

Neuropsychological functioning in children with epilepsy: Generalized Tonic-Clonic Seizures (GTCS) and Complex Partial Seizure (CPS)- an Indian study

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ABSTRACT

Background: Neuropsychological studies confirmed that patients with epilepsy are at considerable risk for cognitive impairment and emotional disturbances. **Aim:** To evaluate the influence of neuropsychological functions in childhood common epilepsy types 1. Generalized Tonic-Clonic Seizures (GTCS) and Complex Partial Seizure (CPS). **Method:** Two groups of 74 children with epilepsy (49 boys and 25 girls), with a mean age of 11.77 (± 2.19) years were screened and selected from Bangalore Neuro Centre, Bangalore, India. **Tools:** NIMHANS Neuropsychological battery was administered to understand the cognitive profile of the epilepsy subjects. To understand their depression level, Centre for Epidemiological Studies – Depression scale for Children (CES-DC) was used. **Statistical Analyses:** Mean, percentage, SD, One-way Analysis of Variance (ANOVA) and post-hoc test was used analyze the difference among the sub-type group children with epilepsy. **Findings:** The present study signify that there are differences in neuropsychological variables between GTCS and CPS children. The CPS children who performed low in cognitive functions reported higher level of depression. In summary, the present study reveals that children with GTCS and CPS explain considerable impairment in cognitive function and struggling with depression.

Keywords: Children with epilepsy, Neuropsychological tests, Epilepsy types & Depression

Epilepsy is a common neurological problem. 3% of the general population suffers from this disease. Epilepsy has its effect on a number of neuropsychological functions such as attention executive functions, learning and memory etc., Delaney et al (1986) concluded that interictal memory deficits are often found in patients with generalized or complex partial seizures, especially with left or bilateral temporal onset. Hermann et al (2002) found that verbal memory impairment was usually seen in left temporal seizure patients, but nonverbal or visual memory deficits were more difficult to lateralize. Dodrill and Wilkus (2002) concluded that perceptual functions, such as response to double simultaneous stimulation, graphesthesia and finger gnosis were not impaired in most forms of epilepsy.

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Neuropsychological functioning in children with epilepsy: Generalized Tonic-Clonic Seizures (GTCS) and Complex Partial Seizure (CPS)- an Indian study

In recent years, important advances have been made in the diagnosis and treatment of seizure disorders. Word finding difficulty or even clinical anomia occurred in patients with left temporal lobe seizures. Anomia and other language dysfunction, such as aural comprehension deficits, may account for some of the verbal memory deficits associated with temporal lobe seizures. Complex problem solving and cognitive flexibility were often impaired in epilepsy. Patients with epilepsy had lengthened reaction times, as well as slowing of pure motor speed. Smith et al (1986) found impaired motor speed and coordination to be common in epilepsy especially in patients with GTCS, mixed seizure types and various EEG abnormalities. Mazzucchi et al (1985) found that laterality affected perceptual ability with left temporal seizures disrupting dichotic linguistic material and right seizures disrupting nonlinguistic auditory perception. Generalized tonic clonic seizures, especially if status epilepticus occurs are more likely to impair cognition than simple and complex partial seizures (Prevey, 1998; Dodrill, 2004). Deficits in motor skills, response inhibition, attention, psychomotor speed working memory, verbal & visual learning and memory, planning, were noted in patients with Temporal lobe epilepsy (Gopukumar et al, 2016). Depression is frequent and usually underdiagnosed and untreated in patients with epilepsy. Depression may involve feelings of being sad, weak, disappointed, frustrated, despairing, helpless, and hopeless (Sarason & Sarason 2002). The link between Depression and Epilepsy Sclerosis has been of great interest to neurologists, psychiatrists and psychologists for many years. Persons with epilepsy have a higher incidence of depression than the general population (David Blum, 1999). Patients with depression, on neuropsychological evaluation exhibited significantly poor performance on measures of intelligence, language, visuo-perceptual ability, memory and executive functions (Paradosoa, et al 2001). The presence of depression can increase the number of seizures in a patient with epilepsy (Ciechanowski, P. et. al., 2010). Epilepsy is known to have its effects on the cognitive functions along with the predisposition for depression. Based on a number of reviews and past studies we have focused on children with GTCS and CPS and its effects on the cognitive performance and depression.

Objectives

1. To evaluate the influence of neuropsychological functions in childhood common epilepsy types Generalized Tonic-Clonic Seizures (GTCS) and Complex Partial Seizures.
2. To understand the cognitive deficits of GTCS and CPS.
3. To study the level of depression in children with epilepsy (GTCS and CPS).

METHODOLOGY

Inclusion Criteria

Patients in the age range of 9-15 years, both boys and girls, right-handed Associated with Generalized Tonic-Clonic Seizures (GTCS) and Complex Partial Seizure (CPS) and Normal or corrected vision and hearing.

Exclusion Criteria

History of any other neurological or psychiatric disorder except interictal psychosis and Clinical evidence of mental retardation

Sample

In the present study a sample of 74 epilepsy children (49 males and 25 females) is been selected from Bangalore Neuro Centre, Bangalore. The sample was selected from 5th to 10th grade and will be divided into two groups, i.e.1. Group-1 GTCS (N=27; Mean Age & SD

Neuropsychological functioning in children with epilepsy: Generalized Tonic-Clonic Seizures (GTCS) and Complex Partial Seizure (CPS)- an Indian study

=11.89 ± 2.19) and 2. Group-2 CPS (N=47; Mean Age & SD = 11.70 ± 2.32). The subjects were chosen by the purposive random sampling method. The sample recruited during 2014 to 2019.

Tools

Clinical Proforma: The clinical proforma was developed to collect the information about the age at onset of epilepsy, type of seizure, duration of the seizures, frequency of seizures, medications tried, current medication and date of last seizure. EEG and MRI findings were also noted.

Neuropsychological Assessment: NIMHANS Neuropsychological battery was administered to understand the cognitive profile of the MTS subjects. The battery comprises of 11 tests [Finger tapping (FT), Controlled Oral Word Association (COWA), Category Fluency (CT), Colour Trails CT-1 &2), Digit vigilance (DV), Rey's Auditory Verbal Learning and memory (RAVLT), Logical Memory (LM), (Rao, et.al., 2004)., [Memory for Designs (MFD) (Kar et.al, 2004)], which assess the aspects of attention, motor speed, mental speed, executive functions, visuospatial ability and learning and memory.

Centre for Epidemiological Studies – Depression Scale for Children (CES-DC): To understand their depression level, Centre for Epidemiological Studies – Depression scale for Children (CES-DC) was used. Score 15 is used as a cut off score. Scores 15 and above are suggestive of significant depressive symptoms (Weissman et al., 1980).

Other Investigations

EEG: Scalp electroencephalography-resting/ spontaneous sleep EEG was done for all the patients. This included conventional activation procedures such as 3 minutes hyperventilation and 3 minutes post-photoc stimulation. This was carried out as per the International EEG Society Guidelines.

MR Imaging: MRI brain was performed on 1.5 T GE equipment. The routine MR examination included imaging in all three orthogonal planes. The imaging protocols included T1W, T2W and inversion recovery sequences (FLAIR).

Procedure

Epilepsy subjects were divided into two groups Group-1 (GTCS) and Group -2 (CPS). Above mentioned Neuropsychological and CES-DC tests take approximately 1 hour 45 minutes to 2 hours 30 minutes depending on the subject's performance. The above-mentioned tests are Indianized according to age, gender and educational background (Kar, Rao, Subbakrishna & Gopukumar, 2004).

Statistical analysis

It was performed using Mean, Standard Deviation, t-test were used analyze the difference among the sub-type group (GTCS and CPS) with epilepsy on Neuropsychological and depression (CES-DC) scores. All statistical analyses were performed using Software Package used for Statistical Analysis (IBM-SPSS version 20).

RESULTS

Individual Analysis

Scores were compared with age, education and gender Indian specific norms, wherein scores falling below the 15th percentile of the normative data were treated as deficits.

Neuropsychological functioning in children with epilepsy: Generalized Tonic-Clonic Seizures (GTCS) and Complex Partial Seizure (CPS)- an Indian study

Group Analysis

Table-1: Comparisons of Neuropsychological measures between GTCS and CPS

NP Test Variables	Groups Compared	N	Mean	Standard Deviation	t
Digit Vigilance- Total Time	GTCS	27	1127.93	286.65	0.90
	CPS	47	1186.14	227.51	
Color Trails-1- Total Time	GTCS	27	96.26	33.05	0.34
	CPS	47	93.26	40.46	
Color Trails-2- Total Time	GTCS	27	147.78	61.04	0.36
	CPS	47	142.34	64.40	
AVLT Total Learning	GTCS	27	32.70	5.29	0.31
	CPS	47	32.66	6.79	
AVLT - Immediate Recall	GTCS	27	6.04	1.45	0.74
	CPS	47	5.77	1.61	

NP Test Variables	Groups Compared	N	Mean	Standard Deviation	t
AVLT - Delayed Recall	GTCS	27	5.48	1.95	0.11
	CPS	47	5.53	1.61	
Logical Memory – Immediate Recall	GTCS	27	8.02	2.1	4.79**
	CPS	47	5.84	1.41	
Logical Memory – Delayed Recall	GTCS	27	6.56	1.85	3.01**
	CPS	47	5.39	1.08	
Memory for Designs Immediate Recall	GTCS	27	9.59	3.59	6.06**
	CPS	47	7.66	2.49	
Memory for Designs Delayed Recall	GTCS	27	21.93	3.98	2.48*
	CPS	47	16.23	3.71	
Digit Symbol Substitution-	GTCS	27	282.04	83.43	0.33
	CPS	47	275.81	62.95	
Finger Tapping- Right Hand	GTCS	27	27.74	3.21	0.29
	CPS	47	27.51	3.33	
Finger Tapping- Left Hand	GTCS	27	24.48	3.62	0.22
	CPS	47	24.68	3.97	
Digit Symbol Substitution	GTCS	27	282.04	83.43	0.33
	CPS	47	275.81	62.95	
Finger Tapping- Right Hand	GTCS	27	27.74	3.21	0.29
	CPS	47	27.51	3.33	
Finger Tapping- Left Hand	GTCS	27	24.48	3.62	0.22
	CPS	47	24.68	3.97	
Category Fluency Animal Names	GTCS	27	7.11	2.11	1.66
	CPS	47	8.00	2.39	
Phonemic Fluency	GTCS	27	6.11	1.81	1.06
	CPS	47	5.66	1.72	
CES-DC	GTCS	27	20.04	7.59	4.40**
	CPS	47	28.13	7.64	

Note: AVLT= Auditory Verbal Learning & Memory; CES-DC= Centre for Epidemiological Studies – Depression scale for Children. ** Significant at 0.01 level; * Significant at 0.05 level

RESULTS

The patients with CPS performed significantly worse on passage memory (verbal) and in learning and memory (Meaning for Designs-visual). Patients with complex partial seizures did not differ from patients with generalized tonic-clonic seizures in tests of motor function or attention, nor in tests of learning and memory (Pulliainen et al ,2000; Bhise et al 2010). Children with CPS performed worse on Digit Vigilance, Auditory Verbal Learning – short-term memory and Digit Symbol Substitution Test. Children with CPS demonstrate significant level depression. Children with GTCS did not differ from patients with CPS in tests of motor function, focused attention, divided attention, sustained attention, processing speed, executive functions and auditory verbal learning and memory.

Individual Analysis: Neuropsychological Impairment based on norms across groups: Neuropsychological impairment amongst the CPS children is highest most of the cognitive tests. Overall, children performed poorly in Auditory Verbal Learning & Memory – Immediate Recall 73% (54/74), Auditory Verbal Learning & Memory –Delayed Recall 58% (43/74), Auditory Verbal Learning & Memory - total score 55% (41/74), followed by Phonemic Fluency 49% (36/74), DV 45% (33/74), Digit Symbol Substitution Test & Finger Tapping left hand speed 38% (28/74) and Meaning For designs test-delayed recall 37% (27/74). Neuropsychological impairment amongst the CPS children is lowest in Verbal Fluency 11% (8/74), and Finger Tapping–right hand speed 16% (12/74).

Group Analysis (GTCS and CPS):

When comparing two groups (GTCS and CPS) based upon the eleven Neuropsychological variables (Phonemic Fluency, Category Fluency, Color Trails 1 & 2, Digit Vigilance, Finger Tapping right hand & left hand, Digit Symbol Substitution, Auditory Verbal Learning and Memory (Total, immediate & delayed recall) there were no significant differences.

Children with CPS showed deficits in focused attention, divided attention, sustained attention, Auditory verbal learning, immediate auditory verbal memory, delayed auditory verbal memory, mental flexibility, verbal fluency, visual learning, visual long-term memory and motor speed – dominant hand.

Overall, 44% of GTCS and CPS subjects had depressive symptoms, of which 20% experienced moderate to severe and 24% experienced mild to moderate level of depression. 58% subjects had no depressive symptoms.

DISCUSSION

The CPS children performed low in the areas of auditory verbal learning, verbal short-term memory, verbal long-term memory, logical short-term memory, visual learning and visual long-term memory. Irrespective of presence or absence of depressive symptoms cognitive dysfunctions are well evident in low depressed MTS children's performance poor in memory and processing speed functions.

Children may show varied number of signs such as problems in concentrating, forgetfulness, indecisiveness and diminished ability to think, analyze, and decide, lack of confidence in one's ability to make good decisions, lack of energy, feelings of fatigue etc. All the above could be indicators of depression in children. The reasons for high depression could be side effects of medication, home and school environment, lack of motivation etc. Since most of the subjects belong to lower middle-income group, the opportunities for growth and development may be

Neuropsychological functioning in children with epilepsy: Generalized Tonic-Clonic Seizures (GTCS) and Complex Partial Seizure (CPS)- an Indian study

restricted. Childhood onset absence epilepsy had subtle cognitive deficits and duration of illness, seizure frequency, antiepileptic drug treatment was related to the severity of the cognitive deficits. Therefore, from the present study we can come to an understanding that depression has significant effect on learning and memory of CPS children.

The present study signifies that there are differences in neuropsychological variables between GTCS and CPS children. The MTS children who performed low in cognitive functions reported higher level of depression. GTCS and CPS children differ in bi-temporal lobe functions viz., verbal learning and memory and visual learning and memory. The GTCS and CPS group showed mild deficits in Phonemic fluency, focused attention, divided attention, motor speed (dominant hand) and visual learning. In spite of the presence or absence of depression, cognitive dysfunctions were seen in GTCS and CPS subjects.

The present study reveals that children with GTCS and CPS explain considerable learning and memory (passage-verbal and visual) impairment in cognitive function and struggling with depression. This finding of the study can help in retraining activities and strategies to enhance GTCS and CPS children's performance mainly in learning and memory function, sustained attention, mental speed, passage memory and their mood level.

Limitations

It includes inadequate statistical power to detect significant small- to medium-sized differences in cognitive function between GTCS and CPS. Future research should consider healthy and Epilepsy sub groups.

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Neuropsychological functioning in children with epilepsy: Generalized Tonic-Clonic Seizures (GTCS) and Complex Partial Seizure (CPS)- an Indian study

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Conflict of Interest

The author declared no conflict of interest.

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