Original Research Paper

Cognitive Performance in Children with Refractory Mesial Temporal Sclerosis (MTS) - an Indian Experience

Gopukumar Kumarpillai[1]*, Samhita K[2]

ABSTRACT

The aim of the present study was to assess the effect of depression on cognitive performance in children with Mesial Temporal Sclerosis (MTS). Thirty-six MTS children were included in the study, and the subjects were set up by a median split of the scores obtained on the Centre for Epidemiological Studies – Depression Scale for Children (CES-DC), high depression (N = 15) and low depression (N = 21). The National Institute of Mental Health and Neurosciences (NIMHANS) Neuropsychological Battery was employed. High depressive subjects displayed impairment in verbal and visual memory functions. Overall, it was revealed that there is a significant relationship between the depression score and cognitive performance. It was concluded that high depression is associated with bi-temporal involvement of the brain.

Keywords: *Cognitive Performance, Mesial Temporal Sclerosis, Depression, Neuropsychological Tests*

It is estimated that worldwide, 10.5 million children under the age of 15 have active epilepsy (Guerrini, 2006).

When seizures occur, abnormal neuronal activity may have a significant impact on the normal cognitive processes of affected individuals (Motamedi & Meador, 2003).

Some researchers have attempted to cull out the separate effects of clinical features such as seizure frequency, age of onset, anti-epileptic drugs (AED) and duration of active epilepsy. Both children with Temporal Lobe Epilepsy (TLE) and Frontal Lobe Epilepsy (FLE) are at risk for cognitive impairments.

Epilepsy being the most common neurological problem, its probability is about 3% of the general population suffering from this illness at some point in their lives. (Annegers JF, 2001).[1] It is known to have complex effects on social, vocational and psychological functions.

[1] Neuropsychologist at Bangalore Neuro Centre, Bangalore, India
[2] Student of Postgraduate Diploma in Technical Writing at Symbiosis International University
*Responding Author

Cognitive Performance in Children with Refractory Mesial Temporal Sclerosis (MTS) - an Indian Experience

In recent years, advances have been made in the diagnosis and treatment of seizure disorders. The most frequent of the epileptic disorders is the Temporal Lobe Epilepsy (TLE). (Schachter SC, 2001).[2]

Epilepsy is marked by loss of neurons in the hippocampus of the temporal lobe and is associated with a decline in memory function. (David Blum, 1999).[3]Epilepsy has its effect on a number of cognitive functions such as learning, memory, attention, and execution.

Another predisposing factor to be considered in epilepsy is depression. A depressed mood is the experience of unhappiness or distress. Depression may involve feelings of being sad, weak, disappointed, frustrated, despairing, helpless, and hopeless (Sarason & Sarason, 2002).[4] Many depressed individuals may be unable to perform well in academic life. They may feel that they are not reaching the standard of performance set for them. As a result they continuously feel disappointed and despairing. They perceive things negatively and consider themselves as failures. This condition can definitely contribute to many serious problems in their academic life such as poor grades.

The link between Depression and Temporal Lobe Sclerosis has been of great interest to both neurologists and psychiatrists for many years. It is said that persons with epilepsy have a higher incidence of depression than the general population (David Blum, 1999).[3]

Depression is frequent and usually underdiagnosed and untreated in people with epilepsy. Patients with depression, at the time of neuropsychological evaluation exhibited significantly poor performance on measures of intelligence, language, visuoperceptual ability, memory and executive functions.

Depression in children and adolescents with epilepsy is a common but often unrecognized and unreported disorder when compared to adults. Both epilepsy and depression are characterized by poor long-term psychosocial outcome.

A study of adult surgical patients found that depression was associated with seizures in the temporal lobe - a common focus for surgically treated epilepsy. However, such evidence is not well established in paediatric patients. (Sanchez-Gistau, 2009).[5] Research studies have shown that the presence of depression can increase the number of seizures a person with epilepsy has. (Ciechanowski et al. 2010).[6]

Epilepsy is known to have its effects on the cognitive functions along with the predisposition of depression. Many studies are in progress to uncover the link between cognitive deficits and depression in children with epilepsy.

Based on a number of reviews and past studies the present author has focused the study on children with depressive symptoms and Mesial Temporal Sclerosis and its effects on the

cognitive performance.

Patient Inclusion Criteria:

1. New case of epilepsy where a diagnosis of epilepsy had not been previously confirmed: the child was seen for the first time by a participating paediatric neurologist within the data collection period;
2. The child was diagnosed between the ages of 4 and 12 years;

Patient Exclusion Criteria:

1. The diagnosis of epilepsy had been previously confirmed by another physician;
2. The patient was diagnosed with other progressive or degenerative neurological disorders;
3. The patient was diagnosed with other major co-morbid non-neurological disorders that would have an impact on quality of life (e.g. asthma requiring daily medication, renal failure);
4. The parent or caregiver had insufficient command over English to complete questionnaires.

Criteria for patients with epilepsy included (i) diagnosis of epilepsy within the past 12 months; (ii) chronological age between 8 and 18 years; (iii) no other developmental disabilities (e.g. autism, developmental delay); (iv) no other neurological disorder; and (v) normal clinical magnetic resonance imaging (MRI).

Epilepsy participants met criteria for classification of idiopathic epilepsy in that they had normal neurological examinations, no identifiable lesions on MR imaging and no other signs or symptoms indicative of neurological abnormality (Engel, 2001).

Cognitive function was considered to be within the normal range (IQ ‡70) for 50% of the participants.

Objectives:

- To examine the difference between depression level (high and low depression) and cognitive functions of Mesial Temporal Sclerosis (MTS) children.
- To understand the relationship between the level of depression, and cognitive performance of Mesial Temporal Sclerosis (MTS) children.

METHOD

Participants:

The sample of MTS children was recruited during the year 2012- 2013. The initial sample consisted of 43 children with Mesial temporal sclerosis (MTS), out of which 2 children had other neurological problems, 1 had psychiatric issue, 2 had mild mental retardation, 2 were incomplete data. Therefore they were excluded from the analysis. The rest of the subjects, that is, 36 constituted the final sample size. The permission and consent of the participants and their parents was taken to include their data for analysis and for the publication of the

paper. They underwent neuropsychological tests, clinical examination, magnetic resonance imaging (MRI) and electroencephalography (EEG). The children's age ranged from eight years to fifteen years. Majority of the MTS subjects (90%) were right handed. The subjects' education ranged from third grade to tenth grade.

Twenty one subjects did not show depression and their mean age was 12.83 years; 15 subjects had high depression with a mean age of 12.73 years. These subjects were referred to Bangalore Neuro Centre, Bangalore, India from the community for treatment.

Procedure:

MTS patients were divided into High-depression and Low-depression groups by the median split of their depression scores on the Centre for Epidemiological Studies – Depression Scale for Children (CES-DC).

- 21 (58%) subjects scored below the CES-DC cut-off score of 15, considered as the low depression group i.e., Group-1. Their mean age is 12.83 and the standard deviation (SD) is 2.28.
- 15 (42%) subjects scored above the CES-DC cut-off score of 15, considered as the high depression group i.e., Group-2. The mean age of this group is 12.73 and SD is 2.60.

Neuropsychological Tests

The NIMHANS Neuropsychological Battery for Children was administered to understand the cognitive profile of the MTS subjects.[7] The battery comprises of 10 tests, which assess the aspects of attention, motor speed, mental speed, comprehension, executive functions, learning and memory.

The above mentioned tests take approximately 1 hour 45 minutes to 2 hours depending on the subject's performance. The above neuropsychological tests are indianised according to age, gender and educational background. To understand their depression level, Centre for Epidemiological Studies – Depression scale for Children was employed.

The aforementioned tests are individual assessments. The instructions and norms for analyses can be referred to from the NIMHANS Neuropsychology Battery (Rao et al., 2004).[8]

- **Color Trails Test:** The Color Trails test (D'Elia, Satz, Uchiyama & White, 1996) was developed by the World Health Organization as part of a multicenter study of human immunodeficiency virus (HIV) infection. The test is an analogue of the Trail Making test and is considered to be free from the influence of language. It has two parts. Part 1 requires sustained attention, perceptual tracking and simple sequencing, while Part 2 requires mental flexibility in addition to the above.
- **Digit Symbol Substitution Test:** The Digit Symbol Substitution Test (Wechsler,1981) is a test of visuomotor coordination, motor persistence, sustained attention and response speed. Rapid information processing is required in order to substitute the symbols

accurately and quickly.

- **Digit Vigilance:** The Digit Vigilance Test (Lezak, 1995) consists of numbers 1 to 9 randomly ordered and placed in rows on a page.[9] There are 30 digits per row and 50 rows per page. The digits are closely packed on the sheet. The subject has to focus on the target digits i.e. 6 and 9 amongst other distracter digits. Inability to sustain and focus attention leads to both increased time to complete the test as well as errors.

- **Motor Speed:** To assess the domain of motor speed the *Finger Tapping Test* (Halstead, 1947) was administered. Number of taps with the forefinger of each hand was recorded. The average number of taps across trials for the right hand and left hand was used for analyses.

- **Verbal Fluency:** To assess phonemic fluency, the *Phonemic Fluency Test* (Rao et al., 2004) was administered.[8] To make the test suitable for use in Indian languages, the phonemes "Ka", "Pa", and "Ma" were used. The score used was the average number of words generated.

- **Category Fluency:** The *Animal Names Test* (Lezak, 1995) was administered to assess category fluency.[9] The score used was the total number of animal names generated.

- **Verbal Learning and Memory:** The *Auditory Verbal Learning Test* (AVLT) was administered which assesses immediate memory span, new learning, susceptibility for interference and recognition memory (Schmidt, 1996).[10] The present study used the World Health Organization (WHO) word lists (Maj et al., 1993) which were translated into different Indian languages.[11] The test was administered and scored according to the procedure given by Schmidt (1996).[10] For analyses, the scores of Trial I-V Total, Immediate recall and Delayed recall of the word list were considered.

- **Visuospatial Abilities & Visual Memory:** Rey-Osterrieth Complex Figure Test (ROCFT) was employed and examinees were asked to reproduce a complex line drawing, first by copying and then from memory. The test therefore permits the evaluation of different functions, such as visuospatial abilities, memory, attention, planning, and working memory (executive functions).

- **Centre for Epidemiological Studies – Depression Scale for Children (CES-DC)** was administered to assess the depression level among children. Score 15 is used as a cut off score. Scores 15 and above are suggestive of significant depressive symptoms (Weissman et al., 1980).

Statistical analysis

Statistical analysis was performed using one-way Analysis of Variance (ANOVA) test to compare the mean difference of the number of high and low depressed and cognitive performances. The correlation between high and low depression groups and cognitive variables were tested using Spearman's correlation. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS version 17).

Table-1: ANOVA Comparisons of High and Low Depression groups of Neuropsychological (NP) Tests

NP Variables	Groups Compared	N	Mean	SD	F	Level of Sig.
Color Trails-1	Low depression	21	114.52	68.43	3.59	0.06
	High Depression	15	165.40	92.84		
Color Trails-2	Low depression	21	220.76	96.34	0.93	0.34
	High Depression	15	255.67	120.16		
Digit Vigilance	Low depression	21	616.81	216.77	1.22	0.27
	High Depression	15	690.8	167.38		
Finger Tapping – Right Hand	Low depression	21	47.56	89.31	0.75	0.39
	High Depression	15	27.36	5.96		
Finger Tapping – Left Hand	Low depression	21	25.86	3.89	0.09	0.76
	High Depression	15	26.43	7.35		
Digit Span - Forward	Low depression	21	5.14	5.02	2.89	0.09
	High Depression	15	2.87	1.40		
Digit Span - Backward	Low depression	21	3.24	2.755	1.33	0.25
	High Depression	15	2.33	1.49		
Digit Symbol Substitution	Low depression	21	303.05	117.87	2.36	0.13
	High Depression	15	361.8	105.98		
Rey's Complex Figure Test (ROCFT) - COPY	Low depression	21	32.19	7.91	6.09	**0.01****
	High Depression	15	24.00	12.02		
NP Variables	**Groups Compared**	**N**	**Mean**	**SD**	**F**	**Level of Sig.**
ROCFT – Immediate Recall	Low depression	21	15.26	5.46	7.44	**0.01****
	High Depression	15	9.23	7.81		
ROCFT –Delayed Recall	Low depression	21	14.02	5.69	7.86	**0.01****
	High Depression	15	8.23	6.64		
LM - Immediate Recall	Low depression	21	5.88	2.61	5.37	**0.02***
	High Depression	15	4.00	2.06		
LM- Delayed Recall	Low depression	21	4.50	2.77	1.86	0.18
	High Depression	15	3.30	2.32		
Category Fluency	Low depression	21	8.26	3.02	0.43	0.51
	High Depression	15	7.47	4.19		
COWA	Low depression	21	5.71	2.32	2.10	0.15
	High Depression	15	4.45	2.89		
AVLT - Total	Low depression	21	43.81	12.27	7.83	**0.01****
	High Depression	15	30.27	16.81		
AVLT – Immediate Recall	Low depression	21	8.95	3.217	7.48	**0.01****
	High Depression	15	5.87	3.50		
AVLT – Delayed Recall	Low depression	21	8.6	4.01	7.03	**0.01****
	High Depression	15	5.27	3.24		

* Values are statistically significant at the 0.05 level

** Values are statistically significant at the 0.01 level.

Table -2: Association between Neuropsychological Test scores and Low Depression and High Depression

Neuropsychological Test Variables	Low Depression group		High Depression group	
	Pearson Correlation	Level of Significance	Pearson Correlation	Level of Significance
Color Trails-1	-0.34	0.06	-0.35	0.09
Color Trails-2	0.76	0.08	0.89	0.15
Digit Vigilance	0.52*	0.03	0.54	0.45
Finger Tapping-Right Hand	-0.30	0.29	0-.65	0.08
Finger Tapping-Left Hand	-0.42	0.18	-0.64	0.29
Digit Span-Forward	-0.41	0.19	-0.77	0.26
Digit Span-Backward	-0.48*	0.03	-0.57	0.50
Digit Symbol Substitution	0.55	.008	0.56	0.02*
ROCFT - COPY	-0.51	0.17	-0.07	0.06
ROCFT –Immediate Recall	-0.47	0.45	-0.63	0.07
ROCFT –Delayed Recall	-0.38	0.41	-0.65	0.05*
LM -Immediate Recall	-0.33	0.47	-0.77	0.02*
LM -Delayed Recall	-0.26	0.24	-0.75	0.02
Category Fluency	-0.49	0.08	-0.30	0.42
Phonemic Fluency	-0.27	0.08	-0.63	0.24
AVLT – Total (Learning)	-0.79	0.06	-0.80	0.08
AVLT –Immediate Recall	-0.74*	0.02	-0.73	0.24
AVLT – Delayed recall	-0.79	0.09	-0.86	0.06

* Values are statistically significant at the 0.05 level.

Note 1.: ROCFT - Rey's Complex Figure Test; LM- Logical Memory; COWA – Controlled Oral Word Association; AVLT – Auditory Verbal Learning and Memory.

Note 2.: Bold values are statistically significant.

RESULTS

The effect of low and high baseline depression on CES-DC, lowest CES-DC scores and maximum CES-DC, are represented in Table -1. When comparing low and high depression

based upon the neuropsychological variable scores, there was a significant effect on the CFT-copy (one-way ANOVA, P=0.019), CFT-IR (P=0.01), CFT-DR- P=0.008), AVLT-Total (P=0.008), AVLT-IR P=0.01) and AVLT-DR (P=0.012), LM-IR (P=0.027).

When comparing low and high depression based upon the Neuropsychological variables CT-1, CT-2, DV, FT-R, FT-L, DS-F, DS-B, DSST, LM-DR, CF and PF, there were no significant effects on the CES-DC.

The Spearman's correlation between CES-DC and neuropsychological variables is represented in Table-2. When comparing low depression based upon the neuropsychological variable scores, there was a significant correlation (Spearman's correlation) in DV (P=0.03), DS-B (P=0.038) and AVLT- IR (P=0.020).

There was a significant correlation between the CES-DC (High – depression) score on CFT-DR (Spearman's correlation, P=0.05), LM –IR (P=0.19), LM-DR (P=0.016) and DSST (P=0.024).

DISCUSSION

The present study investigated the performance of MTS subjects on the cognitive domains. The study also focused on the effect of depression in MTS subjects on the performance level on various cognitive functions such as attention, motor speed, mental speed, execution and memory.

By conducting the various neuropsychological tests on the subjects, MTS children's cognitive impairment was diagnosed. The various tests demonstrated high impairment in the areas of learning and memory followed by attention and mental speed functions. The highly depressed MTS children performed poorly in the areas of sustained attention, processing speed, verbal learning, visuoconstructive ability and visual memory. Irrespective of the presence or the absence of depressive symptoms, cognitive dysfunctions are well evident in low depression MTS children. Their performance is poor in memory and processing speed functions. Children may show varied 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.

Many researchers have conducted studies to find the relation between depression and Mesial Temporal Sclerosis. Many studies have provided the evidence of higher prevalence of depressive symptoms with those presenting MTS. According to one study, the prevalence of depression ranges from 28% in children with uncomplicated epilepsy to 58% in children with refractory epilepsy. (Rutter & Coll,1970). A study conducted in a Brazilian tertiary care facility showed that depression was the most frequent Personality Disorder in children with refractory epilepsy.

(Thome-Souza et al., 2004).[12] As adults, children with epilepsy remain undertreated and under diagnosed, especially those with depression. (Ettinger et al., 1998 & Siddarth.P et al., 2003)[13]. Suicide rates are high even in children and adolescents with epilepsy. (Baker, 2006).[14]

In patients with temporal lobe epilepsy caused by Mesial Temporal Sclerosis (TLE-MTS), the frequency of depression is extremely high even when compared to other types of epilepsy (50–60%).

According to another study, results support a specific association between MTS and lifetime "post seizure onset," - Major Depressive Disorder. The lack of association with current depression is in line with the hypothesis that the link between MTS and depression is more of a chronic than a state-dependent condition (Sanchez-Gistau et al., 2012).[15]

The present study shows that the above problems exist in MTS subjects . There could be a number of reasons for high depression among the MTS 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 the lower middle income group, the opportunities for growth and development may be restricted. Depression, a common psychiatric comorbidity among patients with chronic temporal lobe epilepsy, seems to be undertreated and to have adverse effects on cognitive functioning.[16] Therefore from the present study we can come to an understanding that depression has significant effect on learning and memory of MTS children.

CONCLUSIONS

- In an attempt to understand the difference between depression and cognitive performance, the level of depression of MTS children and cognitive performance were measured.
- The findings of the current study signify that there are differences in neuropsychological variables between low-and high-depressed MTS children.
- The MTS children who performed low in cognitive functions reported higher levels of depression.
- The MTS children with low levels of performance differ in temporal lobe functions viz., verbal learning and memory, and visual learning and memory.
- The MTS children's cognitive impairments are more in attention, mental speed and memory functions.
- The children with MTS are not affected in the areas of motor speed, comprehension and executive functions.
- This findings of the study can help in retraining activities and strategies to enhance MTS children's performance mainly in sustained attention, mental speed, learning and memory function and mood level.

IMPLICATIONS AND FUTURE DIRECTIONS

The study finds its implication in counselling, cognitive retraining, psychotherapy and psychological interventions. A longitudinal study of the MTS children can throw light on the post-intervention effectiveness. It also enables the researcher to learn the number of patients who have stopped taking medications for their seizures. Future studies can focus on the gender differences in cognitive functioning of the children. Since the sample size is just 36, it is not possible to make generalizations of the results obtained.

REFERENCES

1. Annegers JF. The epidemiology of epilepsy. In: Wyllie E, editor. The treatment of epilepsy: Principles and practice. 3 rd ed. Lippincott Williams and Wilkins: Philadelphia; 2001. p. 131-8.
2. Schachter SC, Wheless JW. The evolving place of vagus nerve stimulation therapy.
3. Blum D. Total impact of epilepsy: biological, psychological, social, and economic aspects. Barrow quarterly. 1999;15(1).
4. Sarason, I. G. & Sarason, B. R. (2002). Abnormal Psychology: the Problem of Maladaptive Behaviour. Upper Saddle River, N.J: Prentice Hall.
5. Sanchez-Gistau V, Pintor L, Sugranyes G, Baillés E, Carreño M, Donaire A, Boget T, Setoain X, Bargalló N, Rumia J. Prevalence of interictal psychiatric disorders in patients with refractory temporal and extratemporal lobe epilepsy in Spain. A comparative study. Epilepsia. 2010 Jul 1;51(7):1309-13.
6. Ciechanowski P, Chaytor N, Miller J, Fraser R, Russo J, Unutzer J, Gilliam F. PEARLS depression treatment for individuals with epilepsy: a randomized controlled trial. Epilepsy & Behavior. 2010 Nov 30;19(3):225-31.
7. Kar BR, Rao SL, Chandramouli BA, Thennarasu K. NIMHANS neuropsychological battery for children-manual. Bangalore: NIMHANS publication division. 2004.
8. Rao SL, Subbakrishna DK, Gopukumar K. NIMHANS neuropsychology battery-2004, manual. National Institute of Mental Health and Neurosciences; 2004.
9. Lezak MD. Neuropsychological Assessment, 3rd edR Oxford Univ. Press, New York. 1995:544-6.
10. Schmidt, M. (1996). *Rey auditory verbal learning test: A handbook* (p. 1996). Los Angeles: Western Psychological Services.
11. Maj M, Satz P, Janssen R, Zaudig M, Starace F, D'elia L, Sughondhabirom B, Mussa M, Naber D, Ndetei D, Schulte G. WHO Neuropsychiatric AIDS Study, cross-sectional phase II: neuropsychological and neurological findings. Archives of General Psychiatry. 1994 Jan 1;51(1):51-61.

12. Thome-Souza S, Kuczynski E, Assumpção F, Rzezak P, Fuentes D, Fiore L, Valente KD. Which factors may play a pivotal role on determining the type of psychiatric disorder in children and adolescents with epilepsy?. Epilepsy & Behavior. 2004 Dec 31;5(6):988-94.

13. Ettinger AB, Weisbrot DM, Nolan EE, Gadow KD, Vitale SA, Andriola MR, Lenn NJ, Novak GP, Hermann BP. Symptoms of depression and anxiety in pediatric epilepsy patients. Epilepsia. 1998 Jun 1;39(6):595-9.

14. Baker GA. Depression and suicide in adolescents with epilepsy. Neurology. 2006 Mar 28;66(66 suppl 3):S5-12.

15. Sanchez-Gistau V, Sugranyes G, Baillés E, Carreño M, Donaire A, Bargalló N, Pintor L. Is major depressive disorder specifically associated with mesial temporal sclerosis?. Epilepsia. 2012 Feb 1;53(2):386-92.

16. Paradiso S, Hermann BP, Blumer D, Davies K, Robinson RG. Impact of depressed mood on neuropsychological status in temporal lobe epilepsy. Journal of Neurology, Neurosurgery & Psychiatry. 2001 Feb 1;70(2):180-5.