Neuropsychological Deficits in Children with Epilepsy

Shobini L Rao

Reprints request

,
- *Department of Clinical Psychology, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

Shoba Srinath, - *Department of Psychiatry, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

Suresh Rao Aroor, - *Department of Neurology, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

V G Kaliaperumal, - *Department of Biostatistics, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

Abstract

Neuropsychological deficits have been observed in children with epilepsy. Cognitive deficits in children can affect ongoing school performances and impair new learning in school. Seizures, their type, duration, and frequency, age of onset and the nature of anticonvulsant medication are etiologically related to neuropsychological deficits. The present study examined the effect of seizure duration on neuropsychological functions. 53 children in the acute phase and 42 in the chronic phase of epilepsy and 52 normal controls, were studied. These three groups were matched for age, education and sex ratio. NIMHANS neuropsychological battery was used to assess Frontal, Parietal and Temporal lobe functions. The patient groups did not differ from each other or from the normal group on most of the neuropsychological functions. Other clinical variables such as type of seizures, age of onset, seizure frequency and history of cluster attacks were associated with deficits of attention, kinetic melody, delayed response learning and social functioning. It is hypothesized that a minimal frontal dysfunction is associated with these clinical variables, but not with seizure duration.

Key words -
Epilepsy,
Neuropsychological tests,
Neuropsychology

Neuropsychological deficits have been observed in children with epilepsy. Epileptic children had significantly more neuropsychological impairment [1]. Children are at a double disadvantage when affected by neuropsychological deficits. Cognitive deficits can affect ongoing school performance. It can also impair new learning in the school, which can lead to further deficits in later life. Neuropsychological deficits have been etiologically related to seizures in themselves. Etiology of the seizures, type, frequency, duration of the seizures, age of onset of seizures and the nature of anticonvulsant medication (AED) have been known to affect the nature of cognitive functions in children.

In children with newly diagnosed epilepsy, a fall in I.Q. was associated with toxic levels of AED, presence of more than one seizure type, symptomatic epilepsy and an early age of onset [2]. Early age of onset was associated with poorer I.Q. and a lowering of functioning across a wide spectrum of abilities [3]. Other studies have found the contrary, i.e., early age of onset was not associated with poorer I.Q. [4], [5]. Children with left hemisphere focal discharges had poorer reading skills. But children with generalised seizures did not [6]. However, children with generalized seizures had poorer visuo-perceptual functioning, attention and concentration as compared to those with partial seizures [7]. Decreased I.Q. indicating a slower mental growth was seen in children with uncontrolled seizures. Well controlled seizures resulted in a steady rise in I.Q. [8].

Monotherapy lead to improvements in cognitive functions [9]. Phenobarbitone in high drug levels was associated with fall in I.Q. [10]. Phenytoin was associated with fall in I.Q. [11], poor reading ability [6], mental dulling [12] and poorer memory [13]. Cognitive impairments were less evident with valproate and minimal with carbamazepine [9]. Seizure duration was another important clinical variable which affected neuropsychological functioning. In children years with seizures was inversely correlated with intelligence [1]. Longer seizure duration was associated with fall in I.Q. [14].

It is difficult to simultaneously study the effects of the various clinical variables on neuropsychological functions [15]. However, it is essential to understand their effect on neuropsychological deficits as the latter has an important bearing on the school going child. Thus, in the present study we have studied the association of seizure duration on neuropsychological functions. Neuropsychological functioning was studied in two groups of epileptic children varying in seizure duration

Materials and Methods

Sample

Ninety five patients with epilepsy and fifty two normal controls constituted the sample. The duration of epilepsy was acute in 53 patients and chronic in 42. Patients with seizure duration below one year constituted the acute group, while those with a seizure duration of greater than one year constituted the chronic group. Patients were taken from the Neurology outpatients and Neuropsychiatry clinic of NIMHANS, Seizure etiology was idiopathic in both groups. Normal controls were randomly drawn from the school classmates of the patients. The three groups were matched for age, education and sex. Sample characteristics are given in Table I

Table I - Characteristics of subjects

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Note : X^2 has not been applied where the cell entries were below 5

Method

Neuropsychological assessment was conducted to assess frontal, temporal and pareito-occipital lobe functions, using the NIMHANS neuropsychological battery [16]. The battery consists of the following tests:

Frontal lobe functions:

Attention was assessed clinically, in terms of spontaneous arousal of attention, distractability and fatiguability of attention. A nominal scale was used to categorize it as adequate or inadequate. Allocation of voluntary attention was assessed using numerical and pictorial scanning. The numerical scanning test consisted of 3 parts. Part 1 consisted of numbers 1-20 and parts 2 and 3 of numbers 1-48

respectively, randomly arranged, which had to be crossed serially. The time taken to complete each set and the errors in each set of parts 1 and 2 and the number deleted in 1 minute in part 3 were the scores. Description of 2 pictures was the pictorial scanning test which was scored as adequate or inadequate. Ideational fluency test had two parts. Subject recalled objects made of wood and round objects for 2 minutes each. Score was the number of objects recalled summed over the two parts.

Susceptibility to interference of memory was assessed by the delayed response learning test, wherein arithmetic problems were given. Performance was scored for time taken to complete and accuracy. Adequacy of motivation, kinetic melody and expressive speech was clinically assessed on a nominal scale of adequate or inadequate functioning. Presence of personality change was also noted on a nominal scale.

Parietal Lobe:

Perceptual gestalt and spatial relations were the two tests used to assess visuo spatial perception. Bender Gestalt test assessed perceptual gestalt whose adequacy was rated on a four point scale. In the spatial relations test, a target pattern was compared to 6 other patterns, bigger in size. One of the 6 identical to the standard, had to be detected by the subject. Accuracy and time were the scores. Visuo constructive ability was assessed using the block design test of WAPIS [17]. The first five patterns, using four blocks each were given for construction. Number of patterns correctly constructed and average time were the scores. Adequacy of reading, writing and calculation were assessed on a 4 point scale. Focal signs of ideational and ideomotor apraxia, colour, visual object and tactile agnosias, body schema disturbances were scored on a nominal scale of present or absent.

Right Temporal Lobe:

Visual integration was assessed using the object assembly subtest of WAPIS [17]. 4 items were given, mean, time taken and the number correctly assembled were the scores. Visual memory was assessed using the Benton Visual Retention Test, No. of cards correctly reproduced being the score [18]. Visual memory and learning was assessed by giving the complex figure test, on 3 consecutive trials of 10 sec exposure followed by recall. The fourth trial tested delayed recall after 10 minutes. This is a modification of the Rey Osterich figure [14]. No. of facts correctly reproduced was the score, the maximum being 20.

Left Temporal Lobe:

Receptive aphasia was tested by the verbal comprehension test, wherein 23 questions were asked orally and the number correctly answered formed the score. Sentence repetition test, wherein 20 sentences of increasing complexity were given; assessed verbal memory. Number of sentences correctly repeated formed the score. Logical memory was assessed by 3 successive presentation - recall of a short passage. Delayed recall was assessed after 10 minutes. Number of facts correctly reproduced was the score the maximum being 23.

Subjects below the age of 8 could not be assessed on numerical scanning, delayed response learning and B.V.R.T. tests, due to the difficulty level.

Intelligence was assessed using the Binet Kamath test of intelligence [19]. Social functioning was assessed using the Vineland Social maturity scale [20] which was rated as adequate if the social functioning was age appropriate.

Subjects were tested individually in several sessions.

Results

Both the groups of patients were comparable with the clinical group in terms of age, gender and education. On majority of the clinical variables the patient groups were comparable. However, the acute group significantly consisted of patients with a significantly later age of onset than the chronic group.

Scores on the tests were either continuous i.e., on an interval scale or categorical i.e. on a nominal scale. ANOVA was used to compare performance of the three groups on the scores on an interval scale. None of the F values was statistically significant excepting for that of sentence repetition test (Table II).

Table II - Mean and S.D. of the three groups on the tests with scores on an interval scale

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Note : No group comparison was significant.

Normal subjects had the least scores though the difference was not substantial. Chi square test was used to compare the performance of the three groups wherever the scores were on a nominal scale or wherever the range of scores was very small (Table III).

Table III - Categories, No. of subjects and chisquare values of test scores on a nominal scale

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N.B.: 0 represents inadequate and 1 adequate functioning. X^2 test was not applied (NA) when any cell entry was below 5

Kinetic melody (fist and ring test) was impaired to a greater extent in the chronic group. Fist and outstretched fingers test was impaired to a greater extent in the chronic and normal groups. Again normal children were deficient in performing delayed response tests. i.e., sums with delay. Group differences were not significantly different on any of the other tests. This is an isolated finding, wherein the normal group performed worse than the patients. Normals have performed poorly on two subtests i.e. a subtest (sums with delay test) of the delayed response learning test and a subtest (fist and outstretched fingers test) of the kinetic melody test. These two findings need replication before being interpreted, as the normal group has not performed worse on any other test. In the kinetic melody test on two simpler subtests i.e. fist and ring test as well as fist and outstretched fingers test, the chronic group performed poorer than normals. Even on those results wherein statistical tests could not be applied due to paucity of the requisite number of cases in each cell, visual inspection does not reveal significant differences.

Association of clinical variables with performance on the different tests was tested using the ANOVA, and Median and Chisquare tests. As the two patient groups were not significantly different on most tests, the two groups were combined to arrive at classifications based on clinical variables.

The clinical variables compared were type of seizure i.e. Generalized (N=24) vs partial (N=26) vs. Normals (N=28); Age of onset i.e. early age of onset (> 5 years N=18) vs later age of onset (> 5 years

N=18) vs Normals (N=18); Frequency of seizures i.e.. Very frequent (N=16) vs frequent (N=15) vs Fairly frequent (N=11) vs Infrequent (N=16) vs Normals (N=16); Cluster attacks i.e. H/O cluster attacks present (N=15) vs H/O Cluster attacks absent (N=15) vs Normals (N=15); EEG abnormalities i.e. EEG abnormal (N=14) vs EEG Normal (N=24) vs. Normals (N=24); Nature of therapy i.e. monotherapy (N=12) vs polypharmacy (N=12) vs. Normals(N=12); type of AED in the monotherapy group i.e. Phenytoin (N=13) vs Phenobarbitone (N=14) vs. Normals (N=13).

In each of the above clinical variable, the groups with the lowest sample size determined the number of patients in the comparison groups. Attempt was made to keep the comparison groups in each clinical variable comparable in terms of age, education, sex ratio and other clinical parameters.

The association of type of seizure with the different neuropsychological tests was present on several tests. In the partial seizure group, attention, kinetic melody (fist and ring test) were significantly impaired as compared with normals. In the generalised seizure group, scanning, kinetic melody (fist and ring test), delayed response learning (number of sums correctly done) and social functioning were significantly impaired.

Age of onset was significantly associated with certain neuropsychological functions. Attention was significantly impaired in the early onset group as compared with normals. Kinetic melody (fist and ring test) was significantly impaired in both groups as compared to normals. Delayed recall test was significantly better in patients.

Regarding the clinical variable of frequency of seizures, attention was significantly impaired when the seizures were fairly frequent, as compared with normals. Mental control (subtraction of 3 from 40) in fairly frequent and infrequent seizure groups was significantly better than in the normal group. Delayed response learning (number of sums correctly done) was significantly poorer in all the four categories of seizure frequency as compared with normals.

Patients with history of cluster attacks were significantly poorer in attention as compared with normals. Social functioning was significantly impaired in patients without a history of cluster attacks as compared with normals.

Patients whose EEG was normal had significantly impaired delayed response learning (number of sums correctly done) as compared with normals. Social functioning was significantly impaired in patients with EEG abnormalities as compared with normals.

Patients categorized in terms of nature of therapy, i.e. monotherapy or polypharmacy did not differ significantly from each other or from the normal controls on any of the neuropsychological tests. Again patients on monotherapy who were on phenobarbitone or phenytoin were not significantly different when compared with normal controls on any of the neuropsychological tests. The above findings are summarized in Table IV.

Table IV - Summary of findings from comparison of patient groups with normals

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Discussion

The acute and chronic groups are not significantly different in the neuropsychological profile, I.Q. and

social functioning compared with the normals. The only exception is kinetic melody (fist and ring subtest) wherein the chronic group was significantly poorer. Kinetic melody deficit is indicative of pre motor area involvement. Apart from this finding the results indicate that seizure duration is not significantly associated with neuropsychological functions. The reason could be because of adequate clinical management. Majority of patients in both groups were on monotherapy. Reducing the number of drugs is known to benefit cognitive functions [21]. Thus the lack of significant group differences can be attributed both to the lack of effect of seizure duration, as well as to the effects of monotherapy.

Among other clinical variables independently examined, type of seizures, age of onset, seizure frequency, history of cluster attacks and EEG abnormalities were associated with neuro-psychological deficits. Deficits of attention, kinetic melody, delayed response learning, and social functioning were predominantly associated with these clinical variables. All the above are frontal lobe functions. Even social functioning can be affected by frontal lobe dysfunction, as regulation of activity and behavior including social behavior is a frontal lobe function [22]. Scanning deficit associated with generalized seizures and kinetic melody deficits duration associated with chronicity of seizure duration were also deficits of frontal lobe functioning. It is significant that deficits of parietal and temporal functions were absent when patients were compared with normals. I.Q. of patients was not significantly lower than that of normals. Earlier studies have revealed the influence of clinical variables on neuropsychological functions and IQ in epileptic patients [1], [2], [7]. In particular memory functions has been considered vulnerable in epileptic patients [15]. In view of the above, the absence of intellectual deterioration and generalized neuropsychological deterioration, but the presence of minimal frontal dysfunction can be interpreted as follows. Majority of the patients were on monotherapy. This factor has not influenced the cognitive functioning. Thus patients on monotherapy or polypharmacy were comparable to normals in neuropsychological functions. However, monotherapy could have acted as a modulating factor in that, it might have mitigated the effect of other clinical variables on various cognitive functions. Frontal lobe functions were however vulnerable and though patients were on monotherapy deficits surfaced. An examination of the type of functions reveals that deficits were in the area of attention, susceptibility of memory to interference (delayed response learning) and rapid motor movement (kinetic melody). Regulation of complex behavior was also poor (social functioning). These deficits could represent subtle neuropsychological deficits incorporating factors such as deficits of mental speed and motor speed, which are associated with AEDs [9]. The current findings indicate that even though neuropsychological functions were largely absent in well managed epileptic children, i.e. who were on monotherapy with well controlled seizures, subtle neuropsychological deficits, predominantly of the frontal lobe persists.

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