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Determining the Relationship Between EEG Findings and Prognosis of Patients with Decreased Consciousness Following Head Injury

Zahra Mirzaasgari*, Babak Zamani, Farzan Vahedifard, Parnian Kheirkhah and Amirsina Homayooni

Department of Neurology, Firoozgar Hospital, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

*** Corresponding author**

Zahra Mirzaasgari, MD
Department of Neurology, Firoozgar Hospital, School of Medicine, Iran University of Medical Sciences, Tehran, Iran
Tel: +98 21 8894 2661
Fax: +98 21 8894 2622
Email: mirzaasgari@gmail.com

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Abstract

Background: Head injury is a silent epidemic in developed countries and is one of the leading causes of death and disability. Determining the precise and early prognosis of head injury, especially in severe cases, is essential and will help define treatment actions and rehabilitation plans and counsel other family members. The purpose of this study was to determine the relationship between electroencephalographic findings and prognosis in patients with decreased levels of consciousness due to head injury.

Methods: This is a retrospective descriptive-analytical study on patients with reduced levels of consciousness due to head injury, referred to Tir Hospital (Tehran) in the first half of 2018. Overall, 52 patients were studied and divided according to their GCS into two groups: favorable prognosis (30 patients, 57.7%) and poor prognosis (22 patients, 42.3%). We tried to find the relation between EEG findings such as voltage, electrographic seizures, periodic and rhythmic patterns, and the prognosis.

Results: Normal voltage was associated with a favorable prognosis, with a high specificity (95%) and a less robust sensitivity (63%). The isoelectric voltage (electrocerebral shutdown) was associated with a poor prognosis. Normal and isoelectric voltages were good predictors with 95% and 100% Positive Predictive Values (PPV), respectively. There was a statistically significant relationship between EEG frequency range and prognosis.

Conclusion: This study showed that EEG parameters might provide valuable data regarding the prognosis of decreased consciousness of patients with a head injury, also for the guidance of physicians and informing the patients' family.

Keywords: Craniocerebral trauma, Consciousness, Electroencephalography, Prognosis

Introduction

Head injury is a silent epidemic in developed countries and is one of the leading causes of death and disability (1,2). Determining the precise and early prognosis of head injury, especially in severe cases, is essential and will help set treatment actions and rehabilitation plans and counsel other family members (3).

Various models have been devised to determine the prognosis of head injury, some of which are of poor quality. However, a number of them have passed the evaluation. Of these, two models, IMPACT (International Mission for Prognosis and Clinical Trials in Traumatic Brain Injury) and CRASH (Corticosteroid Randomization after Significant Head Injury), are based on large cohort studies and claim to have statistically significant validity (4). Although these two models have provided accurate prognoses in the patients' population, they are not sufficiently detailed to be used for an individual patient (3).

Loss of consciousness at the time of trauma is caused by acceleration and deceleration of the head, which causes the axons to elongate and tear. The term 'concussion' describes the short loss of consciousness (less than 6 *hr*). Most patients with concussions appear normal on CT and MR imaging since concussion is often caused by physiological rather than anatomical damage to the brain (5).

There are various methods for dividing the loss of consciousness by intensity. Glasgow Coma Scale (GCS) is the most widely utilized method by physicians and emergency health service practitioners to assess the levels of consciousness. However, GCS is not designed to detect focal neurological disorders and does not replace a thorough physical examination (6). The prognosis of severe head injury has improved significantly in the last 20 years although mortality rates have remained at 30%. Patients' age, coma scale, and CT scan findings are important variables in brain injury prognosis (7). Other significant factors in determining prognosis include: lack of response to light, hypotension or hypoxemia at admission, specific patterns on CT scan, persistent high ICP, hyperthermia, and extremely low levels of brain tissue oxygenation (less than ten *mmHg*) (5).

Neurophysiological techniques (including electroencephalograms and evoked potentials), similar to physical examinations, provide a functional assessment of the central nervous system and are applied, in addition to methods that examine anatomy (such as CT scan and MRI). These methods can be used to diagnose the origin of coma, monitor the treatment process, and determine prognosis (8,9).

In recent decades, the role of EEG in determining the prognosis of patients with acute loss of consciousness in the Intensive Care Unit (ICU) has been expanded (10). Hockaday described electro-encephalic changes in post-anoxic comas and divided them into five categories (11). Subsequently, various EEG scoring systems were introduced to evaluate the patients' prognosis in traumatic and non-traumatic comas, including Synek and Young. Nowadays, one of the most commonly used EEG scoring systems in traumatic and anoxic encephalopathies is the Synek Scale, which has emerged from changes in the Hockaday Scale (12,13).

Despite the usefulness of these EEG ratings, using them requires considerable expertise. Also, it is difficult to assign a unique label to an electroencephalogram in many cases since it depends heavily on the interpreter. On the other hand, patients can have different patterns of EEG at the same time (14). The use of standard EEG descriptors, including frequency, amplitude, and irritability, can eliminate the problems above, and make the results more uniform and usable.

The purpose of this study is to determine the relationship between electroencephalographic findings and prognosis in patients with decreased levels of consciousness due to head injury. We also investigated the voltages, paroxysmal EEG findings such as electrographic seizures, periodic and rhythmic patterns. Our hypothesis is, EEG findings can predict the prognosis in patients with decreased consciousness due to head injury.

The results of this study will be valuable in assessing the ability of EEG in providing valuable data considering the prognosis of patients with a head injury. Suppose that standard EEG can determine the prognosis of LOC in patients. In that case, it can be some guide for physicians and inform the patient's family. Since standard EEG is available in most centers, it requires low costs and resources.

Materials and Methods

This study is a retrospective and descriptive-analytical study of patients with a reduced level of consciousness due to blunt head injury in Tir Hospital, Iran, in the first six months of 2018 (convenience sampling method).

Patients younger than 15 years old, and patients undergoing neurosurgical interventions were excluded. Before conducting EEG, sedative drugs (mainly Benzodiazepines, Midazolam, Propofol, narcotics, and ketamine) were discontinued or tapered, if possible. None of the patients were in shock, nor were any hypothermic (temperature below 32°*C*).

Standard EEG of patients was recorded for at least 30 *min* by trained personnel and was interpreted by university neurologists. Twice, within 96 *hr* of entry, the EEG was recorded. Using a portable digital EEG device manufactured by Nihon Kohden, regular EEG was carried out at the bedside. The EEG recording and analysis technique was based on the International Federation of Clinical Neurophysiology recommendations for the use of EEG (15). According to the international 10–20 model, 11 electrodes were set.

The EEG frequency was divided into four bands:

Beta (above 13 *Hz*),
Alpha (8 to 13 *Hz*),
Theta (below 8 to 4 *Hz*),
Delta (below 4 *Hz*).

The voltage was divided into three groups of 'Normal' (greater than or equal to 20 μV), 'Low' (below 20 μV and greater than two μV), and 'Isoelectric' (equal or less than two μV; *i.e.*, electrocerebral shutdown). Paroxysmal EEG activities were also recorded, including electrographic seizures and periodic or rhythmic patterns (16). CT scans of patients were scored based on the Rotterdam scoring system:

Basal cistern state (normal 0, compact 1, and absent 2), midline shift (no midline shift or less than 5 *mm*: 0 points, greater than 5 *mm*: 1 point), Epidural lesion (absent 0, present 1), and ventricular or subarachnoid hemorrhage (absent 0, present 1). One point will be added to the final score (17).

Demographic data (age and sex) and neurological clinical examinations of the patients (GCS, pupil response to light, Rotterdam CT score, and EEG parameters such as voltage, background frequency, electrographic seizures, and periodic rhythmic patterns) were recorded.

Finally, the patients' prognosis at discharge based on the Glasgow Outcome Scale (18) was divided into five categories: 1. Death, 2. Stable vegetative status, 3. Severe disabilities (conscious, but dependent on others), 4. Moderate disabilities (with a disability but independent at tasks) and 5. Good improvements (resuming activities of daily life, although with possible minor neurological or psychiatric problems). GOS 4 and 5 were assumed equivalent to favorable prognosis, and 1 to 3 equivalent to poor prognosis.

IBM SPSS STATISTICS 26 (IBM Inc, New York, USA) software was used for data analysis. The normality of data was measured by the Kolmogorov-Smirnov test. p-values below 0.05 were considered statistically significant. Comparisons of means were performed for quantitative variables with normal distribution using students' T-test and for non-normal distribution using the Mann-Whitney U test. Chi-square or Fischer's Exact test was utilized to compare the qualitative variables.

In this study, ethical guidelines were followed, following the Helsinki resolution. Informed consent was obtained from patients or their relatives. The Ethics Committee of Iran University of Medical Sciences approved this intervention, and the procedures of our study did not cost the patients.

Results

Overall, 52 patients were studied, and divided according to GCS into two groups: favorable prognosis (30 patients, 57.7%) and poor prognosis (22 patients, 42.3%). Demographic data and neurologic findings of the patients grouped by prognosis can be observed in table 1. The EEG parameters are categorized regarding prognosis in figure 1. Some of the significant findings are included:

Age: The age difference between the two groups with favorable and poor prognoses was insignificant (p-value = 0.788).

Gender: Men's prognoses were significantly worse.

GCS: Average GCS in patients with favorable and poor prognoses were 12 (10.75-13) and 6.5 (5-9), respectively. The difference in GCS between the two groups was significant (p-value <0.001).

The pupils' response to light: There was a statistically significant relationship between pupils' response to light and patients' prognoses (One missing data regarding the pupils' response to light).

Table 1. Demographic data and neurologic findings of the patients with traumatic brain injury grouped by prognosis

	Good prognosis N=30	Poor prognosis N=22	p-value
Age (years)** Average (max- min)	32.5 (23.75-45)	34.5 (21.75-50)	0.79
Gender (male/female)	Number: 17/13 Percentage: 56.7% / 43.3%	Number: 19/3 Percentage: 86.4% / 13.6٪	0.03
GCS (Scores)** Average (max- min)	12 (10.75-13)	6.5 (5-9)	<0.001
Pupils' response to light*			
Both reactive	29 Subjects (96.7%)	6 Subjects (28.6%)	<0.001
One reactive – One non-reactive	1 Subject (3.3٪)	5 Subjects (23.8%)	
Both non-reactive	0 Subject	11 subjects (47.6%)	
Rotterdam CT Score** Average (max- min)	1.5 (1-2)	4 (3-4)	<0.001
EEG parameters*			
Voltage			
Normal	19 Subjects (63.3%)	2 Subjects (4.8%)	
Low	11 Subjects (36.7%)	10 Subjects (47.6%)	<0.001
Isoelectric	0 Subject	0 Subject (47.6%)	
Background frequency*			
Beta	4 Subjects (13.3%)	3 Subjects (15%)	<0.001
Alpha	7 Subjects (23.3%)	0 Subject	
Theta	19 Subjects (63.3%)	8 Subjects (35%)	
Delta	0 Subject	11 Subjects (50%)	
EEG Paroxysmal events*			
Electrographic seizure	1 Subject (3.3%)	6 Subjects (27.3%)	0.03
Periodic/rhythmic pattern	2 Subjects (6.7%)	7 Subjects (31.8%)	0.03

(*The numbers listed in the table for the quantitative variables are the percentage of patients in each group, relative to the total number of patients. Number of each group is also mentioned in the parenthesis.

** The quantitative variables are reported as follows: Average (minimum - maximum)).

Rotterdam CT: The Rotterdam CT score was missing for five patients. Among the rest, the Rotterdam CT score did not have a normal distribution. It was on average equal to 2 (1-3) with a minimum of 1 and a maximum of 5. There was a significant difference between the two groups with favorable and poor prognoses regarding the Rotterdam CT score (p-value <0.001).

EEG voltage: There was a statistically significant relationship between EEG voltage and prognosis.

Normal and isoelectric voltages were good predictors with 95 and 100% PPV, respectively.

Background frequency: There was a statistically significant relationship between EEG field ranges and prognosis (Figure 2).

Alpha and theta frequencies were predictors of optimal prognosis with 100 and 73% PPVs, respectively (Table 2). Delta frequency was a predictor of poor prognosis with a PPV of 100% (Table 3).

Electrographic seizures: Patients with electrographic seizures had a significantly worse prognosis (PPV = 100%).

Periodic/rhythmic patterns: Prognosis of patients with periodic/rhythmic patterns was significantly worse (PPV = 86%).

For all the data, the p values below 0.05 were considered statistically significant.

Discussion

The current study showed that normal voltage was associated with a favorable prognosis, with a high specificity (95%) and a less robust sensitivity (63%).

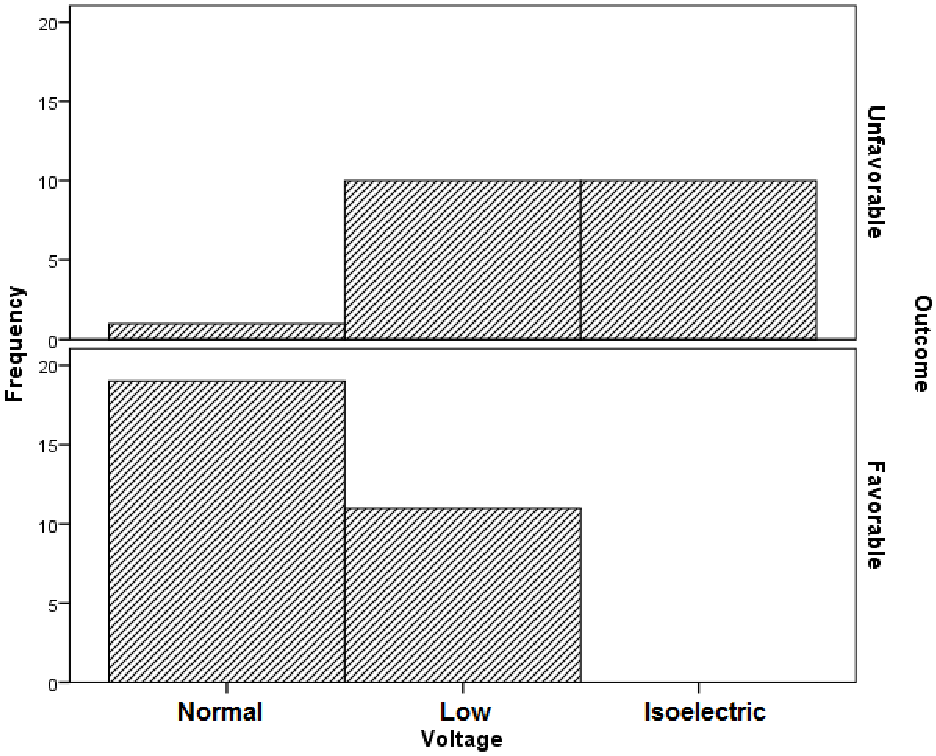

Figure 1. Frequency of different EEG voltages, grouped by prognosis.

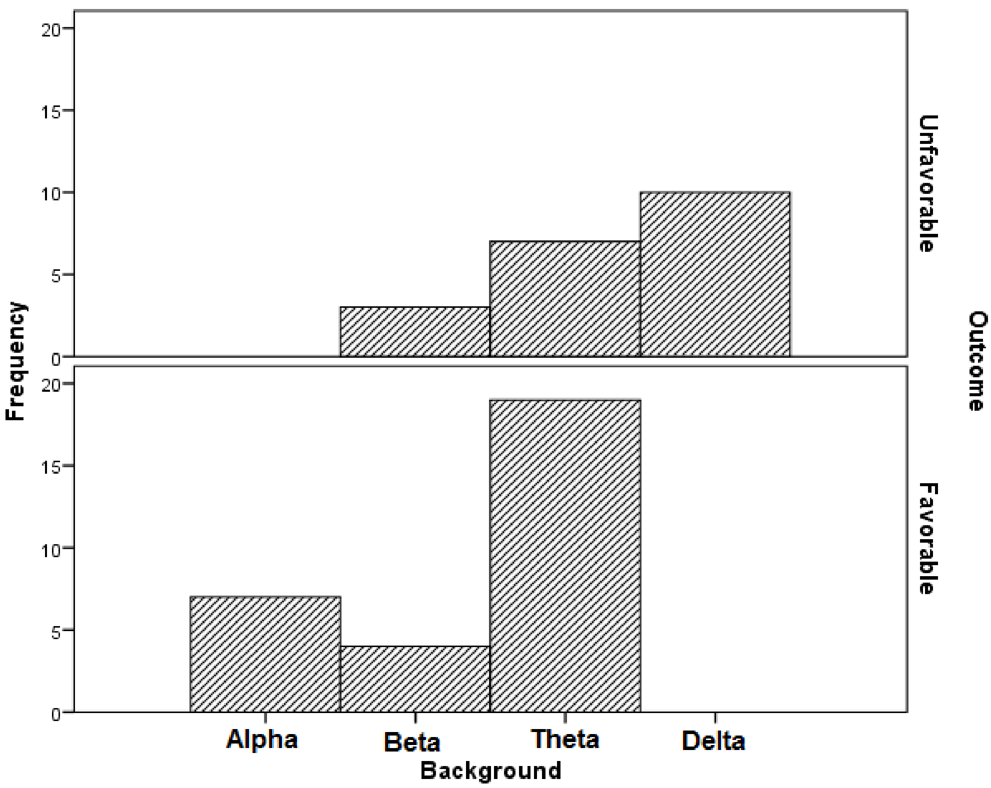

Figure 2. Frequency of EEG background frequency grouped by prognosis.

Table 2. Positive predictive value, negative predictive value, sensitivity and specificity of EEG parameters in predicting favorable prognosis

Predictive variable for favorable prognosis	Positive predictive value	Negative predictive value	Sensitivity	Specificity
Normal voltage	95%	65%	63%	95%
Alpha frequency	100%	47%	23%	100%

Table 3. Positive predictive value, negative predictive value, sensitivity and specificity of EEG parameters in predicting poor prognosis

	Positive predictive value (PPV)	Negative predictive value (NPV)	Sensitivity	Specificity
Isoelectric voltage	%100	%73	%48	%100
Delta frequency	%100	%75	%50	%100
Electrographic seizure	%86	%64	%19	%97
Periodic/rhythm pattern	%78	%65	%32	%93

The isoelectric voltage (electrocerebral shutdown) was associated with a poor prognosis. There was a statistically significant relationship between EEG frequency range and prognosis.

EEG plays a significant role in evaluating patients with altered levels of consciousness. Since EEG assesses supra-tentorial brain activity, its findings complement physical examinations in patients with loss of consciousness. Many EEG changes are nonspecific; still, some results favor a specific cause of loss of consciousness (including epilepsy, herpetic encephalitis, and metabolic encephalopathy). Some results are helpful in determining prognosis. EEG can be used as an adjunctive test to determine brain death. In cases of loss of consciousness, EEG can help answer the following questions:

Are psychogenic factors involved?

Is the process diffused, focal, or multifocal?

Is the loss of consciousness due to a hidden epileptic activity? (Non-convulsive status epilepticus)

Is there evidence of improvement despite a slight change in the patient's clinical picture? Moreover, if so, what are they?

Are there any findings that help determine prognosis?

This cross-sectional study attempted to answer the last question, namely detecting valuable findings in prognosis determination. Therefore, we compared the differences in EEG parameters between the two groups of patients with favorable and poor prognoses. Although the methods of this study (population under study, EEG classification, prognosis classification) differ from previous studies, its results are, in many cases, comparable.

In our study, the normal voltage was associated with a favorable prognosis. Normal voltage was very specific (95%) for a good prognosis but less sensitive (63%). The isoelectric voltage (electrocerebral shutdown) was associated with a poor prognosis.

Other studies investigated this association, too. In a prospective cohort study, Azabou *et al* evaluated EEG parameters in determining the prognosis of post-anoxic coma in 61 patients. It was shown that isoelectric, discontinuous, or dominant delta activity EEG can predict poor prognosis with 100% specificity. Also, non-reactive EEG was a predictor of poor prognosis with 80% specificity (13).

In another study, Azabou *et al* examined the association of EEG findings with prognosis in 110 septic patients admitted to the ICU. EEG of the patients was scored based on Synek and Young systems. Mortality in the ICU was associated with the absence of EEG response, delta predominance, periodic discharge, Synek score greater than 3, and Young score greater than 1 (19).

Also, Poothrikovil *et al* investigated the standard EEG findings and their value in determining the prognosis of 110 ICU patients with reduced consciousness. Patients were prognosticated at the time of discharge based on the mRS (modified Rankin Scale). The good prognosis was defined with a mRS of 0-3 and a poor prognosis with an mRS of 4-6. Regarding the EEG findings, generalized slowing was associated with a good prognosis. Age, GCS <8, and low-voltage cerebral activity were also associated with poor prognosis (20).

Similar results were found in the study of Azabou *et al* and Firosh Khan *et al* (13,21). Isoelectricity had a high specificity (100%) in predicting adverse prognosis, yet with low sensitivity (48%). In other words, although the presence of an electrocerebral shutdown is strongly suggestive of poor prognosis (PPV=100%), its absence does not necessarily guarantee a favorable outcome (NPV=73%). The low voltage difference between the two groups with good and bad prognoses was not significant.

The alpha field frequency was also associated with a favorable prognosis, as shown in the Bagnato *et al*'s study (22). Alpha frequency was very specific for predicting a good prognosis (specificity=100%), but had low sensitivity (23% sensitivity).

Also, the frequency of background theta was associated with a favorable prognosis, but with low sensitivity and specificity (63 and 65%, respectively). In Bagnato *et al*'s study (22), theta frequency was also associated with moderate improvement in consciousness level.

Delta frequency with a very high specificity of 100% and a 50% sensitivity suggested a poor prognosis. Previous studies have also emphasized the association of delta frequency with poor prognosis (12,22,23).

Beta frequency failed to help differentiate the two groups with different prognoses.

In this study, electrographic seizures were detected in 7 patients. This finding, although was highly specific (97%) in predicting poor prognosis, had a low sensitivity (19%).

Although non-convulsive seizures are common in patients with decreased consciousness in ICUs and are thought to be associated with poor prognosis, some studies have failed to show this association. To detect all of these electrical seizure activities, continuous EEG monitoring is required, as many attacks cannot be detected within a short time of standard electroencephalography. Studies with standard EEG are thought to be incapable of demonstrating this relationship (21,24). Although standard EEG was used in this study, the role of these electrical activities in prognosis has been demonstrated. However, most of these electrical activities were probably missed.

Similarly, rhythmic and periodic activities were associated with poor prognosis. The specificity of this finding was high for poor prognosis (93%), but its sensitivity was low (32%). It is thought that some of these activities would not be recorded by the standard EEG.

It has also been shown that gamma activity was linked to the period of epilepticus status. In contrast, theta activity seemed to oppose the development of epilepticus status (25). In the rats study by Costa *et al*, analysis of video-electrocorticographic (v-ECoG) recordings and lesion expansion resulted in the relevant results: The early rise in gamma power before the onset of Status Epilepticu (SE) and the consequent rapid stabilization to below-the-baseline levels prior to the end of SE, both suggest that this ECoG band has a predominant role to play in defining the overall SE period. Further, the steady increase in theta power during SE, reaches the peak coinciding with the maximum duration of stage 4 convulsive seizures (25).

Limitations

One of the practical limitations of performing EEG in these traumatic patients will be technical restrictions, such as: technician's experience, other ICU devices artifacts (*e.g.*, ventilator), scalp and skin injuries in head trauma, which can limit the practicality of EEG to evaluate all traumatic patients.

Considering the short assessment interval from the TBI event (96 *hr*), the EEG may not completely describe and predict the prognosis. However, it can help estimate the prognosis, as the mentioned studies confirmed. Further, the situation at discharge is a predictor of the prognosis of TBI, as well. For example, Oliveira *et al* showed that the Glasgow outcome scale at discharge is a prognostic indicator in patients with TBI (26).

Conclusion

The results of this study showed that EEG parameters might provide valuable data considering the prognosis of decreased consciousness of patients with a head injury, also for the guidance of physicians and informing the patient's family. However, future studies with larger sample sizes are still required to investigate this association further. It is also recommended that similar studies with longer EEG durations be devised regarding electrographic events to predict prognosis better.

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Conflict of Interest

Authors have no competing interests to declare.

Availability of data and material (data transparency)

Authors declare that all data and materials and software application or custom code support their published claims and comply with the field standards.

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