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RESEARCH ARTICLE

ESTIMATION OF EDSS FROM EEG SIGNALS OF MULTIPLE SCLEROSIS PATIENTS

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ABSTRACT

Multiple sclerosis (MS) is an autoimmune, neurodegenerative, chronic disease that affects the central nervous system and manifests itself with attacks. Although there is no definite cure for the disease, it is possible to control these attacks. Follow-up of the disease has great importance in terms of disability. An Extended Disability Status Scale (EDSS) is used to show how much the disease affects. This score is determined by specialized clinicians. In this study, the EDSS score, previously determined by neurologists, was attempted to be estimated using the EEG signals. 32-channel EEG signals were recorded while 17 MS patients with EDSS 1.0, 1.5, and 2.0 were performing a working memory task. Using the band power of these 6-minute EEG signals, EDSS estimation was performed with the Decision Tree Regressor, resulting in a Mean Absolute Error (MAE) of 0.088. With the Leave One Out Cross-Validation, 17 trees were extracted and 12 were found to be identical. As a result, the band power features of F7 and CP2 EEG channels were found to be successful in predicting 3-level EDSS scores with a decision tree regressor with 0.0 MAE. Additionally, the relationship between the scores obtained in the working memory task and the EDSS scores of MS patients was statistically calculated with One-way ANOVA. There was no significant difference between the EDSS score and the task scores (p>.05).

Keywords: *Multiple sclerosis (MS), EEG, EDSS, Working Memory, Decision Tree Regressor.*

1. INTRODUCTION

Multiple sclerosis (MS) is a chronic, autoimmune disease of the central nervous system that affects the brain, cerebellum, brain stem, and spinal cord. The immune system attacks the myelin sheath that surrounds the nerve cells, causing damage. Plaques called sclerosis form in damaged tissues. Depending on the involvement of these plaques, various symptoms are observed in patients [1]. The main symptoms are cognitive problems, fatigue, muscle weakness, vision problems, lack of

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coordination, tingling and numbness, bowel, bladder and sexual problems, mood swings, dizziness, and double vision. The disease is commonly detected using magnetic resonance images (MRI), evoked potentials (EP), and electroencephalography (EEG) signals. Although there is no cure for the disease, the attacks can be brought under control, and the damage caused by the disease can be minimized or reduced to zero. Approximately 2.5 million individuals worldwide are afflicted with MS [2]. Early diagnosis of the disease, monitoring, and controlling its progression are great importance. The disease course of multiple sclerosis (MS) can be classified into five types: Benign MS, Relapsing-Remitting MS (RRMS), Primary Progressive MS (PPMS), Secondary Progressive MS (SPMS), and Progressive Relapsing MS (PRMS) [3]. About 85% of MS patients have the RRMS type. The Extended Disability Status Scale (EDSS), presented by Kurtzke, is used as an indicator of the impact of MS patients [4]. Despite its flaws, it is the most widely used scale in the clinic due to its ease of application. It combines disability and impairment, has moderate inter-rater reliability, and primarily focuses on ambulation-related disability [5]. It is used to monitor the level of disability rather than measuring treatment effects [6]. Additionally, the EDSS scale remains valid [7]–[9], although other scales besides the EDSS [10], [11] are also available in the literature. The EDSS, determined by a detailed neurological examination, corresponds to a value between 0 and 10. Disability status according to the EDSS scores [12], [13] is given in Table 1.

Table 1. Disability status according to the EDSS scores.

EDSS Score	Description
0 - 3.5	No obvious disability.
4.0 - 5.5	Patients have difficulty walking and climbing stairs. They need assistance at distances longer than 100 meters.
6.0 - 6.5	Patients need assistance while walking.
7.0 - 7.5	Wheelchair-dependent.
8.0 - 8.5	The bedridden state.
9.0 - 9.5	Completely immobile with no ability to communicate or safely consume food orally.
10.0	MS-caused death.

Upon reviewing the existing literature, it is evident that no studies have estimated the EDSS score using EEG signals. However, Alexandra et al. [14] demonstrated that cognitive reserve has a significant impact on the association between EDSS score and specific cognitive domains such as processing efficiency, visuospatial learning and memory, and verbal memory disposition. Interestingly, no negative correlation was observed between these cognitive domains and EDSS scores in MS patients with high cognitive reserve.

Kaufmann et al. [15] estimated EDSS based on patient feedback. Based on three questions about patients' mobility, they developed a three-category (EDSS≤3.5, EDSS=4–6.5, EDSS≥7) self-reported disability status scale. With self-reported disability status results, they achieved an accuracy rate of 88.4% in estimating the EDDS determined by clinicians.

Zurawski et al. [16] studied the relationship between time and EDSS. They showed that the time interval between specific EDSS levels showed significant variation. They emphasized that certain functional system scores demonstrated higher predictive ability for future EDDS-related disability, even among patients with the same current EDDS level.

Xiaodong et al. [17] investigated the relationship between Cervical Spinal Cord Atrophy (CSCA) and EDSS scores by synthesizing existing data from MRI images in their review. They analyzed 22 eligible studies involving 1933 participants and showed that the correlation between CSCA and EDSS scores was significant but moderate.

Cao et al. [18] estimated EDSS from posturographic data. The study included 118 volunteers with a range of EDSS scores from 0 to 4.5, who performed the test with their eyes closed. They used second-order polynomial regression models to estimate EDSS based on two postural sway parameters (length and surface) and four recurrence quantification analysis parameters (%Rec, Shannon entropy, mean diagonal line length (LL), and trapping time). To identify the most accurate method for estimating EDSS, they compared the clinical and estimated EDSS scores and demonstrated that the estimates based on surface, %Rec, and LL parameters were correlated with the clinical scores.

In another study by Cao et al. [19], a novel method was presented that utilized decision tree analysis for evaluating the EDSS score using posturographic data. Multiple decision trees were constructed using the training data and evaluated using the test data. A decision tree was presented demonstrating 75% agreement between the clinical and estimated EDSS scores in the test group. The results indicated that the decision tree model effectively automated the evaluation of EDSS scores, and both linear and nonlinear postural sway measures were capable in distinguishing between different EDSS scores.

In a study by Alves et al. [20], the EDSS was estimated using notes and EDSS scores recorded by clinicians in the "OM1 MS Registry data" through the use of machine learning algorithms. The performance of the model was evaluated using metrics such as the area under the curve (AUC), positive predictive value (PPV), and negative predictive value (NPV). The proposed model achieved a PPV of 0.85, an NPV of 0.85, and an AUC of 0.91.

Salim et al. [21] investigated evidence of gray matter brain lesions in patients with MS by evaluating the alpha rhythm of brain electrical activity at rest using EEG recordings. The study included 50 patients diagnosed with MS and 50 control participants. The researchers examined posterior dominant rhythm (PDR) parameters, including wave frequency and amplitude, in the EEG recordings. Functional disability among MS patients was evaluated using the EDSS. One-way analysis of variance and t-test were used to determine the statistical significance. The study found significantly lower PDR frequency and amplitude values in MS patients compared to the control group ($p< .01$), with 34% of MS patients exhibiting PDR frequency lower than 8.5 Hz. Moreover, a negative correlation was found between PDR frequency and the level of functional disability in MS patients ($p<.001$). The study showed that monitoring of the PDR spectrum with EEG could be used as an alternative or complementary tool to other imaging techniques for detecting and monitoring cerebral cortical lesions in MS patients.

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Gschwind et al. [22] investigated whether the millisecond time range in topographic EEG analysis was altered in patients with RRMS, and whether the temporal characteristics of the millisecond time range reflected a link to the clinical characteristics of the patients. The study included 53 patients with RRMS (EDSS ≤ 4, mean 2.2) and 49 healthy controls, and 256-channel EEG signals were used for analysis. The researchers analyzed 5-minute EEG segments at rest and identified four dominant millisecond time ranges for both groups using established clustering methods. Significant differences were found in the temporal dynamics of the EEG signals between RRMS patients and healthy controls. Using stepwise multiple linear regression models with 8-fold cross-validation, they obtained evidence that these electrophysiological measures predict a patient's total disease duration, annual relapse rate, disability score, as well as depression score, and cognitive fatigue measure.

Vázquez-Marrufo et al. [23] conducted a study examining the relationship between EEG signal characteristics and EDSS in MS patients and a healthy control group. They performed correlation analysis using behavioral, neuropsychological test scores, EDSS scores, event-related potentials (ERP), and event-related desynchronization (ERD) parameters, as well as correlation scores between individual participants' P3/ERD maps and the overall average P3/ERD maps. They found that the strongest correlation was between EDSS and reaction time, ERD, and ERP.

Considering the existing literature, it is noted that there is a gap in research on EDSS estimation using EEG signals recorded during cognitive tasks. Therefore, the aim of this study was to contribute to the literature by investigating the estimated EDSS score obtained from EEG signals of MS patients while they performed a working memory task. EDSS was attempted to be estimated using the Decision Tree Regressor based on EEG signals obtained during the working memory task of 17 MS patients with EDSS scores of 1.0, 1.5, and 2.0.

A generalized tree model, which included only 2 features of the EEG signal, was presented for estimating EDSS using the Decision Tree Regressor method. The band power features of the F7 and CP2 EEG channels were identified to be effective in predicting 3-level EDSS scores using a generalized decision tree model, achieving MAE of 0.0. In addition to EDSS estimation, the statistical relationship between the scores obtained in the working memory task and the EDSS scores of MS patients was calculated using One-way ANOVA. The p-value for the comparison between the EDSS score and the task scores was greater than 0.05, indicating that there was no significant difference between the two.

The study flow diagram is given in Figure 1.

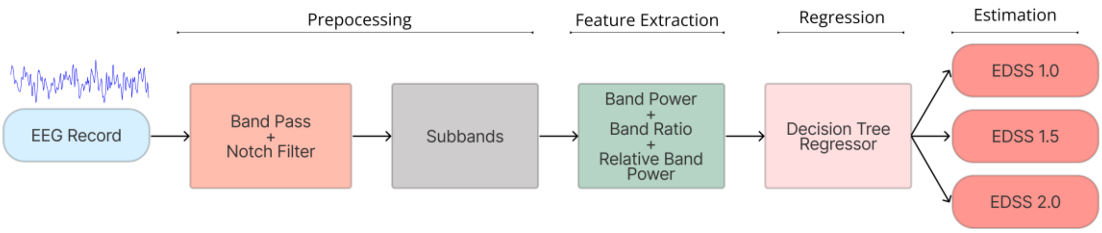

Figure 1. Study flow diagram.

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In the second part of the study, titled "Material and Method", participants, experimental procedure, signal preprocessing, feature extraction, Decision Tree Regressor, and the proposed method are provided. In the third part, the obtained regression and statistical results are presented. The fourth section discusses the results in comparison with other relevant studies. Finally, the conclusion of the study is presented in the final section.

2. MATERIAL and METHOD

2.1. Participants

In this study, EEG signals from 17 patients diagnosed with RRMS and having EDSS score of 2.0 or lower (EDSS=1.0, EDSS=1.5, EDSS=2.0) were used. Healthy individuals were excluded from the study because a detailed examination is required to determine the EDSS score in healthy individuals. The characteristics of MS patients included in the study are as follows:

- No attacks in the last 6 months
- Not taking cortisone treatment
- No comorbid diseases

The distribution of MS patients is given in Table 2.

Table 2. The distribution of MS patients.

Feature	**Distribution**
Count (Female/Male)	17 (11/6)
EDSS (Score+SD)	1.4± 0.38
Age (Mean+SD)	31.11±8.27

2.2 .Experimental Procedure

Study permission was obtained from the Clinical Research Ethics Committee of Kütahya Health Sciences University (18.06.2021-2021/03). In the continuation of our previous study [24], the number of MS patients was increased, and EEG signals were recorded during different cognitive tasks. The experiments were conducted at Kütahya Dumlupınar University Neurotechnology Education, Application and Research Center. MS patients performed a cognitive task for working memory on the computer for 6 minutes [25]. This task is a Visual Pattern Test [26] based task for short-term visual memory and visual attention. The patients were shown a square matrix with a pattern and asked to keep it in their memory and to draw the pattern again with the help of the mouse when the matrix disappeared. As the correct moves were made, the square matrix increased in size, and the level became more difficult. The level decreased with the number of wrong moves. Each participant received a score after the task.

2.3. Data Acquisition and Preprocessing

EEG signals of the volunteers were recorded for 6 minutes with a 32-channel active electrode Brain Products ActiChamp EEG device during the memory task. The sampling frequency was 500 Hz. Electrode placements were made according to the international 10-20 system, and electrode impedances were kept below 10 kohm. The Cz electrode was chosen as the reference.

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As a part of signal preprocessing, a bandpass filter with a frequency range of 0.1-50 Hz was used to eliminate any undesired noise or signal outside of this frequency range. Furthermore, a notch filter with a frequency of 50 Hz was employed to eradicate any electrical interference at this specific frequency. The EEG signal, which was acquired for a duration of 6 minutes, underwent the filtering procedure before subsequent analyses were performed. The filtering process was performed using the MNE library. A 50-second segment of the filtered EEG signal recorded from the participants during the task, according to their EDSS scores, is presented in Figure 2.

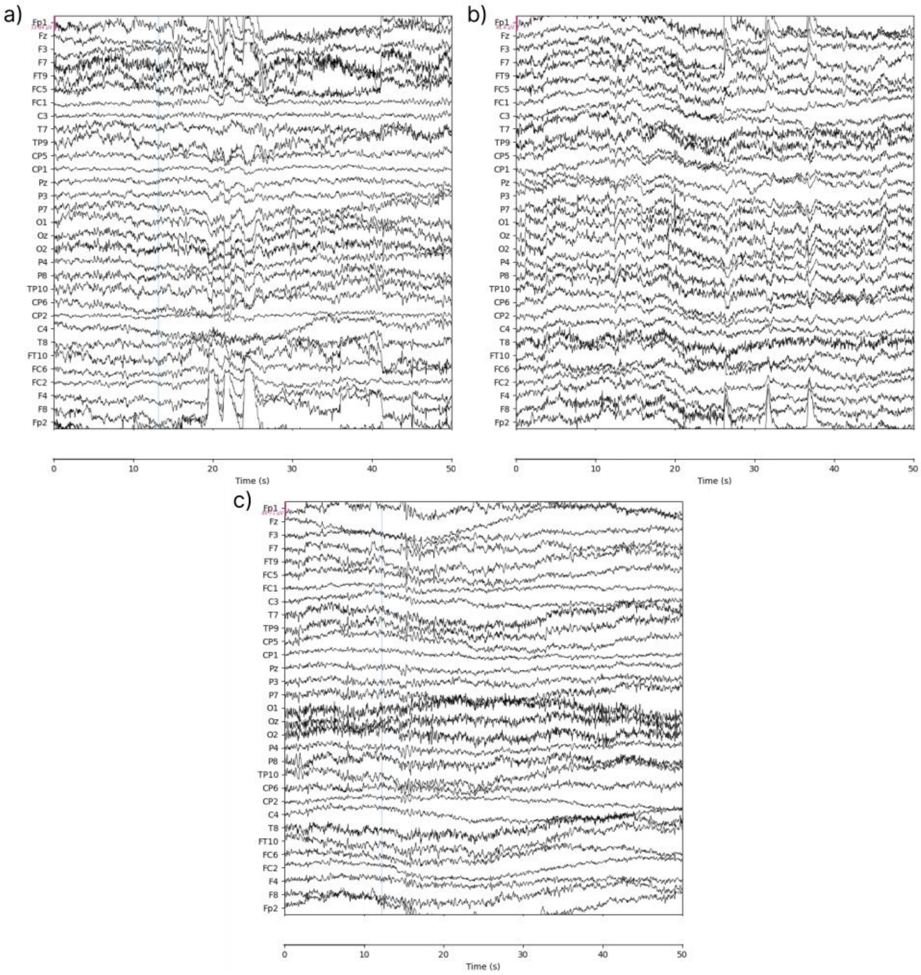

Figure 2. A 50-second segment obtained from volunteers during the task. a) EDSS=1.0. b) EDSS=1.5. c) EDSS=2.0.

2.4. Feature Extraction

The filtered 32-channel EEG signals were divided into subbands using the Welch method. These subbands were delta (δ: 0.5-4 Hz), theta (θ: 4-8 Hz), alpha (α: 8-16 Hz), beta (β: 16-31 Hz), and gamma (γ: 31-50 Hz).

Power Spectral Density (PSD), band ratios, and relative band powers were extracted as features. The features were obtained using the MNE library in Python [27].

2.4.1. Power spectral density

During the feature extraction, the power spectral density of the subbands of the EEG signal was calculated using the Fourier Transform-based Welch method.

The EEG signal was divided into windows with power of 2, and the improved periodogram was calculated for these windows. In the Welch method, which is the improved version of the periodogram method, the windows can overlap while the EEG signal is windowed. Eq. 1 shows the data segments.

$$x_i(n) = x(n + iD);\ i = 0, 1, \dots, L - 1;\ n = 0, 1, \dots, M - 1 \tag{1}$$

An improved periodogram is calculated for these windows, and then the average of these sections is obtained [28].

i. improved periodogram is given in Eq. 2. *f*, *K*, and *w(n)* demonstrate a normalized frequency, normalization factor, and windowing function, respectively.

$$\hat{P}_{xx}^{(i)}(f) = \frac{1}{K.M}\left|\sum_{n=0}^{M-1} x_i(n)w(n)e^{-j2\pi fn}\right|^2,\ i=0,1,\dots,L-1 \tag{2}$$

In Eq. 3, the normalization factor is given.

$$K = \frac{1}{M}\sum_{n=0}^{M-1}(w^2(\mathrm{n})) \tag{3}$$

Eq. 4 shows the power spectrum density.

$$PSD = \hat{P}_{xx}^{w}(f) = \frac{1}{L}\left|\sum_{i=0}^{L-1}\hat{P}_{xx}(f)\right| \tag{4}$$

2.4.2. Band ratios

The band ratios of the EEG signal divided into subbands were calculated and used as a feature in this study. The band ratios used are as follows: α/β, α/γ, α/δ, α/θ, β/γ, β/θ, β/δ, θ/γ, θ/δ, δ/γ.

2.4.3. Relative band powers

After calculating the total PSD of the EEG signal, the relative band powers were calculated using the formulas given in Eq. 5, Eq. 6, Eq. 7, Eq. 8, Eq. 9, and Eq. 10. These relative band powers were used as features in the study.

$$\sum PSD = PSD(\alpha + \beta + \theta + \delta + \gamma) \tag{5}$$

$$Relative\ \alpha = \frac{\alpha}{\Sigma PSD} \quad (6)$$

$$Relative\ \beta = \frac{\beta}{\Sigma PSD} \quad (7)$$

$$Relative\ \theta = \frac{\theta}{\Sigma PSD} \quad (8)$$

$$Relative\ \delta = \frac{\delta}{\Sigma PSD} \quad (9)$$

$$Relative\ \gamma = \frac{\gamma}{\Sigma PSD} \quad (10)$$

2.5. Decision Tree Regression

In the study, a Decision Tree Regressor from the Python Scikit-Learn library [29] was used for regression analysis. Unlike the classification, the aim of regression is to predict continuous numerical values. Independent variables were ranked based on the information gain values, and a comparison is made with this ranking during the testing step. Mean Squared Error (MSE) was used as the measurement for feature selection.

2.6. Proposed Method

In the study, EEG signals were recorded during the working memory task. The recorded EEG signals were filtered using a bandpass filter of 0.1-50 Hz and notch filter of 50 Hz. Subsequently, the EEG signals were separated into sub-bands (alpha, beta, gamma, delta, and theta) using the Welch method on the MNE library in the Python programming language [27]. Spectral features (band powers, power ratios, and relative powers) were extracted from each subband. Using these features, a total of 17 decision trees were trained using a Decision Tree Regressor with Leave One Out Cross Validation (LOOCV). It was observed that 12 out of these 17 trees were identical to each other, and any of these 12 trees could be proposed as a generalized tree. The block diagram of the proposed method is shown in Figure 3.

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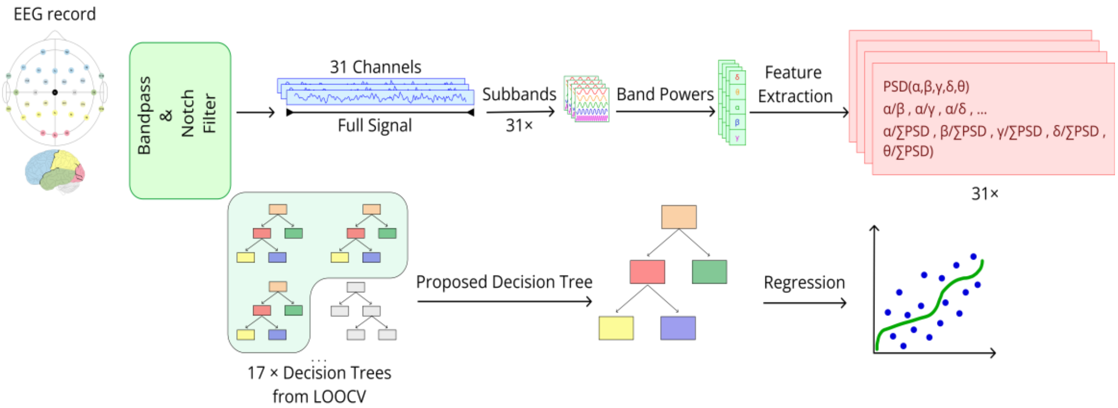

Figure 3. The proposed method block diagram.

2.7. Performance Evaluation Metrics

2.7.1. Mean absolute error

The Mean Absolute Error (MAE) given in Eq. 11 represents the mean of the absolute values of the differences between the real data and the predicted data [30].

$$MAE = \frac{1}{N}\sum_{i=1}^{N}\left|x_i^{real} - x_i^{predicted}\right| \tag{11}$$

2.7.2. Mean squared error

Mean Squared Error (MSE) given in Eq. 12 represents the mean of the squared differences between the real data and the predicted data [30].

$$MSE = \frac{1}{N}\sum_{i=1}^{N}\left|x_i^{real} - x_i^{predicted}\right|^2 \tag{12}$$

2.7.3. Coefficient of determination

The coefficient of determination (R^2) given in Eq. 13 represents the ratio of the variance in the dependent variable that is explained by the linear regression model [31].

$$R^2 = 1 - \frac{\sum\left|x_i^{real} - x^{predicted}\right|^2}{\sum\left|x_i^{real} - x^{mean}\right|^2} \tag{13}$$

3. RESULTS

The statistical features of the EEG signals recorded from the participants during the task are presented in Table 3. The selected features on the nodes of the 17 trees were F7 theta/gamma, FC6 relative alpha, CP2 relative beta, and P3 delta/gamma. These trees are given in Figure 4, showing that 12 of them were identical when analyzing the EEG signals of 17 MS patients using the Decision Tree Regressor with Leave One Out Cross Validation. It was observed that the F7 theta/gamma and CP2

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relative beta feature pairs were used repeatedly in 14 trees. It was also observed that all decision trees could separate the EDSS level using two nodes.

The graphs created according to the EDSS of the features used by the trees are given in Figure 5. F7 theta/gamma and CP2 relative beta features were found to be distinctive in EDSS.

Table 3. Statistical parameters of the EEG signals recorded from the participants during the task.

Channel	Min	Max	SD	Skewness	Kurtosis	VPP
Fp1	-0.00075	0.00101	0.00013	1.54492	19.49554	0.00176
Fz	-0.00011	0.00014	0.00003	0.42954	5.51061	0.00025
F3	-0.00035	0.00035	0.00007	0.18917	6.55013	0.00070
F7	-0.00034	0.00041	0.00007	0.18918	10.81776	0.00074
FT9	-0.00026	0.00033	0.00005	0.81777	15.57779	0.00059
FC5	-0.00020	0.00019	0.00004	-0.06336	5.69386	0.00038
FC1	-0.00015	0.00015	0.00003	-0.13508	5.64678	0.00030
C3	-0.00009	0.00009	0.00002	-0.00865	4.28930	0.00018
T7	-0.00041	0.00059	0.00008	0.43319	13.30249	0.00100
TP9	-0.00038	0.00064	0.00009	0.75868	12.69678	0.00102
CP5	-0.00010	0.00009	0.00002	-0.18525	4.89025	0.00019
CP1	-0.00011	0.00008	0.00002	-0.30563	6.86306	0.00019
Pz	-0.00017	0.00025	0.00003	0.14124	4.89261	0.00041
P3	-0.00008	0.00008	0.00002	0.10255	4.48578	0.00016
P7	-0.00026	0.00023	0.00005	-0.08180	5.14539	0.00049
O1	-0.00020	0.00019	0.00003	-0.05169	6.29524	0.00039
Oz	-0.00016	0.00016	0.00003	0.00548	4.55911	0.00033
O2	-0.00019	0.00019	0.00004	-0.04872	4.88903	0.00038
P4	-0.00007	0.00007	0.00002	0.02542	3.94477	0.00014
P8	-0.00027	0.00027	0.00005	-0.16267	7.75689	0.00054
TP10	-0.00030	0.00039	0.00006	0.37740	8.53761	0.00069
CP6	-0.00010	0.00010	0.00002	-0.19806	6.31914	0.00020
CP2	-0.00008	0.00007	0.00002	-0.18043	5.89390	0.00015
C4	-0.00009	0.00008	0.00002	-0.12843	4.83436	0.00017
T8	-0.00031	0.00029	0.00005	-0.44179	13.14973	0.00060
FT10	-0.00054	0.00070	0.00011	0.65780	14.32443	0.00125
FC6	-0.00020	0.00023	0.00004	-0.02664	5.63375	0.00043
FC2	-0.00007	0.00007	0.00002	0.04355	3.66873	0.00014
F4	-0.00019	0.00020	0.00004	0.11452	5.68868	0.00038

F8	-0.00053	0.00067	0.00012	0.10190	9.45513	0.00120
Fp2	-0.00036	0.00049	0.00007	1.60709	14.17754	0.00084

VPP: Amplitude of peak to peak **SD:** Standard Deviation

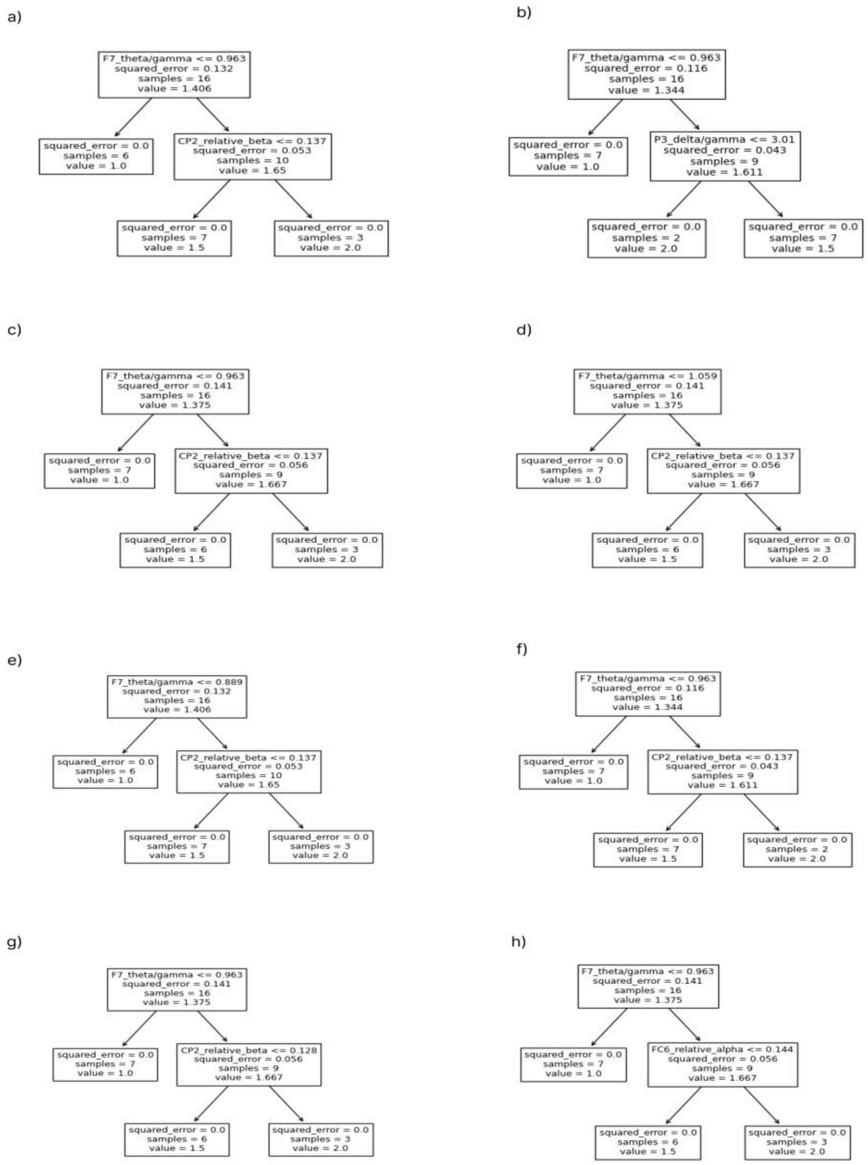

Figure 4. Decision Trees obtained in the LOOCV step a) tree_0, tree_1, tree_2, tree_4, tree_5, and tree_14 b) tree_3 c) tree_6, tree_9, tree_10, and tree_11 d) tree_7 e) tree_8 f) tree_12 and tree_15 g) tree_13 h) tree_16.

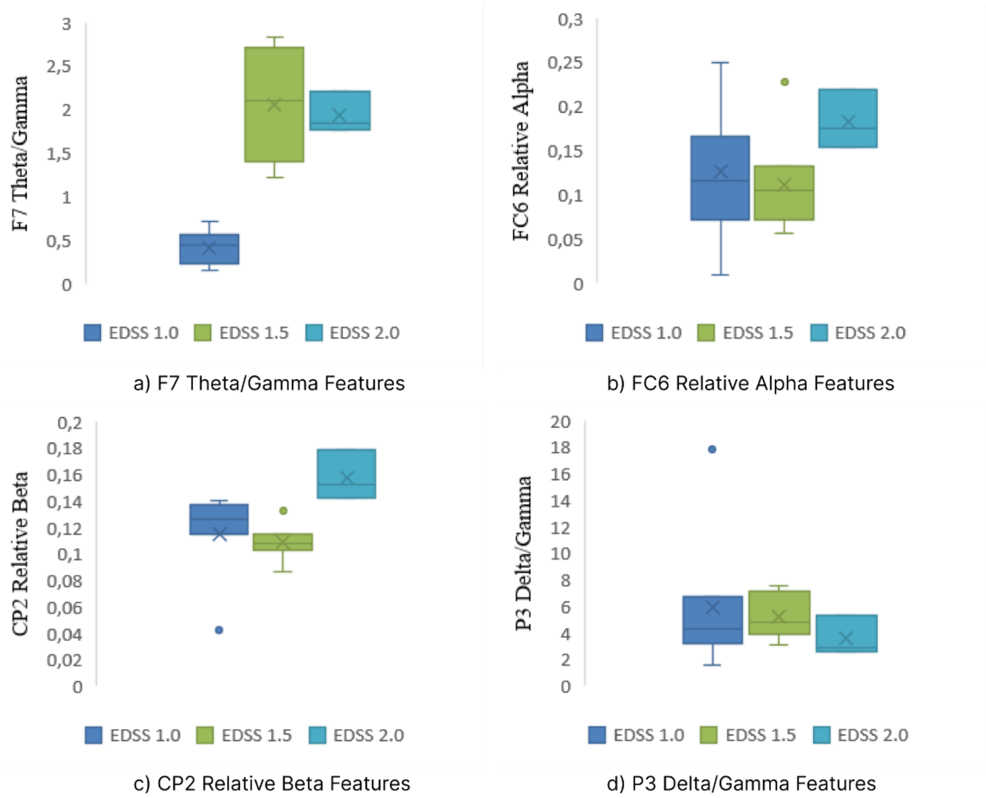

Figure 5. Feature-EDSS graphs used by the decision tree regressor.

The performances of the trees obtained from the Leave One Out Cross Validation steps are presented in Table 4. It is observed that the performances of tree_3, tree_13, and tree_16 are relatively lower compared to the other trees. When the other 14 tree models were used for testing, EDSS scores in the range of 1.0-2.0 (EDSS:1.0, EDSS:1.5, EDSS:2.0) were estimated with an MAE of 0.0, indicating accurate prediction. The overall EDSS estimation using Leave One Out Cross Validation was made with MAE of 0.088.

Table 4. The performances of the trees belonging to the Leave One Out Cross Validation steps.

tree_ID	EDSS	MAE	MSE	R^2	EEG Features
tree_0*	1.0	0	0	1	F7 theta/gamma, CP2 relative beta
tree_1*	1.0	0	0	1	F7 theta/gamma, CP2 relative beta
tree_2*	1.0	0	0	1	F7 theta/gamma, CP2 relative beta
tree_3	2.0	0.029	0.015	0.890	F7 theta/gamma, P3 delta/gamma

tree_4*	1.0	0	0	1	F7 theta/gamma, CP2 relative beta
tree_5*	1.0	0	0	1	F7 theta/gamma, CP2 relative beta
tree_6*	1.5	0	0	1	F7 theta/gamma, CP2 relative beta
tree_7	1.5	0	0	1	F7 theta/gamma, CP2 relative beta
tree_8	1.0	0	0	1	F7 theta/gamma, CP2 relative beta
tree_9*	1.5	0	0	1	F7 theta/gamma, CP2 relative beta
tree_10*	1.5	0	0	1	F7 theta/gamma, CP2 relative beta
tree_11*	1.5	0	0	1	F7 theta/gamma, CP2 relative beta
tree_12*	2.0	0	0	1	F7 theta/gamma, CP2 relative beta
tree_13	1.5	0.029	0.015	0.890	F7 theta/gamma, CP2 relative beta
tree_14*	1.0	0	0	1	F7 theta/gamma, CP2 relative beta
tree_15*	2.0	0	0	1	F7 theta/gamma, CP2 relative beta
tree_16	1.5	0.029	0.015	0.890	F7 theta/gamma, FC6 relative alpha
LOOCV	**-**	**0.088**	**0.044**	**0.669**	

tree_ID: States the subject selected from MS patients for the Leave One Out Cross Validation steps. Identical trees are indicated with asterisks (*).

While making the EDSS estimation, 12 decision trees with the same node parameters were obtained in the LOOCV steps. The proposed decision tree is shown in Figure 6.

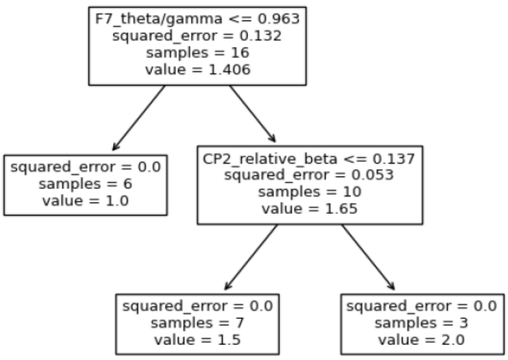

Figure 6. The proposed decision tree.

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The actual-predict performance of the decision tree is shown in Figure 7.

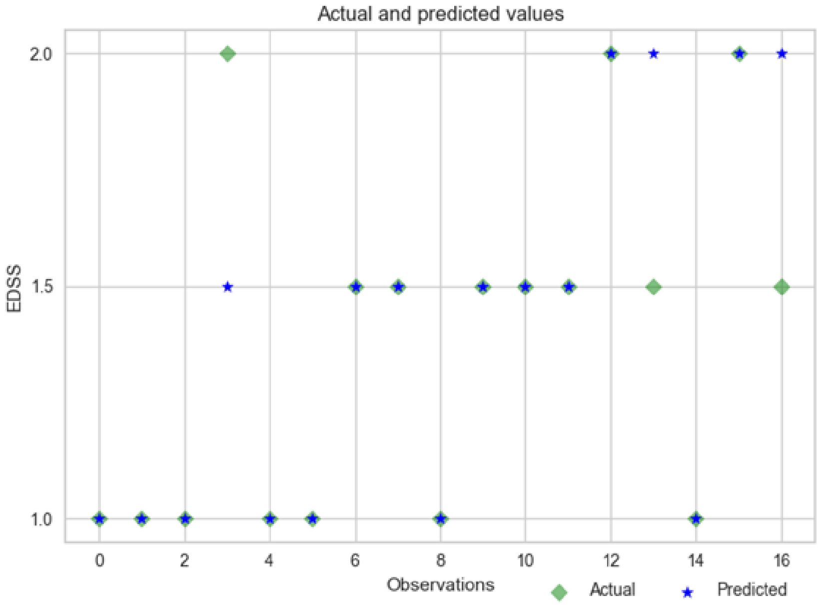

Figure 7. The actual-predict performance of the decision tree.

Statistical results of MS patients' scores obtained during the task according to EDSS are presented in Table 5. One-way ANOVA results showed that there was no significant difference between the cognitive task scores of MS patients with EDSS 1.0, 1.5, and 2.0 (p>.05). However, it was observed that the mean task score decreased as the EDSS increased.

Table 5. Statistical results of MS patients' task scores according to the EDSS score.

EDSS		N	Task Score (Max)	Task Score (Min)	Task Score (Mean)	SD	p
1.0	1.5 2.0	7	83.00	49.00	66.00	10.89	.907 .082
1.5	1.0 2.0	7	86.00	28.00	62.43	20.02	.907 .144
2.0	1.0 1.5	3	53.00	25.00	40.33	14.19	.082 .144

SD denotes the standard deviation, **p** denotes the p-value obtained as a result of the One-way ANOVA test.

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4. DISCUSSION

Since MS is a chronic and inflammatory disease of the central nervous system, monitoring disease progression and control is crucial. MRI is commonly used for disease follow-up as the lesions seen on MRI are known to correlate with EDSS scores. However, in this study, EDSS estimation was performed using EEG signals, which are more accessible and easier to apply compared to MRI. By using the theta/gamma ratio of the F7 channel and the CP2 relative beta features, accurate EDSS score estimations were achieved for 17 MS patients using a decision tree regressor. Table 6 presents comparisons with relevant studies from the literature that have also attempted EDSS estimation.

Table 6. The EDSS estimation studies in the literature.

Study	Subject	EDSS	Feature	Method	Performance Metrics
Kaufmann et al. [15]	173 MS	≤3.5, 4–6.5, ≥7	Self-report on patient mobility	Statistical analysis	Accuracy:88.4%
Cao et al. [18]	89 MS 29 Healthy	0-4.5	Postural sway parameters	Second-order polynomial regression models	Agreement:70.49% Mean error:0.63
Cao et al. [19]	89 MS 29 Healthy	0-4.5	Postural sway parameters	Decision trees	Agreement:75.00%
Alves et al. [20]	684 MS	0-10	Clinical notes from neurologist visits (OM1 MS Registry data)	XGBoost gradient-boosting regression models	PPV: 0,85 NPV: 0,85 AUC: 0,91
Gschwind et al. [22]	53 MS 49 Healthy	0-4.0	EEG topographies	Stepwise Multiple Linear Regression Models	R^2:0.97
This Study	**17 MS**	**1.0, 1.5, 2.0**	**EEG band powers**	**Decision Tree Regressor (LOOCV)** **Decision Tree Regressor (Proposed Tree)**	**MAE: 0.088** **MSE: 0.044** **R^2: 0.669** **MAE: 0.0** **MSE: 0.0** **R^2: 1.0**

In previous studies, Kaufmann et al. achieved an accuracy of 88.4% in classifying 3-class EDSS estimation based on self-reported mobility status of MS patients with EDSS scores between 0-10 using statistical methods. Cao et al. estimated EDSSs between 0 and 4.5 with a mean error of 0.63 using second-order polynomial regression models based on postural sway parameters of MS patients. In another study by Cao et al., EDSS estimation with 75.00% agreement was achieved using the Decision Tree method with the same data. Alves et al., used the XGBoost gradient regression model to estimate EDSS scores between 0 and 10 using data recorded by neurologists, achieving an AUC of 0.91. Gschwind et al. Obtained an r-squared value of 0.97 using Stepwise Multiple Linear Regression Models based on EEG topographies of MS patients with EDSS scores between 0-4. In the current study, the Decision Tree Regressor method was used with features extracted from the band powers of EEG signals. It was observed that 14 out of the 17 decision trees obtained in the LOOCV steps were similar, with 12 of them being identical. Using these 12 identical trees, accurate 3-category EDSS estimation with 0.0 MAE was achieved.

The results of the study showed that the theta/gamma ratio of the F7 channel and the relative beta features of the CP2 channel were significant in the EDSS estimation between 0-2.0.

The study has several limitations, including the inclusion of a limited number of MS patients with only the RRMS type and the low range of EDSS scores. Further research with larger sample sizes and inclusion of other types of MS patients in a more homogeneously distributed population is needed. Thus, the stability and reliability of the proposed method will be understood.

5. CONCLUSION

In the study, for the first time, EDSS was estimated using decision tree regression with PSD features of EEG signals from volunteers with MS during a cognitive task. The proposed tree model achieved EDSS estimation with 0.0 MAE, indicating high accuracy. This proposed method could be an important tool for the monitoring the progression of MS disease. The theta/gamma features of the F7 channel and the relative beta features of the CP2 channel were found to be significant in the proposed decision tree; however, further investigation is warranted for these features.

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