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Frontal lobe cognitive functions and electroencephalographic features in juvenile myoclonic epilepsy

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ABSTRACT

Purpose: The study aimed to examine the relationship between frontal lobe functions and interictal electroencephalography (EEG) discharge characteristics of patients with juvenile myoclonic epilepsy (JME).
Method: Thirty patients with JME who had EEG with asymmetrical generalized discharge (aEEG), 15 patients with JME who had EEG with symmetrical generalized discharge (sEEG), and 15 healthy controls were included in the study. To evaluate attention, the digit span and Corsi block tests were used; to evaluate memory, we applied verbal and visual memory tests; to evaluate frontal lobe functions, we used clock drawing, verbal fluency, the Stroop test, trail making, mental control, and antisaccadic eye movement tests as well as the continuous performance (CPT) tests.
Ethical Considerations: The research was approved by the Research Ethics Committee of the Bakirkoy Research and Training Hospital for Psychiatry, Neurology, Neurosurgery, with protocol number: 41340010/4891-262, date: 05.02.2013.
Results: The mean age of the 45 patients with JME was 22.89 ± 6.77 years, and 34 (75.6%) were female. The age at onset of seizures and disease duration of the patients with JME was 15.56 ± 4.06 years (range, 9–26 years) and 7.20 ± 5.59 years (range, 1–25 years), respectively. All patients were under valproate (VPA) treatment, and the mean VPA dosage was 783.33 ± 379.14 mg/day. Patients with JME scored worse than the control group in attention, memory, and frontal lobe functions. In patients with aEEG, scores of attention, memory, and frontal lobe function tests were lower than in patients with sEEG; however, with the exception of CPT, they were not statistically significant.
Conclusion: Cognitive functions in JME have been shown to be impaired. Furthermore, we concluded that the frontal lobe cognitive functions may be worse in patients with aEEG than in patients with sEEG. Further studies in patients with JME with aEEG abnormalities may lead to a better understanding of the pathophysiology of JME.

1. Introduction

Juvenile myoclonic epilepsy (JME) is an idiopathic generalized epilepsy (IGE) syndrome characterized by myoclonia, absence, and generalized tonic–clonic seizures (GTCS) [1]. Ictal and interictal electroencephalography (EEG) demonstrates fast, generalized, usually irregular wave and spike and polyspike and wave discharge activities [1,2]. Further focal or asymmetric abnormalities on EEG occur in approximately 30–40% of patients [3,4]. Photosensitivity is frequently seen, and the response to appropriate drug treatment is generally good [5].

In recent years, it is emphasized that patients with JME are affected by cognitive functions. Sonmez and Ataklı demonstrated cognitive impairment in patients with JME compared with healthy subjects [6]. Piazzini et al. found that the tests they designed for the evaluation of frontal lobe cognitive functions of patients with JME determined cognitive impairment similar to patients with JME when applied to patients with frontal lobe epilepsy [7]. The most important risk factors for the cognitive impairment were reported as age at seizure onset, family history, and the existence of absence seizures. The relation between the cognitive impairment and existence of spike–wave discharges on EEG was not exactly understood [8]. Demir et al. demonstrated that frontal lobe functions were important for provoking the EEG discharges [9].

We aimed to investigate whether the frontal lobe was more affected, and if so, which functions were affected more prominently in patients whose EEGs showed persistent asymmetry for a particular side.

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2. Method

2.1. Study ethics and participant recruitment

The participants consisted of voluntary patients with JME as diagnosed according to the International League Against Epilepsy classification who were attending an epilepsy outpatient clinic [10]. Forty-five voluntary patients who had normal neurological examinations and cranial magnetic resonance imaging (cMRI), generalized spike and wave discharges in at least two EEGs performed with an interval of one month, no myoclonic seizures in the last 24 h, and no generalized seizure in the last seven days were included in the study. All participants were under valproate (VPA) treatment. We excluded patients with learning disabilities, those who were illiterate, those using drugs or substances other than VPA, and patients with any systemic disease that affects cognitive functions.

Subjects were divided into two groups according to seizure frequency: (1) patients with at least one generalized tonic–clonic seizure per year or two and more myoclonic seizures per month despite appropriate and enough dosage of treatment and appropriate living conditions and (2) patients without any seizure.

2.2. Study design

The demographic and clinical features of patients including age at onset and duration of disease, history of febrile convulsion, family history, and seizure type were noted. Electroencephalography was recorded using a 21-channel Nihon Kohden 1100K device with the 10–20 international recording system. All EEGs were evaluated by a neurologist who was also a clinical electrophysiology specialist. Participants were divided into two groups based on the type of discharges found in at least two EEGs recorded with at least 1-month interval: those who had EEG with symmetric generalized spike and wave discharges (sEEG) and those with asymmetric generalized spike and wave discharges (aEEG). Electroencephalography showing generalized spike and wave discharges with more than 50% amplitude difference between the right and left hemispheres was accepted as aEEG. Patients whose EEG findings were normal or with focal discharge or combined symmetrical and asymmetrical discharges were excluded (Table 1).

The control group consisted of 15 participants who had normal neurological examination, did not have any systemic disease affecting cognitive function, and did not use any drug or substance. The neuropsychological test battery (NPTB) included tests evaluating verbal attention (digit span test), visual attention (Corsi block test), verbal memory (modified Rey auditory verbal learning test), visual memory (Wechsler memory scale—nonverbal memory subtest), and frontal lobe executive functions (clock drawing test, Stroop test, verbal fluency animal test, verbal fluency fruit/human test, trail making tests A–B, nonverbal fluency test, continuous performance test (CPT), mental control test, antisaccadic eye movement test). The NPTB was administered to both the patient and control groups.

Table 1
Evaluation of demographic characteristics.

		Group with aEEG (n = 30)	Group with sEEG (n = 15)	p*
Age (years)		22.70 ± 6.93	23.27 ± 6.67	0.795[a]
Sex	Woman	23 (76.7%)	11 (73.3%)	1.000[c]
	Man	7 (23.3%)	4 (26.7%)	
Level of education	Primary school	9 (30.0%)	4 (26.7%)	
	Secondary school	7 (23.3%)	4 (26.7%)	1.000[c]
	High school	7 (23.3%)	4 (26.7%)	
	University	7 (23.3%)	3 (20.0%)	
Age at seizure onset		15.47 ± 3.88	15.73 ± 4.54	0.838[a]
Disease duration		7.10 ± 5.77	7.40 ± 5.41	0.904[b]
Drug dosage		825.00 ± 400.16	700.00 ± 330.04	0.391[b]
Febrile convulsion story	None	25 (83.3%)	14 (93.3%)	
	Yes	5 (16.7%)	1 (6.7%)	0.647[c]
Family epilepsy story	None	21 (70.0%)	10 (66.7%)	
	Yes	9 (30.0%)	5 (33.3%)	1.000[c]
Consanguineous marriage	None	22 (73.3%)	12 (80.0%)	
	Yes	8 (26.7%)	3 (20.0%)	0.726[c]

[a] Student's *t* test.
[b] Mann–Whitney U test.
[c] Fisher's exact test.
* $p < 0.05$.

2.3. Data analysis

The Number Cruncher Statistical System 2007 and Power Analysis and Sample Size 2008 Statistical Software programs were used for the statistical analysis. Besides the descriptive statistical methods, for two-group comparisons of parameters with and without normal distribution, Student's *t* and Mann–Whitney U tests were used, respectively. The Kruskal–Wallis test was used for the comparison of three and more groups without normal distribution, and the Mann–Whitney U test was used to determine the group causing the difference. Fisher–Freeman–Halton and Fisher's exact tests were used for the comparison of three and more groups with normal distribution. Statistical significance was evaluated at $p < 0.01$ and $p < 0.05$.

3. Results

Of the 45 patients with JME, the mean age was 22.89 ± 6.77 years; 34 (75.6%) were female. The mean age of the 15 participants in the control group, 11 of whom (73.3%) were female, was 23.20 ± 4.72 years. There were no statistically significant differences between age, sex, and education status ($p > 0.05$).

Age at onset of seizure and disease duration of the patients with JME was 15.56 ± 4.06 years (range, 9–26 years) and 7.20 ± 5.59 years (range, 1–25 years), respectively. The mean VPA dosage was 783.33 ± 379.14 mg/day with a range of 250–1500 mg/day. Six patients (13.3%) had a history of febrile convulsions, 14 patients (31.1%) had a family history of epilepsy, and 11 patients (24.4%) had a history of consanguineous marriage.

There were no statistically significant differences between the participants with aEEG and sEEG with regard to age, sex, education status, age at onset of seizure, duration of disease, drug dosage, history of febrile convulsion, family history of epilepsy, and consanguinity between the parents ($p > 0.05$).

3.1. Cognitive test results

1- *Attention*: Verbal and nonverbal attention test scores were statistically lower in patients with JME compared with those of the control group ($p < 0.05$). However, there was no statistically significant difference between participants with aEEG and sEEG ($p > 0.05$) (Table 2).

2- *Memory*:

a) Verbal memory: There was no statistically significant difference of recall, recognition, and total memory scores between the patients with JME and control group and between the groups with aEEG and sEEG ($p > 0.05$). Immediate memory, repeat count, item count, and total learning scores were statistically lower in the patients with JME compared with those of the control group; however, there was no difference between the aEEG and sEEG groups.

b) Visual memory: Short-term memory (STM) score was significantly lower in patients with JME compared with that of the control group and in the aEEG group compared with that of the control group ($p < 0.005$). However, there was no statistically significant difference between the aEEG and sEEG groups or between the sEEG group and the control group ($p > 0.005$) (Table 3).

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