

Children With Partial Epilepsy And Its Effect On Reading And Writing

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Abstract— Introduction. Several neuropsychological deficits have been observed in children with partial epilepsy crises, however, few studies have focused on their reading and writing aspects of them. Objective. To assess the alterations in reading and writing of children that were recently diagnosed with partial epilepsy. Methods. A sample of 19 children between ages 6 to 8 with a recent diagnosis of partial epilepsy under valproic acid treatment were compared with a Control group. The intelligence scale of Wechsler WISC-R and the battery Macotela (IDEA) were employed. Results. There were no significant differences between the two groups when the scale of Wechsler was applied. When the Macotela battery was applied, differences in dictation and redaction were found as well as some omissions. Conclusions. Children with a recent diagnosis of partial epilepsy under treatment with valproic acid present a verbal, executive, and total intellectual coefficient at the same levels as the control group, with minimal alterations in the learning battery.

Keywords: *partial epilepsy, children, cognitive damage, learning.*

I.- INTRODUCTION

According to the World Health Organization, epilepsy is defined as a chronic and repetitive disorder, secondary to neuronal discharge from multiple etiologies, with a myriad of epileptic crises as clinical manifestations and electroencephalographic findings as preclinical manifestations [1].

Epilepsy is relatively frequent in the young population with a prevalence of 3.4 – 11.3 cases per 1000 children [2,3]. However, prevalence can vary between countries, in Mexico oscillating between 1.8 and 2%, which represents more than half a million cases [4]. Regarding types, partial beginning epilepsy constitutes the most frequent one and represents around 65% of all cases of epilepsy [5].

Neurocognitive alterations are common in consequence of child epilepsy [6]. The more common are memory impairment, slowness, comprehension issues, verbal expression, the deficit in logic reasoning, behavioral alterations, social interactions, and attention deficit [7-12]. All of the above can be a

direct consequence of epilepsy, but also secondary to pharmacological treatment and psychosocial factors [6-12].

Adverse effects of antiepileptic drugs (AED) are a common issue and limit significantly the quality of life of epileptic patients. Thus, to a great proportion of them, the adverse effects of AED are their first priority and cause a clear social stigma [13, 14]. Studies carried out with epileptic children show that the biggest issue to them and their parents are the neurocognitive and behavioral aspects derived from treatment with AED [13, 14]. If treated carefully and early, children with epilepsy can reach a good level of basic education similar to the general population [16-18]. Research in the neuropsychological component of children with partial epilepsy can be ambiguous, thus it is of great interest to carry out a study focused on analyzing the effect of the disease over learning, mainly in reading and writing.

II.- MATERIAL AND METHODS

Subjects.

The sample was taken from the neurology service from the Child Psychiatric Hospital "Dr. Juan N. Navarro" in Mexico City. All pediatric patients were under pharmacological treatment with valproic acid for at least one month. The children from the Control Group were taken from a local school under supervision from teachers. Special consideration was taken to choose right-handed children. All parents and children were informed about the study and signed informed consent.

Instruments.

The neuropsychological assessments were performed by means of the instruments WISC-R [19] and the IDEA battery [20]. WISC-R measures three components, the first one is verbal comprehension, education-based knowledge, and the capacity to apply verbal communication in novel situations; the second one focuses on spatial and perceptive organization;

the third one measures the capacity to remain focused on a task. The IDEA battery is an instrument developed and tested for the Mexican population and allows to evaluate different two kinds of errors in writing, the first one is incorrect or inadequate employment of grammatical rules and the second one refers to specific discriminative mistakes.

Statistical analysis.

All variables were tested for Normality and descriptive and inferential statistics were developed accordingly. Fisher exact test was employed for testing differences between sex, Mann-Whitney U to compare ages, and lastly X² to compare educational level. A value of P < 0.05 was considered for statistical differences. GraphPad Prism 7.0 was employed for all analyses.

III.- RESULTS

The Experimental Group was formed by 19 children, 10 males and 9 females, and the Control Group by 19 children, 11 males and 8 females. The Experimental Group presented an age mean = 7.25 and Control group an age mean = 7.35. Not presenting differences in age nor sex distribution; both groups were homogeneous.

Analyzing data from the WISC-R test, in executive function and verbal profiles no significant differences were found (Fig. 1 and Fig. 2), the same was found in the analysis of comprehension of writing (Fig. 3). In contrast, the incomprehension of hearing the parameter that showed a significant change was word dictation (p < 0.04).

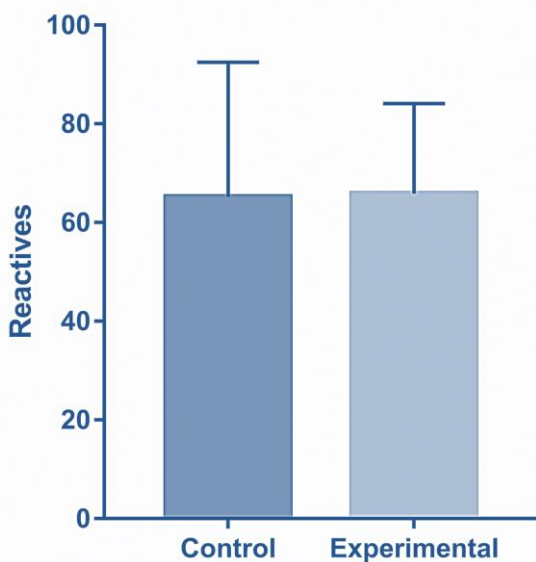


Figure 1. Comparison between Cases and Controls in the WISC-R test's executive scale.

Regarding the IDEA battery, each subset was analyzed; the children from the Experimental group presented significant less punctuation than the ones in

the Control group in the subset "Mistakes on grammatical orthography" and "Omission of punctuation signs" (p < 0.05), in the subset of "Specific mistakes in dictation" the Experimental group presented a significant difference compared with the Control group (p < 0.01). No significant differences were found when analyzing accents omission, punctuation signs omission, the substitution of capital letters, incorrect separation of syllables, and addition of error rules (Table 1).

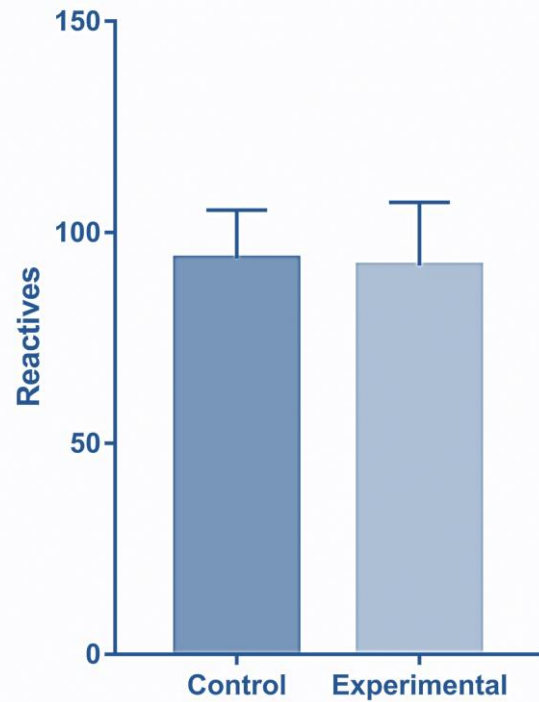


Figure 2. Comparison between Cases and Controls in the WISC-R test's verbal scale.

Table 1. P values of the comparison between Cases and Controls in the IDEA battery.

	Copy	Dictate	Redaction
Orthographic substitution	0.83	0.59	0.18
Orthographic omission	0.38	0.22	0.01*
Accent omission	0.68	0.25	0.89
Punctuation signs omission	0.86	0.76	0.03*
Upper- and lower-case errors	0.33	0.08	0.67
Syllable separation errors	0.35	0.16	0.16
Rule summatory errors	0.51	0.17	0.06
Specific errors	0.90	0.001*	0.09
Transposition	0.16	0.13	0.33
Omission	0.65	0.17	0.96
Substitution	0.41	0.88	0.42
Inversion	0	0.13	0.04*
Union	0.11	0.02*	0.40
Specific summatory errors	0.57	0.04*	0.51

When the test of transposition, omission, and substitution in the field, copy, dictation, and redaction, no significant differences were found. On the other hand, in the union test, the cases group presented significant differences in dictation when compared

with controls ($p < 0.02$), in the summary of specific errors the same was visible ($p < 0.04$).

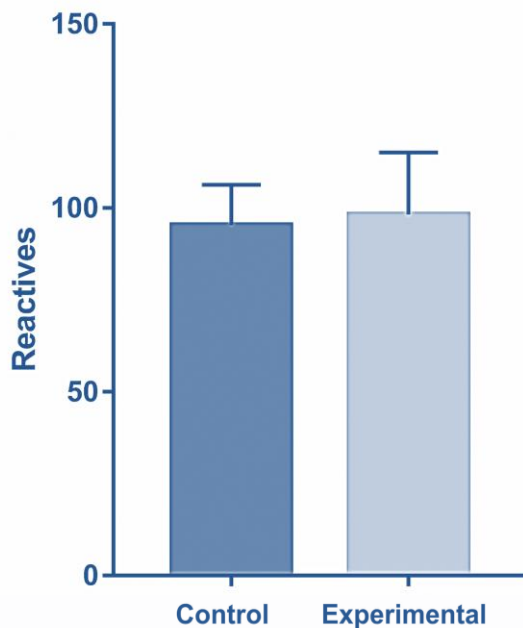


Figure 3. Comparison between Cases and Controls in the WISC-R test's drafting on redaction.

IV.- DISCUSSION

Children with partial epilepsy under treatment with valproic acid present some alterations in memory, nevertheless, they are not really significantly different from healthy children, Dodson et al [21] point out that children with epilepsy present three times more risk of cognitive issues that individuals without neurologic diseases. Difficulties in learning have been observed in children with partial epilepsy, but we have to keep in mind that nearly 20% of the general school population also presents these disorders [22].

Regarding the characteristics of the epileptic crisis, studies evaluating neuropsychological deficits have centered mainly on children with the idiopathic partial crisis. In them, attention disorders, visual-motor and fine motor skills have been found [23, 24 along with some other problems in executive functions and language and immediate verbal memory [23-25].

The work of Nehlig [26] shows that if epileptic patients did not suffer any brain damage, the distribution of their intelligence would be the same as a healthy individual. In a recent study, Oscar Papazian by means of tomography and electroencephalography evaluated the learning process of children with partial idiopathic epilepsy aged 6 to 12, employing the Weschler and Connors scales they determine that the cognitive impairments are strongly associated with interictal epileptic discharges, to the partial and complex crises and to the left temporal lobe crisis, only when this hemisphere is the dominant one [27, 28].

Some antiepileptic drugs (AEDs) like phenobarbital, phenytoin, and primidone impact the memory process, however, benzodiazepines affect it more than carbamazepine and valproic acid just as we see in the present study [29, 30]. It is worth noticing that the adverse effects of antiepileptic drugs diminish when the correct dosage is given to the patient [22].

The degree of cognitive impairment could depend on etiologic factors like the age at which the first epileptic episode presented; the younger the worse, the duration of the disease, the frequency of crises in the active phase [22].

In the present work children with partial epilepsy under treatment with valproic acid presented problems in writing when compared with a control group, which has been reported previously [3].

The adverse effect of AEDs, previously warned by Lennox [31], over cognitive functions has been the subject of research for the last 30 years [3]. These effects depend on the type of drug, the dose employed and the interactions between drugs, the effects could be beneficial as is the case with carbamazepine (CBZ) over the visual-perceptive tasks [33], like negatives. Generally, among the called "first line AED", the ones that have more reported adverse effects are phenobarbital and phenytoin and on the opposite side, the more beneficial are CBZ and valproic acid.

Macotela et al. [20] pointed out that mistakes in rules are related to an inadequate comprehension and employment of grammatical and orthographic rules, in other words, are mistakes associated with the practice that children have in the learning process of these rules. On the other hand, specific mistakes that refer to difficulties of the discriminative kind where the children alter the perception of the stimuli that are presented to them are directly related to the previous abilities that children need to develop in order to obtain adequate learning in reading and writing.

These results seem to concur with the findings of other studies where the researchers showed that reading and writing acquisition of certain abilities are percurrent and that children develop these abilities before the beginning of their school-life or during pre-school [34, 35].

The point previously exposed could explain why in the present study there no significant differences in the learning process of children with partial epilepsy under treatment with valproic acid when compared with healthy individuals. It is worth noticing that all children in the experimental group had achieved a more than adequate control of their epilepsy with only one AED, plus it being one of the less associated with learning alterations and good in maintaining a good

balance in memory, attention, and information process.

V.- CONCLUSION

In conclusion, the objective of evaluating the effect of partial epilepsy in children over learning, mainly in reading and writing was achieved, finding differences in dictation and redaction, showing that valproic acid did not heavily impact cognition and learning.

Likewise, it was observed that the general neuropsychological evaluation carried out by a global instrument such as the Wisc-R does not show specific deficits, it is necessary to carry out a focal evaluation of the cognitive domain to be investigated to detect the specificity of the deficit; as well as a deep investigation of the premorbid state, which can show the consolidation or not and the practice that the children have had in the reading and writing process, as indicated by the present investigation.

VI.- ETHICAL RESPONSIBILITIES

Protection of people. The authors declare that the procedures followed were in accordance with the ethical standards of the responsible human experimentation committee and in accordance with the World Medical Association and the Declaration of Helsinki.

Confidentiality of the data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Conflict of interest: The authors declare that there is no conflict of interest.

VII.- REFERENCES

- Engel J., Pedley T. *Epilepsy* Editorial Lippincott-Raven Publishers; 1998 Philadelphia.
- Durá-Travé T, Yoldi-Petri ME, Gallinas-Victoriano F. Estudio descriptivo de la epilepsia infantil. *Rev Neurol.* 2007; 44: 720-4.
- Conde-Guzon PA, Cancho-Candela R. Idiopathic generalized epilepsies with absence seizures with valproic acid treatment: neuropsychological disorders]. *Rev Neurol.* 2012; 16;55(2):65-73.
- Reséndiz-Aparicio JC, Rodríguez-Rodríguez E, Contreras-Bernal J, Ceja-Moreno H, Barragán-Pérez E, Garza-Morales S, Malagón-Valdéz J, Ortega-González F. [A randomised open trial comparing monotherapy with topiramate versus carbamazepine in the treatment of paediatric patients with recently diagnosed epilepsy]. *Rev Neurol.* 2004; 1-15;39(3):201-4.
- Cockrell OC, Johnson AL, Sander JW, Hart YM, Shorvon SO. Remission of epilepsy: results from the national general practice study of epilepsy. *Lancet.* 1995; 348: 140-4.
- García-Peñas JJ, Fournier-Del Castillo MC, Domínguez-Carral J. [Epilepsy and cognition: the role of antiepileptic drugs]. *Rev Neurol.* 2014; 24;58 Suppl 1:S37-42. Review.
- Hamiwka LD, Wirrell EC. Comorbidities in pediatric epilepsy: beyond 'just' treating the seizures. *J Child Neurol.* 2009; 24:734-42.
- Campos-Castelló J. Neuropsicología de la epilepsia: ¿qué factores están implicados? *Rev Neurol.* 2006; 43: S59-70.
- Sánchez-Carpintero R. Variabilidad de la evolución cognitiva en los distintos tipos de epilepsia del niño. *Rev Neurol* 2010; 50: S31-6.
- García-Peñas JJ. Repercusión neurocognitiva de las descargas epileptiformes interictales en el niño. *Rev Neurol.* 2011; 52: S43-52.
- Motamedi G, Meador K. Epilepsy and cognition. *Epilepsy Behav.* 2003; 4: S25-38.
- Vinayan KP. Epilepsy, antiepileptic drugs and educational problems. *Indian Pediatr.* 2006; 43: 786-94.
- Hirtz D, Berg A, Bettis D, Camfield C, Camfield P, Crumrine P, et al. Quality Standards Subcommittee of the American Academy of Neurology; Practice Committee of the Child Neurology Society. Practice parameter: treatment of the child with a first unprovoked seizure: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology.* 2003; 60: 166-75.
- Perucca E, Kwan P. Overtreatment in epilepsy: how it occurs and how it can be avoided. *CNS Drugs.* 2005; 19: 897-908.
- Hamiwka LD, Wirrell EC. Comorbidities in pediatric epilepsy: beyond 'just' treating the seizures. *J Child Neurol.* 2009; 24: 734-42.
- Taras H, Potts-Datema W. Chronic health conditions and student performance at school. *J Sch Health,* 2005; 75: 255-66.
- Cornaggia CM, Gobbi G. Learning disability in epilepsy: definition and classification. *Epilepsia.* 2001; 42: S2-5.
- Austin JK, Huberty TJ, Huster GA, Dunn DW. Does academic achievement in children with epilepsy change over time? *Dev Med Child Neurol.* 1999; 41: 473-9.
- Wechsler D. *Escala de Inteligencia Wechsler para niños revisada (WISC-R).* Madrid: TEA Ediciones; 1993.
- Macotela, S., Bermúdez, P., & Castañeda, I. *Inventario de Ejecución Académica: un Modelo Diagnóstico-prescriptivo para el Manejo de Problemas Asociados a la Lectura, la Escritura y las Matemáticas.* 1991. México: Facultad de Psicología, U.N.A.M.

21. Dodson WE, Kinsbourne M, Hiltbrunner B. The assessment of cognitive function in epilepsy. Nueva York: Demos; 1991.
22. Campos-Castelló J. Neuropsicología de la epilepsia: ¿qué factores están implicados? *Rev Neurol* 2006; 43: S59-70.
23. Baglietto MG, Battaglia FM, Nobili L, Tortorelli S, De Negri E, Calevo MG, et al. Neuropsychological disorders related to interictal epileptic discharges during sleep in benign focal epilepsy of childhood with centrotemporal or rolandic spikes. *Dev Med Child Neurol*. 2001; 43: 407.
24. Metz-Lutz MN, Kleitz C, De Saint Martin A, Massa R, Hirsch E, Marescaux C. Cognitive development in benign focal epilepsies of childhood. *Dev Neurosci*. 1999; 21: 182-90.
25. Yung AW, Park YD, Cohen MJ, Garrison TN. Cognitive and behavioral problems in children with centrotemporal spikes. *Pediatr Neurol*. 2000; 23: 391-5.
26. Nehlig A, Moñe J, Moshé P. Childhood Epilepsy and Brain development. 1999. Editorial John Libbey & Company Lt.
27. Papazian O, Alfonso I, García Galarreta V. Efecto de las descargas epileptiformes interictales sobre las funciones cognitivas en niños con epilepsia idiopática. *REV NEUROL*. 2003; 36(3):282-284.
28. Tirosh E. Learning disabilities with and without attention-deficit hyperactivity disorder: parents' and teachers' perspectives. *J. Child Neurol*. 1998;13(6):270-6.
29. Warren A. Neuroanatomic Substrate of Developmental Specific Learning Disabilities and Select Behavioral Syndromes. *Journal of Child Neurology*. 1995;10:S78-S80
30. Aldenkamp A. Efectos de los fármacos antiepilépticos en la cognición. *Rev Neurol*. 2002; 34(9):851-56.
31. Lennox WG. Brain injury, drugs an environment as causes of mental delay in epilepsy. *Am J Psychiatry*. 1942; 99: 174-80.
32. Cramer JA, Fisher R, Ben-Menachem E, French J, Mattson R. New antiepileptic drugs: comparison of key clinical trials. *Epilepsia*. 1999; 40: 590-600.
33. Cowdry RW, Gardner DL. Pharmacotherapy of borderline personality disorder: alprazolam, carbamazepine, trifluoperazine and tranlycypromine. *Arch Gen Psychiatry*. 1988; 4: 111-9.
34. Leppänen, U., Niemi, P., Aunola, K., & Nurmi, J. E. Development of reading skills among preschool and primary school pupils. *Reading Research Quarterly*. 2004;39 72-93.
35. DiLalla, L. F., Marcus, J. L., & Wright-Phillips, M. V. Longitudinal effects of preschool behavioural styles on early adolescent school performance. *Journal of School Psychology*. 2004; 42, 385-401.
36. Rains, GD., Principios de Neuropsicología Humana. McGraw-Hill Interamericana. 2004