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ORIGINAL ARTICLE / KLİNİK ÇALIŞMA

The Effect of Cognitive Functions on EEG in Patients with Juvenile Myoclonic Epilepsy

Jüvenil Miyoklonik Epilepsi Hastalarında Kognitif Fonksiyonların EEG Üzerine Etkisi

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Summary

Objectives: In this study, we aimed to show any effect of different types of cognitive activities on the electroencephalography (EEG) of patients with juvenile myoclonic epilepsy (JME).

Methods: 30 patients with JME who stated that their seizures are not effected by any mental activity were submitted to a 30-minute standard awake video EEG. A neuropsychological activation battery (NPA) was performed during the ongoing video EEG.

Results: The provocative effect of at least one test of NPA was observed in seven of 30 patients (23.3%) and the inhibitory effect of NPA was observed in nine of 30 patients (30.0%).

Conclusion: We demonstrated that increased attention, concentration, and the tests associated generally with the frontal lobe functions were crucial for provocating the EEG discharges. This may support the studies with neuropsychological tests and structural neuroimaging techniques showing focal cortical abnormalities mainly associated with frontal lobe in JME.

Key words: Juvenile myoclonic epilepsy; neuropsychological EEG activation.

Özet

Amaç: Bu çalışmada, jüvenil miyoklonik epilepsi (JME) hastalarında, değişik tipte mental aktivitelerin elektroensefalografi (EEG) üzerinde yapabileceği değişiklikleri göstermeyi amaçladık.

Gereç ve Yöntem: Herhangi bir kognitif aktivite ile nöbetinin tetiklendiğinin farkında olmayan 30 JME hastasına, 30 dakikalık standart uyanıklık video EEG çekimi yapıldı. EEG devam ederken, bir nörofizyolojik aktivasyon bataryası (NAB) uygulandı.

Bulgular: Otuz hastanın yedisinde (%23.3), NAB'nin en az bir testinin provokatif etkisi gözlenirken, 30 hastanın dokuzunda (%30.0), NAB'nin inhibitör etkisi gözlendi.

Sonuç: Artmış dikkat, konsantrasyon ve genel olarak frontal lob fonksiyonları ile ilişkili testlerin EEG deşarjlarını provoke etme açısından önemli olduğunu saptadık. Bu durum, JME'de özellikle frontal lob ile ilişkili fokal kortikal anormallikleri gösteren nörofizyoloji ve yapısal nörogörüntüleme teknikleri ile yapılan çalışmaları destekleyebilir niteliktedir.

Anahtar sözcükler: jüvenil miyoklonik epilepsi; nörofizyolojik EEG aktivasyonu.

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Introduction

Juvenile myoclonic epilepsy (JME) is classified as an idiopathic generalized epilepsy (IGE) with age related onset, characterized by myoclonic jerks associated with generalized tonic-clonic (GTC) and absence seizures; It accounts approximately 5-11% of all epilepsies.[1-6] Seizures are known to be triggered by conditions such as sleep deprivation, sudden awakening, fatigue, alcohol intake, flashing lights, menstruation and stres.[1-4] It has been also demonstrated that spesific or nonspecific complex cognitive activities such as calculations, constructive activities, drawing, playing strategic board games are able to precipitate seizures. [7-15] In the treatment of JME not only antiepileptic drug therapy but also identification and regulation of seizure precipitant factors are important.

In our study, we purposed to examine the effects of higher mental activities on the electroencephalography (EEG) of patients with JME who are not aware of any mental activity precipitating or inhibiting their seizures.

Materials and Methods

We evaluated 30 JME patients who had been followed up at the epilepsy outpatient clinic of Bakirkoy Reserch and Training Hospital for Psychiatry, Neurology and Neurosurgery. Inclusion criteria were age between 15-45 years, well documented diagnosis of JME according to criteria of the Commission on Classification and Terminology of the International League Against Epilepsy (ILAE), and having a minimum five year-education. All patients were interviewed for the seizure precipitating factors, especially for mental activities. Only the patients who stated that their seizures were not effected by any mental activity were included into the study. Presence of an illness other than JME and any abnormal neurological finding, use of any medication except antiepileptic drugs, occurrence of a GTC seizure within the last week and of myoclonic jerks or absence seizures within the last 24 hours were exclusion criteria.

After the ethical committee approval, risks for participation were explained and informed concents were obtained from the patients.

Electrode placements for video EEG recording were in accord with the international 10-20 Electrode System. All patients were submitted to a 30-minute standard awake video EEG recording, including 3-minute hyperventilation and intermitant photic stimulation. After the Standard EEG, a neuropsychological EEG activation battery (NPA) was performed during the ongoing EEG and video monitoring to show any effect of higher mental activity on the EEG. The battery test lasted approximately 35 minutes. Our neuropsychological test protocol was founded on those reported by Matsuoka et al.[11]

The NPA protocol included:

(1) Immediate memory test: Patients repeat four words aloud after listening
(2) Writing test
  (a) Spontaneous writing
  (b) Spontaneous writing blindfolded
  (c) Writing with dictation
  (d) Writing with dictation blindfolded
  (e) Writing by copying
  (f) Writing by foot
(3) Long-term memory test: Patients tried to remember the four words which they heard in the immediate memory test.
(4) Global attention test: Patients tried to repeat 4, 5, 6, 7, 8 numbers in sequence after listening.
(5) Speaking and reading
  (a) Repeating the words and sentences containing 2-4 words in Turkish
  (b) Reading letters
  (c) Reading silently
  (d) Reading aloud
(6) Complex attention test: Patients described a text after reading silently.
(7) Calculation
  (a) Mental arithmetic calculation
  (b) Written arithmetic calculation
  (c) Mental arithmetic problem solving
  (d) Written arithmetic problem solving
(8) Spatial construction
  (a) Drawing spontaneously
  (b) Copying figures
  (c) Copying a figure by matchsticks
  (d) Reproducting matchstick pattern spontaneously
(9) Gnosia: Patients try to recognise
  (a) Famous faces
  (b) Recognise objects
  (c) Recognise objects blindfolded

(d) Recognise fingers
(e) Recognise colours
(10) Praxia: Patients were evaluated by:
(a) Giving simple verbal orders
(b) Testing the use of objects
(c) Testing complex processes
(11) Testing complex plays: (make puzzles).

Data analysis

We analysed the EEGs in two steps, first the standard EEG during relaxed wakefulness state, and later EEGs during performing the NPA tests. To evaluate the effect of each NPA test on the EEG, the number of discharges per total recording time of a NPA battery test was divided by the number of discharges per standard EEG time.

The formulation was as: (number of discharges during a test / total recording time of the test) / (number of discharges during the standard EEG / total recording time of standard EEG).

We regarded the test as 'provocative' if the result was above 2.0, 'inhibitory' if below 0.5, 'without any effect' if between 0.5 and 2.0 as used in the study of Matsuoka et al.[11] Also, in the case of any epileptic discharge on the EEG during a test of a patient who did not have any discharge on the standard EEG, the test was regarded as 'provocative'. Otherwise, the condition was regarded as 'inhibitory' if any discharge was not found on the EEG during the NPA battery of a patient who had discharges on the standard EEG.

Statistical analysis

SPSS 10.0 statistical programme was used for the analyses. Descriptive statistical values (mean, standart deviation), Mann Whitney-U test for comparing the numerical data as well as the chi-square test for comparing the categorical data were used in the study.

Results

In this study, 30 JME patients (23 female, 7 male) were studied. The mean age was 23.83+6.41 and the mean duration of the disease was 7.5+5.5 years.

There was not any statistical difference between the female and male patients when comparing the age (p=0.25), seizure type (p=0.71), antiepileptic drug usage (p=0.98), duration of disease (p=0.14) and the duration of seizure-free time (p=0.53). However, the epileptiform discharges were present in 60.9% of the female and 14.3% of the male patients during the standard EEG. Also, the median number and the duration of spontaneous discharges per minute on the standard EEGs were statistically higher in the female compared to the male group (p=0.03; p=0.04).

We evaluated the patients in two groups, first group (Group 1) included the patients who showed epileptiform discharges on their standard EEGs and the second group (Group 2) had no such findings. Half of the patients (50.0%) belonged to group 1, and the other half belonged to group 2. The only statistical difference between the groups was sex distribution, there was a female predominance in group 1 (p=0.03). There was not any difference in other variables such as age (p=0.72), family history (p=0.33), type of seizure (p=0.17), treatment (p=0.42), duration of epilepsy (p=0.78), and duration of seizure free time (p=0.48). Six of the 15 patients in group 1 (40.0%) showed provocative and 9 of them (60.0%) showed inhibitory effect of NPA on the EEG. However, only one of the 15 patients in group 2 (6.7%) showed provocative effect of NPA which was during the complex-play test. There was not any effect of NPA on EEG of the remaining 14 patients (93.3%). Overall, the provocative effect of at least one test of NPA battery was observed in seven of 30 patients (23.3%) and they were all female. All of them belonged to group 1, except one patient. Otherwise, the inhibitory effect of NPA was observed in nine of 30 patients (30.0%) in whom eight of them were female (88.9%) and one of them was male (11.1%). All of these patients with inhibitory effect of NPA were from group 1. There was not any effect of NPA tasks on the EEG's of the remaining 14 (46.7%) patients (eight female; 57.1%, six male; 42.9%) in group 2.

The NPA tasks with provocative effect on seven patients were analysed and results revealed that; a single patient was affected by 11 tasks; whereas two patients were sensisitive to two and four patients, to a single test. Those tests were oriented to global attention, complex game play, figure copying, object recognition blinfolded, complex attention, complex processes, repeating, sentence copying, finger recognition, written calculation, mental calculation, long-term memory, writing blindfolded spontanously, and writing blindfolded with dictation. They are shown in Table 1.

We did not observe the provocative effect of any NPA task when the patients regarded the task as difficult to do and thought that they could not do and did not deal with it. The

Table 1. The NPA tests with the provocative effect

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Global attention							
	–	–	–	–	–	+	+
Complex game play	+	–	–	–	–	+	–
Figure copying	–	–	+	–	–	–	+
Object recognition blindfolded	–	–	–	–	+	–	+
Complex attention	–	–	–	–	–	–	+
Complex processes	–	+	–	–	–	–	–
Repeating	–	–	–	–	–	–	+
Sentence copying	–	–	–	+	–	–	–
Finger recognition	–	–	–	–	–	–	+
Written calculation	–	–	–	–	–	–	+
Mental calculation	–	–	–	–	–	–	+
Long-term memory	–	–	–	–	–	–	+
Writing blindfolded spontanously	–	–	–	–	–	–	+
Writing blindfolded with dictation	–	–	–	–	–	–	+

epileptiform discharges of our patients which were seen on the standard EEGs or during the NPA battery application were only interictal, we did not observe any type of seizure activity throughout the study.

Discussion

The seizures of JME patients are able to be precipitated by stress, anxiety, expectation, thinking, decision making or concentration in addition to sleep deprivation, awakening, alcohol intake, flashing lights.[1-4] The relation between spontaneous epileptiform activity and cognitive functions has been studied with an increasing interest since present.[7-14]

Seizures induced by higher mental activities have encouraged studies which were designed with special EEG activation methods to show any effect of mental tasks on the EEG of epileptic patients.[11-14] Matsuoka et al.[11] used a neuropsychological method testing for various mental activities as a part of routine EEG examination for patients with epilepsy. They reported that 36 of 38 patients who had epileptic discharges provoked by NPA tests were related to IGE's including 22 patients with JME. In our study, we aimed to explore the effects of mental functions on EEG of the patients with JME who were not aware of any mental activity precipitating or inhibiting their seizures.

The number and the duration of spontaneous discharges per minute in the standard EEG was statistically higher in the female compared to male patients although there was not any statistical difference in other variables. The female predominance of the study may contribute to this result. At least one NPA test provocated EEG discharges in the seven of 30 JME patients (23.3%) in our study. Matsouka et al.[11] showed the provocative effect of NPA in the 46.7% of JME patients. In another study of patients with JME, Karachristianou et al.[12] reported that 23 of 30 patients (76.6%) showed EEG activation in response to at least one neuropsychological task. In a more recent paper, Guaranha et al.[14] showed that 29 of the 76 patients with JME (38.2%) were affected by at least one cognitive task of video-EEG neuropsychological protocol. A distinguishing feature from the similar studies in the literature, is that patients with any previous perception of mental activity precipitating or inhibiting their seizures were not included in the present study. The lower incidence of activatory effect of NPA in our study may be explained on that basis.

In a paper, Senanayake et al.[15] reported that the frequency of epileptiform anomalies were increased during the NPA task protocol in patients with JME, especially when the patients were solving puzzles. Matsuoka et al.[11] found that mental acitivities mainly associated with the use of hands such as writing, written calculation, and spatial construction provoked discharges in 46.7% of their JME patients.Similarly, Guaranha et al.[14] showed that the action programming tasks were more effective than thinking in provoking epileptiform discharges and suggested that the more tissue

involved in a network with more complex function may explain the greater probability of the provocative effect. However, Karachristianou et al.[12] showed that both manual (doodling figures, written calculations) and non-manual activities (solving arithmetic problems mentally, mental spatial manipulaton) activated the epileptogenic discharges in the EEG of patients with JME. In our study, each of the most provocative tests including global attention, complex game playing, figure copying, and object recognition blinfolded induced epileptiform discharges in two patients. We concluded that these provocative tasks which are shown in Table 1 are associated with the frontal, parietal and temporal lobe activities, but they primarily affect the frontal areas. The NPA battery of other similar studies did not include the global attention test, however the other three activatory tests were all manual activities in accordance with the previous reports.[11-14] Matsouka et al.[11] reported that the provocative effect of NPA tasks was observed in 6.6% of the patients without paroxysms and 9.6% of the patients with paroxysms on the standard EEG. In our study however, although the NPA tasks induced provocative effect in a similar percentage of patients (6.7) without discharges on standard EEG; affinity to provocation was present in 40% of the patients with discharge. The patients with discharges on standard EEG obviously were more affected by mental tasks.

Matsouka et al.[11] reported 63.9% of inhibitory versus 7.9% provocative effect of NPA tests in a population of 480 patients with epilepsy. On the other hand, Guaranha et al.[14] observed the inhibitory effect was more frequent than the provocative effect as such that. Twenty-eight of the 31 patients (90.3%) with epileptiform discharges on standard EEG presented inhibitory effect. The mental calculation was a powerful inhibitor which may be explained by the activation of parietal cortex without motor involvement. However, a nonspesific effect of major categories of tasks seemed to account for the significant inhibition in most of the patients. The authors proposed that this may show the relation of the inhibitory effect with the cognitive activation in general, suggesting widespread inhibitory pathway, such as cortical-thalamic feedback loops.[14] Since these inhibitory tasks also elicited epileptogenic discharges, it is concluded that the same functions could be exitatory or inhibitory depending on the state of network at that moment. In our study, nine of the 30 patients (30.0%) showed inhibitory NPA effect. They were all subjects with the epileptiform discharges on their standard EEGs. Although this incidence is quite high, the 'inhibitory effect' can not be clearly seperated from the 'no effect' result. Also, apparent inhibitory affects are reported to be difficult to distinguish sufficiently from spontaneous fluctuations of the epileptogenic discharges. To account the spontaneous fluctuations, Beniczky et al.[16] divided the baseline EEG into 5-min epochs and calculated the 95% confidence interval for the baseline EEG discharges. Modulation was assumed when the number of EEG discharges during any 5-min test period was outside the 95% confidence interval. Cognitive tasks seemed to inhibit the EEG discharges in 94% of the patients, and to provoke in 22%. However, inhibition was found in only 29% of the patients when the spontanous fluctuations were accounted.

In summary, we found that at least one of the NPA tests associated mainly with the attention and frontal lobe activities provocate the subclinical epileptiform EEG discharges in all patients with the provocative NPA effect. Matsuoka et al.[11] concluded that the action programming type activities were crucial among the precipitating events which were mental activities that needed frontal lobe processes with increased attention similar to our results.

Interestingly, we did not observe the provocative effect of any NPA task when the patients regarded the task as difficult to do and thought that they could not do and did not deal with it which may show that the attention and concentration for a task results in the increase of subclinical EEG discharges.

We concluded that the increased attention, concentration, and the tests associated generally with the frontal lobe functions were critical for provocating the subclinical EEG discharges. This may support the studies with neuropsychological tests and advanced structural neuroimaging techniques showing focal cortical abnormalities mainly associated with frontal lobe in patients with JME.[17-23]

Results of ours and similar studies seem to be challenging for further trials designed with tasks more spesific to the critical regions of cortical network.

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