Study of Executive Dysfunctions in Epileptic Patients and its Correlation with Demographics and Seizure Characteristics

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ABSTRACT
Introduction: Epilepsy is one of the most common neurological disorders known to man with a global prevalence of 50-70 million and an annual prevalence of 2.4 million per year. This disease process affects the overall quality of life due to its psychosocial and cognitive outcomes. In recent times, the concept of executive dysfunction in patients with epilepsy has emerged. This phenomenon has widespread therapeutic implications. This study is aimed to assess the executive function in epileptic patients using Frontal Assessment Tests and to analyze its correlation with demographic and seizure characteristics.

Materials and Methods: This was a prospective observational study, conducted on 100 epileptic patients in Department of neurology, during period between Jan.2021 to Dec.2021. All patients were screened for executive dysfunction using six subsets of frontal assessment tests - Similarity, Fluency, Luria motor test, Go-No-Go task, Conflicting instructions, Prehension behavior. Abnormalities in the applied test were correlated with demographic and seizure characteristics.

Results: Out of 100 epileptic patients, 56 (56%) were female, 44 (44%) male. The most common abnormality noted   in similarity task (27%) followed by fluency test (24%). There was significant association between abnormality in subtest of FAT - Similarity test, Fluency test, Go-No-Go task and duration of seizure. But no significant association found   between number of AEDs and any aspect of FAT.

Conclusion: it is concluded that deficits in different aspect of executive functions was common in epileptic patients. So these tests can be used as representive tests for evaluation of executive dysfunction.

Keywords: Executive dysfucnction, Frontal assessment test, Epilepsy

I. INTRODUCTION

Epilepsy is one of the most common neurological disorders known to man with a global prevalence of 50-70 million and an annual prevalence of 2.4 million per year.[1] This disease process affects the overall quality of life due to its psychosocial and cognitive outcomes. Executive functions are mediated by complex neural circuits or feedback loops that connect discrete regions in the prefrontal lobes with other cortical regions in the brain and sub cortical structures.It constitutes three basic functions working memory operations such as the maintenance and updating of relevant information ('updating'), inhibition of prepotent impulses ('inhibition'), and mental set shifting ('shifting').[2] In recent times, the concept of executive dysfunction in patients with epilepsy has emerged. This phenomenon has widespread therapeutic implications. Most of the studies were mainly focusing on either memory or language abnormalities, which often times are due to focal symptomatic seizures. In the study by Borai et al, impaired executive function among adult patients with idiopathic epilepsy was demonstrated.[3] Different factors contribute to adverse cognitive effects in epileptic patients including anti-epileptic drugs, particularly the older generations; the underlying brain lesions; and infections (e.g. HIV encephalopathy). In addition, age at seizure onset; seizure type and frequency, duration of the seizure and refractoriness tend to affect the prevalence of CAE in epileptic patients. Although the magnitude of cognitive function of epilepsy has been known for a long period of time, there is scarcity of data from the developing countries, particularly in India. Several neuropsychological studies have assessed executive functioning. The standard neuropsychological tests for the assessment of executive functions are time-consuming and require quite experienced administrators. Thus, a screening tool which can detect executive dysfunction in a short time seems to be beneficial. Frontal Assessment Battery (FAB), which was first

introduced in 2000 by Dubois et al. is a sensitive test for evaluating executive functioning. It takes about 10 minutes to be completed and is designed to investigate the aspects of executive functions, which are predominantly reliant on the intact integrity and functionality of frontal lobes. FAB consists of six subtests and measures different aspects of frontal lobe function.These six subtests include conceptualization (similarity), mental flexibility (fluency), motor programming (Luria motor series), sensitivity to interference (conflicting instructions), inhibitory control (Go-No-Go task), and environmental autonomy (prehension behavior). This study is aimed to assess the executive function in epileptic patients using Frontal Assessment Tests and to analyze its correlation with demographic and seizure characteristics.

II. METHODOLOGY

This study was observational cross sectional study conducted on 100 epileptic patients in Department of Neurology, TVMCH, Tirunelveli during period from Jan. 2021 to Dec.2021 after getting Institutional ethical committee approval and informed written consent from all patients included in this study.

Inclusion criteria: 100 patients both male and female with seizure disorder diagnosed as per International league Against Epilepsy (ILAE) were included.

Exclusion criteria: presence of fronto-temporal lesion on CT/MRI, mental retardation, blindness, hearing impairment, inability to read, known case of depression, dementia, pregnancy, terminally ill patients were excluded in this study.

All patients were interviewed about their demographic data, detailed clinical and seizure history. Then all patients were screened for executive dysfunction by using Frontal Assessment Tests. The tests consists of six subtests and measures different aspects of frontal lobe function, include conceptualization (similarity), mental flexibility (fluency), motor programming (Luria motor series), sensitivity to interference (conflicting instructions), inhibitory control (Go-No-Go task), and environmental autonomy (prehension behavior). Abnormalities in the applied test were correlated with demographic and seizure characteristics.

Data analysis: All obtained data were entered in excel sheet and analyzed by appropriate statistical tests. The correlation of various factors with executive dysfunction is assessed by tests of significance. A multivariate analysis is attempted by SPSS software to look for the independence of any factor. A p value of less than 0.05 is taken as significant.

III. RESULTS
Table 1: Demographic and Seizure Characteristics of epileptic patients

Variables	No. of patients (N=100)	Percentage (%)
Age group (in yrs)		
< 40	68	68%
40-60	20	20%
>60	12	12%
Sex		
Female	56	56%
Male	44	44%
Education status		
Illiterate	20	20%
Primary	42	42%
Secondary	26	26%
Higher Secondary	12	12%
Age at seizure onset (in yrs)		
<20	80	80%
>20	20	20%
Family history		
Yes	5	5%
No	95	95%
Duration of seizure disorder		

<10	36	36%
>10	64	64%
Type of epileptic seizure		
Generalized	53	53%
Focal	39	39%
Myoclonic	8	8%
Seizure frequency		
Once in 6 month	30	30%
No for > 6 month	70	70%
Type of AED		
Mono-therapy	79	79%
Poly-therapy	21	21%
Duration of AED (in yrs)		
<10	75	75%
>10	25	25%
Brain CT/MRI findings		
Normal	45	45%
Abnormal	20	20%
EEG findings		
Normal	40	40%
Abnormal, nonepileptiform	5	5%
Abnormal, epileptiform	20	20%

Type of AED	No. of patients (N=100)	Percentage (%)
Mono-therapy		
CBZ	8	8%
PHN	36	36%
PHB	8	8%
VAL	20	20%
CLO	4	4%
Poly-therapy		
PHN+CBZ	5	5%
PHN+VAL	8	8%
PHB+VAL	3	3%
CBZ+VAL	3	3%
PHN+CBZ+VAL	5	5%

Table 2: Distribution of epileptic patients according to FATsubsets

Subsets of FAT	Abnormal	Normal
Similarity	27 (27%)	73 (73%)
Fluency	24 (24%)	76 (76%)

Luria motor test	19 (19%)	81 (81%)
Go-No-Go test	14 (14%)	86 (86%)
Conflicting instruction	9 (9%)	91 (91%)
Prehension behavior	7 (7%)	94 (94%)

Table 3: Correlaton between abnormality in subsets of FAB and clinical variables of epileptic patients

Variables	No. of patients (N=100)	Subsets of FAT						P Value
Age group (in yrs)		Similarity	Fluency	Luria motor test	Go-No-Go test	Conflicting instruction	Prehension behavior	
< 40	68	17	13	19	10	5	4	0.0513
40-60	20	10	2	0	1	4	3	
>60	12	0	9	0	3	0	0	
Sex								
Female	56	20	19	1	6	6	4	0.0701
Male	44	7	5	18	8	3	3	
Education status								
Illiterate	20	4	6	1	2	5	2	
Primary	42	14	11	5	6	1	5	0.0524
Secondary	26	6	5	12	1	2	0	
Higher Secondary	12	3	2	1	5	1	0	
Family history								
Yes	5	1	1	1	0	1	1	0.7234
No	95	26	23	18	14	8	6	
Duration of seizure disorder (in yrs)								
<10	36	2	6	3	14	7	4	<0.0001*
>10	64	25	18	16	0	2	3	
Type of epileptic seizure								
Generalized	53	20	10	11	6	4	2	0.0753
Focal	39	6	13	3	8	5	4	
Myoclonic	8	4	1	3	0	0	1	
Type of AED								
Mono-therapy	79	23	21	12	13	9	1	0.0860
Poly-therapy	21	4	3	7	1	0	6	
Brain CT/MRI findings(N=85)								
Normal	65	17	23	8	8	5	4	0.0525
Abnormal	20	8	0	2	5	3	2	
EEG								

findings(N=85)								
Normal	50	20	12	8	0	5	5	0.0620
Abnormal, nonepileptiform	15	1	2	2		10	0	0
Abnormal, epileptiform	20	6	4	2	4	4	0	
Age at seizure onset (in yrs)								
<20	78	23	22	18	11	2	2	0.0512
>20	22	4	2	1	3	7	5	
Duration of AEDs regimens (in yrs)								
<10	70	19	16	11	12	7	5	0.6436
>10	30	8	8	8	2	2	2	

Demographic and seizure variables: Out of 100 epileptic patients, 56(56%) were females and 44 (44%) were males. They were divided into three groups. Group-1, 2 and 3 included patients of age < 40 years and consisted of 68 patients (68), age between 40-60 years consisted of 20 patients (20) and group-3 included patients of age > 60 years and consisted of 12(12%). The educational status varied between illiteracy to higher education, were 20(20%) illiterate, 42 (42%) upto primary, 26(26%) secondary and 12(12%) higher secondary education level and above. 80(80%) had seizure onset at age < 20 years followed by 20(20%) at age >20 years. 5(5%) had positive family history of epileptic seizure, in 36(36%) patients duration of seizure disorder was < 10 years followed by 64(64) patients had > 10 years of duration. 30(30%) patients had seizure once in six month and 70(70%) patients were seizure free atleast more than six month. Majority of patients had GTC seizure in 53(53%) followed by focal in 39(39%) and myoclonic in 8 (8%). Out of 100, 65 patients had atleast one EEG study during their follow up, out of them, 40 were normal and rest were abnormal in 5 with abnormal non-epileptiform discharges and 20 with abnormal epileptiform discharges. 65 patients had atleast one brain iwere normal. Phenytoin alone was the most commonly used AED in 36 (36%) patients. The most commonly used combination was phenytoin with sodium valproate in 8 (8%) patients. 5 (5%) of patients were on triple therapy. Patients were on AED for atleast 10 years, while patients were on AED for >10 years (Table 1).

Executive function assessment: The executive function was assessed using six subsets of frontal assessment test-similarity, fluency, luria motor test, Go-No-Go test, conflicting instruction and prehension behavior. Most commonly affected test was similarity task in 27(27%) followed by fluency in 24(24%), luria motor test in 19(19%), Go-No-Go in 14(14%), conflinting instruction in 9(9%) and prehension behavior in 6(6%). Female patients had more abnormality in different task of FAT than males (Table 2).

Correlation analysis: None of demographic variables showed significant association with any aspect of FAT. Duration of seizure disorder was significantly correlated with abnormality in similarity, fluency, Go-No-Go Task but Age of seizure onset, family history of seizure, seizure frequency, seizure types, neuroimaging , EEG findings, number of AEDs and duration of AEDs treatment showed no significant association with any aspect of FAT (Table 3).

IV. DISCUSSION
In this study, executive functions in epileptic patients was assessed by using standard frontal assessment tests (FAT).

The major findings of this study are as follows: (1) Epileptic patients showed lower performance in most tests in similarity, fluency, luria motor test and conflicting instruction (except Go-No-Go task and prehension behavior. (2) Duration of seizure disorder was significantly associated with abnormality in similarity, fluency, Go-No-Go task. (3) Duration of time since the last seizure had no significant effect on any subsets of FAT. (4) Age of seizure onset, family history of epilepsy, seizure types and seizure frequency showed no significant effect on any subsets of FAT. (5) Number of AEDs, duration of treatment had no significant effect on any subsets of FAT.

Although it seems that FAT is a most sensitive test for evaluating the frontal lobe

function. In fact, it was shown that FAT subsets abnormality could be explained by the performance of other neuropsychological tests such as word list memory, constructional praxis, constructional, recall and stroop color word test. The performance on these tests is dependant on both frontal and nonfrontal regions, including the precuneus, right temporo-parietal region and posterior cingulated cortex. The majority of reviewed studies have used digit span, TMT, Stroop test to assess the executive dysfunction in epileptic patients. TMT-A is test of visual attention, while TMT-B is tests of inhibitory control and mental flexibility. Stroop test assess different domains of executive functions, including inhibition, switching, sensitivity to interference and mental flexibility. The almost all studies reported worse performance on TMT, Stroop test in patients with seizure disorders. In our study, we found the epileptic patients have deficits in various subsets of FAT, which might not be the result of frontal dysfunctioning but also because of the disruptions in the connection between frontal regions with other non-frontal regions. Similar to our study, several previous studies have evaluated the association between cognitive deficits in epileptic patients and different clinical variables but previous results are not entirely consistent.

V. CONCLUSION

In this study, it is concluded that deficit in various aspect of executive functions was common in epileptic patients. Most commonly affected subset of FAT for executive dysfunction was similarity task. We found significant association between duration of seizure disorder and abnormalities in tests especially in similarity, fluency and Go-No-Go task used for executive dysfunction. So these test can be considered as representative tests for executive dysfunction in epileptic patents.

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