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Research Article

Differences in Cognitive Functioning of Patients Related to the Type of Epilepsy, Time of Onset and Type of Therapy

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Abstract

Introduction: Our aim in this paper was to investigate and establish the differences in general cognitive abilities among children taking into account different types of epilepsy.

Methods: It was a historical prospective study involving 51 patients. The patients were children treated for the diagnosis of epilepsy in the period of 12 years, from January 1, 1994 to December 31, 2006. The information was collected by way of reviewing patients' medical records.

Results: The study involved 51 patients with epilepsy. There were 22 patients (43.1%) with partial, and 29 (56.9%) with generalized epilepsy number of examinees, in 22 patients (43,1%) intellectual difficulties were present, and in 29 (56,9%) there were no intellectual difficulties, but the difference was not statistically significant ($\chi 2 = 0,706$; df = 1; P = 0,401).

Conclusion: With patients with lower cognitive abilities, polytherapy is often applied, and they spend more time in rehabilitation than patients with higher cognitive abilities. In order to successfully treat epilepsy there is a need for a better definition of the clinical phenotype and early inclusion of correct treatment. Treatment should not be reduced to control the seizures, but is an essential psychological aspect of illness because fear of the next attack cannot be ignored.

Keywords: *Epilepsy; Cognitive Functioning; Rehabilitation; Type of Therapy*

Introduction

Epilepsies represent chronic diseases of the brain characterized by multiple causes, repeated seizures and, as a rule, associated with electroencephalographic (EEG) abnormalities. The chronicity, i.e. recurrent seizures, is one of the essential properties of epilepsy [1,2]. The prevalence of epilepsy in the general population ranges from 0.5% to 1%, being about double in childhood only [1]. Almost all major central nervous system disorders may be the cause of epilepsy (congenital malformations, infections, tumors, vascular diseases, degenerative diseases, metabolic disorders or traumas). In childhood, the most common cause is birth or neonatal trauma, followed by vascular malformations, congenital disorders (including metabolic diseases), head traumas, infections and neoplasms. Almost 70% of epilepsies are the so called idiopathic or cryptogenic, where the exact cause cannot be identified. In recent decades, the development of genetics in the area of epilepsy has been particularly interesting. It has been established that there are at least 100 different genetic disorders which can be associated with clinical manifestations of epileptic seizures, and at present gene loci abnormalities have been shown to be associated with several specific epileptic syndromes [3-5].

The International League Against Epilepsy (ILAE) Classification of the Epilepsies and Epileptic Syndromes classifies epilepsy into:

- Focal (partial);
- Generalized;
- Unknown (cannot be established whether focal or generalized);
- The so called special syndromes, i.e. situation-related seizures (ILAE, 1989).

It is generally thought that partial epilepsies are more common (around 60%) than generalized ones (40%) [6]. The disease prognosis is mostly favorable, with the average disease duration of about 10 years. In 50% of the affected the disease lasts for even a shorter period of time, sometimes for less than 2 years [7]. The treatment can be medicamentous and surgical [5,8,9]. It is thought that about 70% of patients have a well controlled disease with monotherapy. Out of the remaining 30%, about one half are stable using two or three antiepileptic drugs. Out of the remaining 15%, 5% are candidates for surgery, and 10% are treatment failures in whom the disease transforms into its malignant form. The most important indications are the suspicion of drug intoxication, recurrent seizures despite therapy, and extremely long-lasting polytherapy [1,10]. Behavioral disorders are present in 30 - 50% of children with epilepsy, while their prevalence in the general population is around 8.5%. It is well recognized in clinical practice that many children with epilepsy have disorders of various cognitive functions, ranging from learning difficulties, poor outcomes and achievement at school, all the way to intellectual impairments [11,12]. It has been estimated that 20 - 30% of children with epilepsy have intellectual difficulties [13-19].

Aim of the Paper

Our aim in this paper was to investigate and establish the differences in general cognitive abilities among children taking into account different types of epilepsy (partial vs generalized), time of onset, type of therapy, and time spent for rehabilitation at the Department for Psychophysiological and Speech Disorders, Primary Health Care Center in Mostar.

Hypotheses:

- It is supposed that there will be a statistically significant difference in cognitive abilities in children with respect to the type of epilepsy and that lower cognitive abilities will be more frequently encountered in children with generalized epilepsy;
- It is supposed that there will be a statistically significant difference in cognitive abilities in children with respect to the time of onset of epilepsy; worse cognitive functioning will be more common with earlier onset of the disease;
- It is supposed that there will be a statistically significant difference in cognitive abilities in children with respect to the administered therapy; worse cognitive functioning will be more common in children on polytherapy;
- It is supposed that there will be a statistically significant difference in cognitive abilities in children with respect to the length of time spent on rehabilitation; children with lower cognitive abilities would have spent much more time on rehabilitation.

Methods

The study took place at the Department for Psychophysiological and Speech Disorders, Primary Health Care Center in Mostar. It was a historical prospective study involving 51 patients. The patients were children treated for the diagnosis of epilepsy in the period of 12 years, from January 1, 1994 to December 31, 2006. The information was collected by way of reviewing patients' medical records.

The observed parameters of interest were as follows:

- Type of epilepsy (partial or generalized);
- Time of onset of epilepsy;
- Type of therapy (monotherapy, polytherapy);
- Length of rehabilitation;
- Patient's cognitive abilities.

Statistical data processing

SPSS for Windows (version 13.0, SPSS Inc, Chicago, Illinois, USA) was used for statistical analysis, as well as Microsoft Excel (version 11, Microsoft Corporation, Redmond, WA, USA).

Results

The study involved 51 patients with epilepsy. There were 22 patients (43.1%) with partial and 29 (56.9%) with generalized epilepsy number of examinees, in 22 patients (43,1%) intellectual difficulties were present, and in 29 (56,9%) there were no intellectual difficulties, but the difference was not statistically significant (χ^2 = 0,706; df = 1; P = 0,401). With regard to the prevalence of intellectual difficulties by epilepsy types, in generalized epilepsy intellectual difficulties were present in 13 patients (59,1%), while in partial epilepsy they were present in 9 (40,9%), which was not statistically significant either (χ^2 test = 0,078; df = 1; P = 0,780).

Cognitive status	Number (%) of patients by type of epilepsy		Total
	Partial epilepsy	Generalized epilepsy	
Neat cognitive status	13 (44,8%)	16 (55,2%)	29
Intellectual difficulties	9 (40,9%)	13 (59,1%)	22
Total	22 (43,1%)	29 (56,9%)	51

Table 1: *Prevalence of intellectual difficulties by the type of epilepsy.*

The following table presents the prevalence of forms of cognitive status in partial and generalized epilepsy in patients enrolled in our study (χ^2 test = 3,068; df = 4; P = 0,587; Fisher's exact test) (Table 2).

Cognitive status	Number (%) of patients by type of epilepsy		Total
	Partial	Generalized	
Neat cognitive status	13 (44,8%)	16 (55,2%)	29
Borderline intellectual disabilities	0 (,0%)	2 (100,0%)	2
Mild intellectual disabilities	3 (75,0%)	1 (25,0%)	4
Moderate intellectual disabilities	4 (36,4%)	7 (63,6%)	11
Severe intellectual disabilities	2 (40,0%)	3 (60,0%)	5
Total	22 (43,1%)	29 (56,9%)	51*

Table 2: *Display of cognitive status with respect to the type of epilepsy.*

The average age of onset of epilepsy in our study was 4,00 ± 8,50 years (median ± interquartile range). The earliest age of onset of epilepsy was 0.33 years, and the latest was 15 years. Comparing the age of onset of epilepsy with cognitive functioning of patients, it was found that the disease tended to appear at an earlier age in cases with poor cognitive functioning, and that proper cognitive functioning was associated with the disease appearing at a later age (Kruskal-Wallis test = 12,104; P = 0,017) (Figure 1).

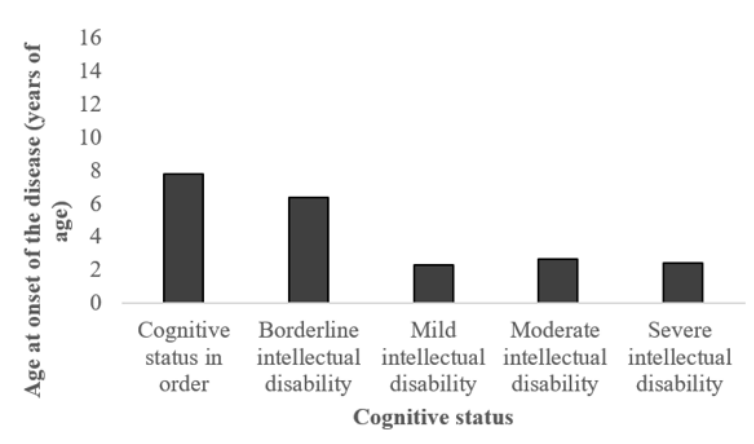

Figure 1: *Distribution of cognitive status (cognitive status in order; borderline intellectual disability; mild intellectual disability; moderate intellectual disability; severe intellectual disability) by the age of onset of epilepsy.*

There was a statistically significant difference in the type of therapy as to the cognitive functioning of the studied patients. In those with normal cognitive status, monotherapy was used in 25 patients (86,2%), and polytherapy in 4 patients (13,8%). In those with severe intellectual disability monotherapy was not used at all, while polytherapy was used in 5 patients (100,0%) (χ^2 test = 23,427; df = 4; P < 0,001; Fisher's exact test) (Table 3).

Cognitive status	Number (%) of patients according to the type of treatment		Total
	Monotherapy	Polytherapy	
Neat cognitive status	25 (86,2%)	4 (13,8%)	29
Borderline intellectual disabilities	2 (100,0%)	0 (,0%)	2
Mild intellectual disabilities	4 (100,0%)	0 (,0%)	4
Moderate intellectual disabilities	3 (27,3%)	8 (72,7%)	11
Severe intellectual disabilities	0 (,0%)	5 (100,0%)	5
Total	34 (66,7%)	17 (33,3%)	51*

Table 3*: Distribution of cognitive status with regard to therapy (monotherapy or polytherapy).*
**χ^2 test = 23,427; df = 4; P < 0,001 (Fisherov exactly test).*

The average duration of rehabilitation was 0,50 ± 4,00 years (median ± interquartile range). In this study, the period of rehabilitation ranged from 0 to 5 years. Comparing the duration of rehabilitation with patients' cognitive status it was found that those with poorer cognitive status statistically significantly spent more time in rehabilitation programs than those with normal cognitive status (Kruskal-Wallis test = 36,968; P < 0,001).

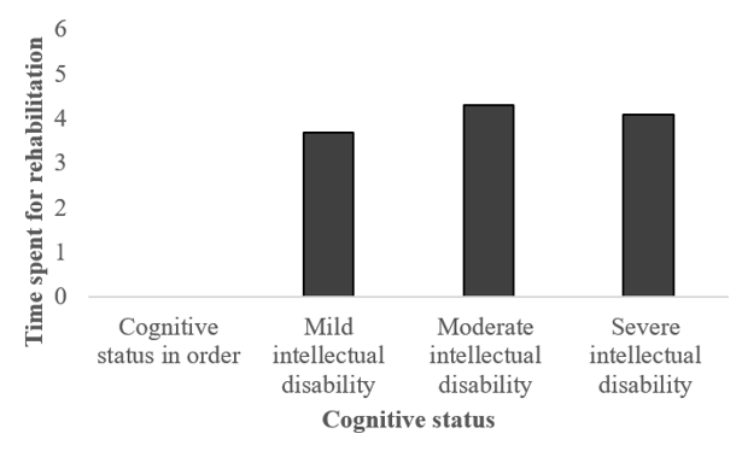

Figure 2: *Distribution of cognitive status (cognitive status in order; borderline intellectual disability; mild intellectual disability; moderate intellectual disability; severe intellectual disability) by the duration of rehabilitation.*

Comparing the duration of rehabilitation with type of therapy it was shown that polytherapy was significantly more common in patients who had spent more time on rehabilitation [4,0 ± 2,25 years (median ± interquartile range)] in contrast to those on monotherapy [0,0 ± 2,0 years (median ± interquartile range)] (Mann-Whitney U test = 132,500; P = 0,001).

Discussion

Epilepsy is more than just seizures. In a Swedish study, the frequency of intellectual disability in patients with epilepsy was 38% [20-24]. In our study, in 22 (43,1%) intellectual disabilities were found, while the remaining 29 (56,9%) were free of intellectual disabilities, which was not a statistically significant difference (P = 0,401). While some studies reported the difference in cognitive status between partial and generalized epilepsy, with poorer outcomes observed in generalized epilepsies [25], there were studies reporting no difference in the mean value of intelligence quotient between those with partial and those with generalized epilepsy [26]. There were more patients with intellectual disabilities in the group of those with generalized epilepsy [13 (59,1%)] compared to the group with partial epilepsy [9 (40,9%)], but there was no statistically significant difference in cognitive status distribution by epilepsy types (P = 0,587).

It is well known that epilepsy at an early age may expose the brain to abnormal nervous activity during a critical period of brain maturation and consequential diffuse structural and functional damage of the brain [27]. In our study, relating the age of onset of epilepsy to cognitive status, we found that earlier age at onset of the disease was associated with poorer cognitive status, and if the disease appeared later cognitive status was better. In the study of O'Leary., *et al*. in 73% of children who had intellectual disabilities accompanying epilepsy (regardless of the type), epilepsy appeared before the age of 5 years [28]. Comparing our results with these, we can say that severe, moderate and mild intellectual disabilities were present in those in those with the onset of epilepsy before 5 years of age.

All antiepileptic agents have side effects affecting congitive functioning and these are usually moderate in case of monotherapy and if prescribed therapeutic regimen is abided by, but the induced damage may increase with polytherapy [29,30]. Out of the total number, 25 examinees (86.2%) with normal cognitive status used monotherapy, in contrast to 5 examinees (100%) with severe intellectual disabilities who were treated with polytherapy (P < 0,001).

When the duration of rehabilitation was related to cognitive status, it was shown that children with moderate and severe intellectual disabilities were longer on rehabilitation than those with mild intellectual disabilities ($P < 0,001$). The average duration of rehabilitation was 0,50 ± 4,00 years.

Further statistical data processing showed that there were differences in the cognitive status of patients with epilepsy with regard to their age at onset of the disease and type of administred therapy. Worse cognitive status was more common with earlier disease onset, and polytherapy is thus more often applied in patients with more severe intellectual disabilities. There are numerous multicentric studies reporting that early treatments can improve the probability of achieving adequate control of seizures, since active epilepsy demonstrates a natural tendency to progress. When starting a treatment, monotherapy is preferred to polytherapy [7,31,32], especially considering the fact that in this study a greater number of examinees with intellectual disabilities used polytherapy. In children, adequate socialization is often difficult to achieve, and active involvement of parents, teachers and psychologists is therefore required, especially in the light of the fact that timely introduction of therapy would reduce patients' anxiety as well. Only the comprehensive care and concern about our patients' overall success, all the way from seizure control to socialization, will ultimately lead to better quality of life of both the patients and their families [33,34].

Conclusion

1. There is not any statistically significant difference in cognitive status with regard to the type of epilepsy.
2. Worse cognitive status is encountered with an earlier onset of epilepsy.
3. In patients with severe intellectual disabilities polytherapy is administered.
4. Patients with worse cognitive status spent more time in rehabilitation, in contrast to those with better cognitive status.

Disclosure

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