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Original Research Article

To Study the Clinical Correlation of Cognitive Domains in Patients with Seizure Disorders

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Abstract

Aim: To study the clinical correlation of different cognitive domains like Executive function, mental speed and attention in subjects with seizure disorders.

Methods: The study was conducted in a tertiary care hospital over a period of 1yr after taking informed consent from 100 patients by random sampling after fulfilling the inclusion criteria.

Results: In our study , We found Controlled oral word test & Digit symbol substitution test for executive function and mental speed was statistically significant with duration of seizure (p value 0.04 and p value 0.000 respectively) while rest clinical variables were not statistically significant P value >0.05. Color trails test for attention was statistically significant with duration of AED (p value 0.02) and medication status (p value 0.03) while rest clinical variables were not statistically significant.

Conclusions: The high prevalence of cognitive impairment among epilepsy patients calls for early neuropsychological assessment soon after the diagnosis of epilepsy.

Keywords: Cognitive Impairment, Attention, Mental Speed, Seizures Duration, Seizures.

Introduction

Patients with epilepsy are at significant risk for cognitive impairment and behavioral abnormalities.[1]Poor adherence to Antiepileptic Drugs (AEDs) may contribute to poor seizure control, cognitive impairment, behavioral disorders, and excess mortality.[2]

Cognitive difficulties may affect multiple domains, including memory, language, attention, and executive function. [3] Other studies have shown the effects of epilepsy on intelligence, language, attention, executive function and psychomotor speech.[4]

Verbal memory, language, executive functions, and attention are domains of cognitive consequences in epilepsy. However, most of the studies focus on one or two domains in a relatively small sample. For example, 31 studies have probed into the temporal lobe epilepsy with cognitive impairment in 357 patients and the meta-analysis focuses on the social cognitive impairment. [5]

Another study enrolled 247 newly onset untreated epileptic patients, who showed 49.4% impairment in attention or executive function, 47.8% impairment in episodic memory, and 39.3% subjective

deficits in attention and 35.2% subjective deficits in memory.[6] Therefore, it is crucial to evaluate the cognitive function of epileptic patients and to seek interventions as soon as possible.

Cognition includes the brain's response to the objective world, having range from simple perception of the people themselves and the environment, attention, judgment, to the ability of performing complex mathematical calculation, language ability, memory, space ideation, executive function, etc. [7]

There are many cognitive domains, such as memory barriers, or falling of executive function, psychomotor speed, naming ability, visual–spatial ability etc. which are the manifestations of cognitive impairment in epileptic patients.[8, 9] The life quality of epileptic patients is significantly declined by these cognitive deteriorations and eventually cripple them .

Material and methods

Study Setting: This is a hospital based cross-sectional study, which was conducted in outpatient department of psychiatry, MGM Medical College and mental hospital Banganga, after clearance obtained institutional ethic committee of MGMMC, Indore. Patients were included after the meeting inclusion criteria and those patients who do not meet inclusion criteria are excluded from the study.

Study Design: The study was carried out with a cross sectional observational study the as per the designed objective of the study.

Sample: Purposive sampling technique was used. The study sample was consisted of 100 subjects of seizure.

Inclusion and exclusion criteria-

- The patients included were in the age group of 18 to 60 years of either sex and diagnosed as having epilepsy as per ILAE Classification. Patients with mental retardation, head injury, substance dependent. Any medical co morbidity, Pregnancy and lactation were excluded.
- Written informed consent was obtained from all participants after complete description of the study to the subjects. Evaluation of the samples was done as per procedure of methodology.

Ethical consideration

The study was approved by Institutional Ethics Committee. Written informed consent was taken from the study subjects. They were informed about the purpose of the study and were ensured confidentiality. They were also informed about their right to withdraw any point of time during the study and told that their withdrawal from study would not have any impact in the treatment of the condition. All voluntary participants were informed of possible risks and benefits of participating in the research.

NIMHANS Neuropsychological test: All study participants completed a comprehensive battery of well-established neuropsychological tests including:

1. Attention and pyschomotor speed:

a. Digit symbol substitution and test: DSST is a test of visuomotor coordination, motor persistence, and sustained attention response speed.

b. Trail making test -A: Participants are asked to connect a series of 25 numbered dots in ascending order as quickly as they can (e.g., 1–2–3, etc.). Time to completion is recorded.

c. Trail Making Test—B: This test adds a set-shifting component to Trail Making Test—A and requires participants to alternate between numbers and letters in ascending order (e.g., 1–A–2–B, etc.).Time to completion is recorded.

2. Executive functions:

Controlled Oral Word Association (COWA): It is a measure of verbal fluency. Participants are asked to generate

as many words as they can that begin with a given letter. A total of three letters are given. Participants have 60 s for each letter and cannot use proper nouns or numbers, or provide different endings to a root word already given.

Methodology

- Protocol is made after discussion with Guide and approval from ethics committee of the institute.
- Subjects were included in the study from epilepsy clinic in mental hospital Banganga and OPD of department of psychiatry, MGM, medical college, & M.Y. hospital and Mental hospital, Indore after meeting inclusion criterion. Subjects not meeting inclusion criteria or meeting exclusion criteria were excluded from the study.
- Department of psychiatry runs epilepsy clinic on every Thursday during OPD hours in mental hospital Banganga. Subjects visiting in epilepsy clinic were precisely evaluated for seizure and other comorbidities then diagnosis of seizure accordance to ILAE classification expended version Then subject precisely were screened for study. After applying strict inclusion and exclusion criteria participants were included in the study.
- Subjects who were included for study where explained the study procedure in detail containing Information about study its procedure, duration, participant selection, risk, benefits, voluntary participation and confidentiality of the study. Relevant questions asked about the study procedure were answered satisfactorily. After explaining the procedure in detail, the subject were ask to provide written consent form for the participation in study without any under force and willingly.
- A detailed assessment of the patient's complaint was done on the basis of seizure questionnaire and diagnosis was formulated clinically in accordance with international league against epilepsy classification for seizure Disorders. Afterwards NIMHANS neuro-psychological battery test was administered for assessment of cognitive domain in seizure patients. After establishment of diagnosis appropriate treatment was provided to the patient on the same consultation. All the collected information was stored and later digitized for interpretation.

Statistical analysis

The statistical analysis of data was done by SPSS version 23.0 (SPSS South Asia Pvt Ltd., Bengaluru, Karnataka, India) .Test of significance was seen by chi square test and fisher exact test was applied for correction wherever applicable.

Results

Table 1: Association of clinical variables with cognitive domain - controlled oral word test (COWT)

Variables	COWT <15 Percentiles	COWT > 15 Percentiles	P Value
Type of seizure			0.99
CPS	0	6	
CPS with generalization	0	7	
GTCS	11	76	
Seizure frequency			0.07
<10 episodes/years	3	50	
>10 episodes/years	8	39	
Duration of seizure			**0.04**
0-2 years	2	14	

3-5 years	0	28	
>5 years	9	47	
Duration of AED			0.197
Drug naive	3	35	
0-1years	0	10	
1-2years	0	12	
2-5years	3	12	
>5years	5	20	
Medication status			0.66
Drug Naïve	3	35	
Monotherapy	5	28	
Polytherapy	3	29	

Table 2: Association of clinical variables with cognitive domain –Digit symbol substitution test (DSST)

Variables	DSST <15 Percentiles	DSST > 15 Percentiles	P Value
Type of seizure			0.07
CPS	4	2	
CPS with generalization	7	0	
GTCS	50	37	
Seizure frequency			0.892
<10 episodes/years	32	21	
>10 episodes/years	29	18	
Duration of seizure			**0.000**
0-2 years	4	12	
3-5 years	13	15	
>5 years	44	12	
Duration of AED			0.07
Drug naive	19	19	
0-1years	6	4	
1-2years	5	7	
2-5years	12	3	
>5years	19	6	
Medication status			0.164
Drug Naïve	19	19	
Monotherapy	21	12	
Polytherapy	21	8	

Table 3: Association of clinical variables with cognitive domain – color trail test (CTT)

Variables	<15 Percentiles		>15 Percentiles		P Value	
Color trail test	**CTT-1**	**CTT-2**	**CTT-1**	**CTT-2**	**CTT-1**	**CTT-2**
Type of seizure					0.69	0.06
CPS	1	0	5	6		
CPS with generalization	1	0	6	7		
GTCS	26	27	61	60		
Seizure frequency					0.41	0.55
<10 episodes/years	13	13	40	40		
>10 episodes/years	15	14	32	33		
Duration of seizure					0.713	0.407
0-2 years	5	4	11	12		
3-5 years	6	5	22	23		
>5 years	17	18	39	38		

Duration of AED					**0.02**	0.07
Drug naive	16	13	22	25		
0-1years	0	0	10	10		
1-2years	2	1	10	11		
2-5years	6	6	9	9		
>5years	4	7	21	18		
Medication status					**0.03**	0.30
Drug Naïve	16	13	22	25		
Monotherapy	8	9	25	24		
Polytherapy	4	5	25	24		

Discussion

Over the disease process, seizure duration had greater impact on cognitive performance of the epileptic patients. Previous studies indicate that specific cognitive impairment, such as decline in memory, attention, executive function, naming ability, and verbal fluency deteriorates with the extending disease duration (Taylor & Baker [10], 2010). [Table 1 &2] In our study, we found duration of seizure had statistically significant association with impairment in verbal fluency and mental speed (P value 0.04 and 0.000) respectively, 9% and 44% cases shown impairment in verbal fluency and mental speed respectively having duration of seizure > 5 years while only 2% and 17% cases shown impairment in verbal fluency and mental speed had <5years of seizure duration. Similar finding was seen by WANG et al [11], disease duration was negatively correlated with the digit symbol test (Dsy) scores. The reason behind that is longer disease duration may causes neuronal damage and produce a cumulative effect, which might lead to abnormal cerebral morphological, structural and metabolism which gradually aggravate the cognitive impairment.

[Table 3] in our study we found that there is a statistically significant association between attention and duration of AEDs (P value 0.02) and medication status (P value 0.03). We found drug naïve patients (16%) and patients on monotherapy (8%) have more impairment in attention as compared to patients on polytherapy (4%).Similarly we found more duration on AED i.e.>5 years have less impairment in attention as compared to drug naïve and< 5 years of duration on AED this is because of less sample size and most of the patients were on single AEDs. Other studies, which support our study finding [9] they suggest that cognitive impairment is not associated with the kind of AEDs, but with other contributing factors or mechanisms or that cognitive impairment may appear before AEDs treatment [12]. In against of our finding WANG et al study[11],found that more AEDs causes more impairment in cognitive function was, including a decline in verbal memory, nonverbal memory, attention, executive function and patients with monotherapy had less cognitive impairment. For patients with poor seizure control, more AEDs may decreases or control attack, thus decreasing cognitive impairment, but at the same time, also increase the risk of cognitive impairment. Therefore, a balance should be maintained between seizure control and reducing drug side effects (Wang et al, 2019) [11].

In epileptic patients, it is observed that seizure frequency has been closely associated with the cognitive impairment. [Table 1]In our study, we found that seizure frequency >10 episodes/years was positively associated but not statistically significant with executive function i.e. verbal fluency (8%), and [Table-3] attention (CTT-1&2 are 15% & 14%),because seizure causes neuronal damage and excessive synchronous discharge from brain neurons causes

epileptic seizure. As a result of it, hypoxia in the neuronal membrane and electricity failure cause irreversible damage to neurons and frequent seizures increases the time of abnormal discharge in the grey matter which affect the brain function and resulting in an impairment in the cognitive function. Abnormal white and grey matter associated with the decline in cognitive function [13] and also frequent seizures are closely related to cognitive impairment of memory and executive function [14]. Similar finding was present in, Wang et al. [11] study, the more frequent the seizures, the more affected the memory and executive functions were. Notably, we found that controlled seizure for >1 year has a protective effect on cognitive as function of epileptic patients. Some incompatible studies report that cognitive function is not related to seizure frequency miller et al [15] this is because of the enrolment of different sample and the employment of different study methods.

[Table 1, 2, 3] In epileptic patients, generalized seizure type has been resulted to exert significant effect on the cognitive function[10]In the present study, generalized tonic clonic seizure shows 11% cognitive decline in verbal fluency, 50% in mental speed, 26% in attention in our study generalized seizure was compared with partial seizure, was strongly correlated with the cognitive performance of epileptic patients it might be because of epileptic discharge of the generalized seizure exist in the bilateral cerebral hemisphere, causing greater control difficulty and exerting a more effect on the cognitive function and in our study, there is no statistically significant association exist between cognitive domains and seizure type this may be because of 87% cases had generalized seizure and different results related to different patients with different seizure type so the results might be secondary to an overlap effect, or different seizure types may operate through the same mechanism or pathways that lead to inconsistent results of Wang et al, 2019 [11].

Conclusion

Seizure related factors like duration of seizure, duration of AED and polytherapy are statistically significantly associated with cognitive function and have negative impact on cognition. High educational level, well controlled seizure, monotherapy and healthy psychological state are protective factors for cognitive function of epileptic patients.

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