed using MATLAB® to determine the latency time, maximum amplitude and elapsed time between two stimulations.

## 5. ARTIFICIAL NEURAL NETWORKS

A multi-layer feed-forward neural network (MLFFNN) was used in this study. It consists of three basic layers such as input layer, hidden layer and output layer. A layer's input is the output of the previous layer. Input layer forward the input data to hidden layer without any

change. The data is processed only in the hidden layer and output layer. The mission of input layer is only multiplexing the input. When the structure of ANN is created typically one or two hidden layers are sufficient. This type of ANNs works according to supervised learning strategy and back propagation learning algorithm is used efficiently in training of these networks. Therefore, these networks also referred to as back propagation networks. Operating procedures of this type network involve the following steps in generally.

**Collecting Samples:** Samples are collected for the training set and test set. During the network training, only training data are given to ANN. Thus, the learning process of the network is provided. After learning process is done the network performance is measured by giving test data to the network. 100% of the training results to be consistent in terms of training are important.

- **Determining Topological Structure of the Network:** The numbers of input unit, hidden layers and neurons in layers are determined in this section.

- **Determining the training parameters:** Parameters such as learning coefficient of the network, the momentum coefficient, collecting and activation functions is determined.

- **Training Stage:** The test data is given to the network. The network output corresponds to the given data to Hidden and output layer is calculated. Until the expected output value reaches to the acceptable error rate, training is continued by updating the weight of the layers. The weights updating process is done in accordance with the selected learning rule. Training is completed by calculating the output with an acceptable error.

- **Test Stage:** After training the network, the network performance is measured with test data is not given previously [19].

MLFFNN network which includes an input layer consisting of 17 neurons and an output layer consisting of one neuron was used in this study. Tansig activation function was preferred in the hidden layer and purelin linear activation function was preferred in the output layer. The better results were obtained when between 20 and 40 neurons used in the hidden layer. The best result was obtained when used 35 neurons. A single output is seen as “0” for diseased subjects input and “1” for healthy subjects input at the exit part. "Levenberg-Marquardt (LM)" learning algorithm was chosen as the learning algorithm.

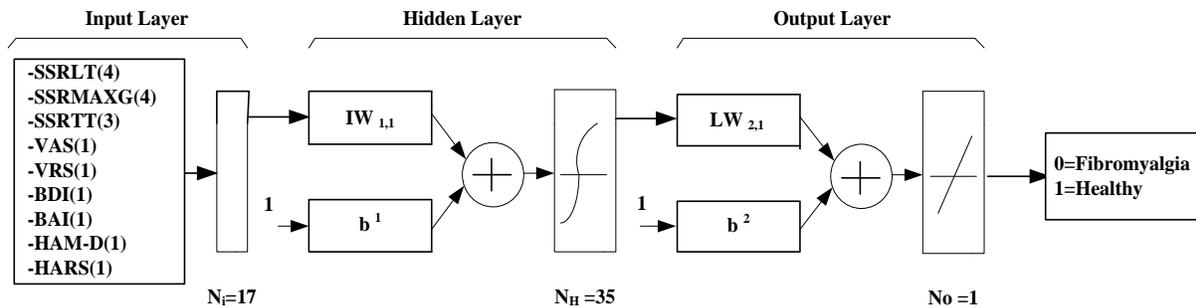


Figure 2: MLFFNN for SSR associated with the psychological test scores

## 6. SIMULATION RESULTS

Flow chart of this study was shown in Figure 3 and the artificial neural network model was shown in Figure 4. In the input layer, nine features which contain three features of SSR and six features of psychological tests were used as inputs.

42 of 57 FMS subjects were chosen to participate in experiment one that its results to be used as the training data, remaining 15 reserved for testing procedure and 22 of 29 control subjects were chosen to participate in experiment one that its results to be used as the training data, remaining 7 reserved for testing procedure.

The goal was 10<sup>-6</sup> for a mean squared error. Levenberg-Marquardt Algorithms reached the goal at 6 epochs as seen figure 4.

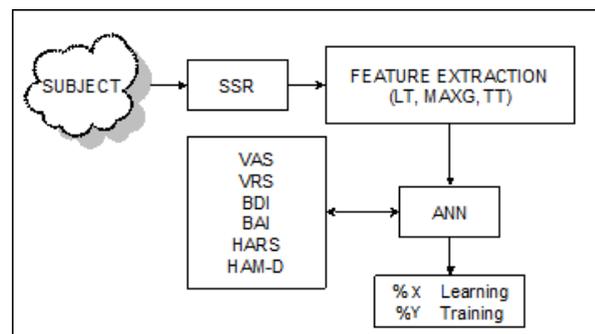


Figure 3: Flow chart of the study

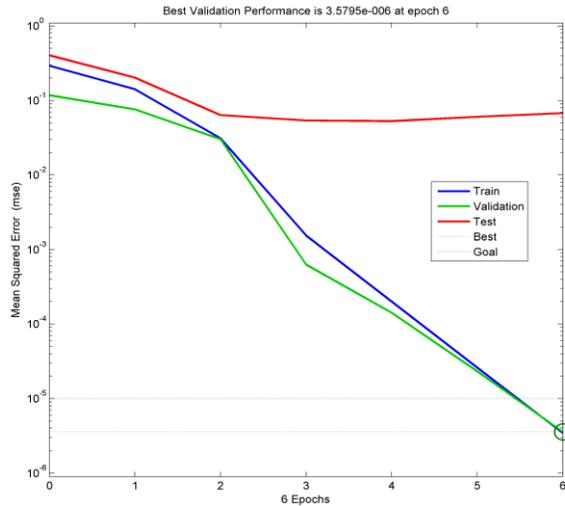


Figure 4. Training with Trainlm

Table 2. Training and test simulation results

|         | Training  |           |              | Test      |          |              |
|---------|-----------|-----------|--------------|-----------|----------|--------------|
|         | Patient   | Control   | Accuracy (%) | Patient   | Control  | Accuracy (%) |
| Patient | <b>42</b> | <b>0</b>  | <b>100</b>   | <b>14</b> | <b>1</b> | <b>92,86</b> |
| Control | <b>0</b>  | <b>22</b> | <b>100</b>   | <b>0</b>  | <b>7</b> | <b>100</b>   |
| Average |           |           | <b>100</b>   |           |          | <b>95</b>    |

## 7. CONCLUSION

The aim of this study was to investigate the effect of SSR parameters to the psychological test scores in FMS patients. In this context, values of the SSR parameters were added to the psychological test scores. Diagnosis accuracy percentages of subjects calculated by using ANN and 100% success was achieved in the training data, while 95% success was achieved in the test data. Consequently, accuracy percentages achieved in the validity of SSR analysis in classification of FMS.

If the study is analyzed from the medical aspects, VAS scores were obtained between 6 and 8 in FMS patients. But they were obtained between 0 and 5 in control subjects. On the other hand, VRS scores were obtained between 2 (moderate pain) and 4 (unbearable pain) in patients, while 0 (no pain) - 2 (moderate pain) were obtained from the control subjects. 12 of the FMS patients had no depression by looking at the BDI scores. One of the control subjects might have depression according to the BDI scores. According to the obtained psychological test scores, HAM-D supported the BDI in terms of depression status. Anxiety levels of the FMS patients were not too high but anxiety predispositions of them were higher than the control subjects according to the BAI and HARS scores.

The best accuracy percentages of data obtained from results of the ANN by testing and training are given in Table 2. Accordingly, data of 42 patients and 22 healthy subjects used in training were trained with 100% accuracy. Output of 14 patients data used for testing was calculated correctly. However, output for one patient data was calculated incorrectly and they were recorded as healthy. 92.86% accuracy percentage was calculated in testing of the patient parameters by using ANN. On the other hand, the output for all of the data, used for testing and obtained from healthy subjects, was calculated as target value "1" and one hundred percent accuracy percentage was reached. Generally, 100% accuracy percentage was calculated in training of 86 parameter values. 95% accuracy percentages were calculated in testing of the same values.

In future researches related to this study, correlation between the effect of physiological factors such as heart rate, skin temperature and respiration rate on FMS and SSR appears as further research topics.

## 8. ACKNOWLEDGEMENTS

This research was supported by The Scientific and Technical Research Council of Turkey (TUBITAK) through The Research Support Programs Directorate (ARDEB) with project number of 108E036 and by The Coordination Unit of Scientific Research Projects of Sakarya University.

## REFERENCES

- [1] Krypel L.L., "Fibromyalgia: A Review of Its Pathophysiology and Drug Treatment", *Journal of Pharmacy Practice*, 22(1):6-16, Feb 2009.
- [2] Eisinger J., "Dysautonomia, fibromyalgia and reflex dystrophy", *Arthritis Research & Therapy*, 9(4):105, 2007.
- [3] Fietta P., Fietta P., Manganelli P., "Fibromyalgia and psychiatric disorders", *Acta Biomed.*, 78(2):88-95, Aug. 2007.
- [4] Martinez-Lavin, M., "Biology and therapy of fibromyalgia. Stress, the stress response system, and

fibromyalgia”, *Arthritis Research & Therapy*, 9(4):216, 2007.

[5] Toyukara, M., “Sympathetic skin responses: the influence of electrical stimulus intensity and habituation on the waveform”, *Clinical Autonomic Research*, 16(2):130-135, 2006.

[6] Özkan Ö., Yıldız M., Köklükaya E., “The Correlation Of Laboratory Tests And Sympathetic Skin Response Parameters By Using Artificial Neural Networks In Fibromyalgia Patients”, *Journal of Medical Systems*, 36(3):1841-1848, June 2012.

[7] Ahuja N.D., Agarwal A.K., Mahajan N.M., Mehta N.H., Kapadia H.N., “GSR and HRV:Its Application in Clinical Diagnosis”, *Computer-Based Medical Systems*, 2003, Proceedings, 16th IEEE Symposium, 279-283, India, 26-27 June 2003,.

[8] Martinez-Lavin, M., Vargas, A., “Complex adaptive systems allostasis in fibromyalgia”, *Rheumatic Disease Clinics of North America*, 35(2):285-298, July 2009.

[9] Özkan, Ö., Yıldız, M., Bilgin, S., Köklükaya, E., “Measuring the Sympathetic Skin Response on Body and Using as Diagnosis-Purposed for Lung Cancer Patients by Artificial Neural Networks”, *Journal of Medical Systems*, 34(3):407-412, June 2010.

[10] Özkan, Ö., Yıldız, M., Köklükaya, E., “Fibromiyalji sendromunun teşhisinde kullanılan laboratuvar testlerinin sempatik deri cevabı parametreleriyle desteklenerek teşhis doğruluğunun artırılması”, *Sakarya Üniversitesi Fen Bilimleri Enstitüsü Dergisi*, 15(1): 1-7, Haziran 2011.

[11] Ries, A.L., Bauldoff, G.S., Carlin, B.W., Casaburi, R., Emery, C.F., Mahler, D.A., Make, B., Rochester, C.L., Zuwallack, R., Herrerias, C., “Pulmonary rehabilitation: Joint ACCP/AACVPR evidence based guidelines”, *Chest*, 131(5):4-42, May 2007.

[12] Perez-Higueras, A., Alvarez, L., Rossi, R., Quinones, D., Al-Assir, I., “Percutaneous vertebroplasty: Long term clinical and radiological outcome”, *Interventional Neuroradiology*, 44(11):950-954, 2002.

[13] Çakır, T., Evcik, D., DüNDAR, Ü., Yiğit, İ., Kavuncu, V., “Evaluation of sympathetic skin response and F-wave in fibromyalgia syndrome patients”, *Turkish Journal of Rheumatology*, 26(1):38-43, 2011.

[14] Ulusoy M., Şahin N.H., Erkmén H., “Turkish version of the Beck Anxiety Inventory: Psychometric properties”, *Journal of Cognitive Psychotherapy*, 12(2):163-172, 1998

[15] Shear, M.K., Bilt, J.V., Rucci, P., Endicott, J., Lydiard, B., Otto, M.W., Pollack, M.H., Chandler, L., Williams, J., Ali, A., Frank, D.M., “Reliability and validity of a structured interview guide for the Hamilton Anxiety Rating Scale (SIGH-A)”, *Depression and Anxiety*, 13(4):166-178, 2001.

[16] Aben, I., Verhey, F., Lousberg, R., Lodder, J., Honig, A., “Validity of the Beck depression inventory,

hospital anxiety and depression scale, SCL-90, and Hamilton depression rating scale as screening instruments for depression in stroke patients”, *Psychosomatics*, 43(5):386-393, 2002.

[17] Wolfe, F., Smythe, H.A., Yunus, M.B., “The American College of Rheumatology 1990 criteria for the classification of fibromyalgia”, Report of the Multicenter Criteria Committee., *Arthritis Rheumatology*, 33(2):160-172, Feb. 1990.

[18] Chroni, E., Argyriou, A.A., Polychronopoulos, P., Sirrou, V., “The effect of stimulation technique on sympathetic skin responses in healthy subjects”, *Clinical Autonomic Research*, 16(6):96-400, 2006.

[19] Öztemel, E. , “Yapay Sinir Ağları”, Papatya Yayıncılık, 2003.