Original Article

Cognitive Dysfunction in Juvenile Myoclonic Epilepsy (JME) – A Tertiary Care Center Study

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Abstract

Background and Aim: Epilepsy often leads to cognitive impairment. Idiopathic generalized epilepsy as a group is considered to be benign in terms of its effects on cognition. Though, neuropsychological testing reveals subtle frontal impairment in patients with juvenile myoclonic epilepsy (JME). The aim of this study is to evaluate cognitive dysfunction in patients with JME. **Method:** We compared 50 JME patients and 50 age and sex matched healthy controls above 12 years of age on various cognitive tests which included Mini Mental State Examination (MMSE), Frontal Assessment Battery (FAB), Executive Interview (EXIT), PGI Memory Scale (PGIMS), Clock Drawing Test (CDT), Cube copying test (CCT), and Nahor Benson Test (NBT). We correlated the cognitive dysfunction with education level, age of onset, duration of epilepsy, electroencephalogram (EEG) abnormalities, treatment, and seizure control status. **Results:** JME patients performed significantly worse on MMSE (P = 0.001), PGI MS (P value = 0.001), FAB (P =.001), EXIT (P =.001), CDT (P =.02), and CCT (P =.001) when compared to the controls. JME patients had impaired attention, verbal fluency, design fluency, verbal memory, visual memory, conceptualization, set shifting, mental flexibility, response inhibition, and visuospatial functions. Cognitive dysfunction correlated with education level, duration of epilepsy and EEG abnormality. No correlation was seen with seizure frequency or type of antiepileptic therapy. **Conclusions:** JME patients demonstrate both frontal and parietooccipital lobe dysfunction. Hence detailed higher mental function tests supplemented by functional neuroimaging studies should be done in JME patients for their comprehensive management. This would also enhance our knowledge about the pathogenesis of JME.

Keywords: Factors associated with cognitive dysfunction, frontal executive dysfunction, juvenile myoclonic epilepsy, visuospatial impairment

Introduction

Juvenile myoclonic epilepsy (JME)—also known as impulsive petit mal—first described by Janz in 1985, has been classified as a syndrome of idiopathic generalized epilepsy (IGE) and comprises of 5–11% epilepsy cases, with an age of onset predominantly between 12 and 18 years.[1] JME is characterized by myoclonic jerks, generalized tonic clonic seizures and, less frequently, by absence seizures with characteristic precipitation with sleep deprivation.[2] It is considered a benign epilepsy as it is not associated with any apparent cognitive decline or structural abnormalities and seizure freedom can be achieved with a single antiepileptic drug in 85%–90% of the cases.[2]

Cognitive impairment frequently occurs secondary to epilepsy. Memory impairment, mental slowing and attentional deficits are the most frequently reported cognitive disorders.[3] Neuropsychological performance in patients with epilepsy is affected by structural brain damage; type, duration, frequency, severity and age of onset of seizures; total number of seizures; localization and lateralization of seizure focus; antiepileptic used, efficacy of treatment, features of laboratory findings and congenital and acquired diseases.[4,5]

Various studies employing sensitive neuropsychological tests have demonstrated frontal lobe dysfunction in patients with JME.[6-9]

In addition, a number of studies based on sensitive imaging techniques and autopsy studies have, provided evidence of multiregional cerebral dysfunction, involving primarily the frontothalamic circuit in JME.[10-12]

Cognitive impairment is often overlooked in patients with idiopathic epilepsy but the subclinical cognitive dysfunction can have a profound negative impact on the academic, professional and social life of an individual. Therefore, it is important to study the cognitive impairment in JME patients and determining particular areas of cognition affected, as well as, the factors which might influence the degree of cognitive dysfunction.

Therefore, the aim of our study was to assess cognitive dysfunction in patients diagnosed as JME and in addition to study the factors associated with the cognitive dysfunction

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such as age of onset, duration of epilepsy, antiepileptic drug therapy (AED), electroencephalographic (EEG) abnormalities and seizure control status.

Materials and Methods

This was an observational cross-sectional study conducted in a tertiary care hospital in New Delhi from August 2016–July 2017. We included 50 JME patients and 50 healthy volunteers. All the participants were explained about the purpose of the study and a written informed consent was obtained from them or from their guardians in cases of minor patient. A formal ethical clearance certificate was duly acquired from the ethical clearance committee.

Demographic characteristic

The inclusion criteria for patients were age more than 12 years with a minimum of primary school education, fulfilling the diagnostic criteria of JME and with no generalized seizure within last 1 week and myoclonus or absence seizure within 24 hours. Exclusion criteria included mental retardation (IQ Score <70), history of dementia/psychosis, chronic medical disorder like chronic renal disorder, chronic liver disease etc., stroke or neurological deficit, CNS Infection, alcohol or drug abuse, recent (<6 weeks) traumatic brain injury.

A control group comprised 50 healthy individuals who were age and sex matched with no history of any chronic medical illness or drug/substance abuse.

Neuropsychological tests

Both the cases and controls were subjected to various cognitive tests.

General cognitive testing was done employing the MMSE.

Memory and Learning were evaluated with PGIMS.

Frontal lobe function assessment was done using FAB and EXIT test.

Clock drawing test, Cube copying test and Nahor Benson test were also employed which predominantly assessed the parietooccipital functions.

The components and normative values of the above-mentioned tests are given in Annexures 1 and 2, respectively.

We compared the results of all neuropsychological tests for JME patients with the controls.

Statistical analysis

The continuous variables were assessed using Mean ± SD (standard deviation) whereas categorized variables were depicted as frequencies. The results were analyzed using SPSS software version 17.0. Comparison between two groups was done using *t* test and chi square test. Pearson correlation test was used for correlation analysis of cognitive dysfunction with various factors. The level of significance was set at <0.05.

Results

Demographic profile

There were no significant differences between JME patients and controls with respect to age, gender, and education level. The results pertaining to the demographic parameters have been summarized in Table 1.

Out of the 43 patients on treatment 46.5% were controlled, 13.9% had a seizure frequency of ≤1 seizure in 6 months, 25.5% had ≥1 seizure in 3 months, another 13.9% had only myoclonic jerks.

Table 1: Demographic profile of cases and controls

Demographic parameters	JME (*n*=50)	Control (*n*=50)	Significance
Age (Mean±SD)	22.8±7.76	22.44±4.708	NS* (*p*=0.78)
Gender			
Males %	34	40	NS* (*p*=0.53)
Females %	66	60	
Education level (%)			
Junior high school	14	16	NS* (*p*=0.448)
High school	58	50	
Graduates	22	30	
Post graduate	6	4	
Age at onset (Mean±SD)	14.5±6.3		
Duration of epilepsy (Mean±SD)	9.08±6.95		
Range	1-28 years		
Family history [*n* (%)]	2 (4%)		
Abnormal EEG [*n* (%)]	26 (52%)		
Type of therapy (%)			
Drug naïve	14		
Monotherapy	58		
Polytherapy	28		

*NS- Not significant

EEG abnormalities were seen in 26 patients i.e. 52% of the patients studied had EEG typical of JME. 43.8% patients with seizure control showed abnormal EEG and no correlation was seen between EEG findings and seizure control status ($P = 0.456$)

Cognitive assessment

The comparative results of all the cognitive assessment scales have been summarized in Figure 1.

General cognitive evaluation—MMSE

It was observed in our study that mean MMSE score for cases was 27.78 ± 2.17 which was significantly lower than the controls with a mean of 29.12 ± 1.27 (P <.001). The JME patients made errors in attention, calculation, and recall.

Memory and Learning—PGIMS

JME patients obtained a significantly (P <.001) lower mean raw score (76.94 ± 8.28) and lower mean dysfunctional rating score (8.80 ± 4.88) on PGIMS as compared to the controls who had a mean raw score of 88.48 ± 8.25 and mean dysfunctional score of 3.18 ± 4.3.

Upon analysis of the individual components of the scale it was detected that the JME patients had significantly lower scores on mental balance (P <.001), digit span forward (P <.001), digit span backward (P <.001), delayed and immediate recall (P <.001), retention of similar pairs (P = 0.019), retention of dissimilar pairs (P <.001) and visual retention (P =0.003) indicating attention, verbal memory, and nonverbal memory deficits.

Frontal lobe function assessment

FAB

Total mean score on FAB for JME patients was 15.22 ± 2.27. This was significantly lower as compared to total mean FAB score of controls i.e. 17.02 ± 1.67 (P < 0.001). JME patients had significantly lower scores for similarities (P = 0.005), lexical fluency (p = <0.001), Luria test (P = 0.003) and Go/No Go (GNG) (P < 0.001) in comparison to controls. Mean lexical fluency i.e. number of words generated per minute by patients was 7.3 ± 2.64 words vs 9.92 ± 3.23 words by controls. This difference was found to be statistically significant (P < 0.001).

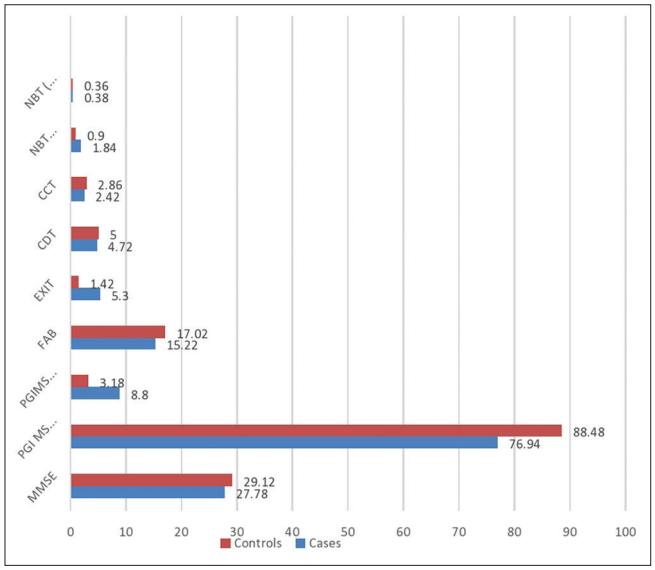

Figure 1: Bar diagram comparing cases and controls on different Cognitive assessment scales

EXIT

Higher score on EXIT indicated worse performance. JME patients secured a mean score of 5.30 ± 3.33 which was significantly higher than the mean score obtained by the controls i.e. 1.42 ± 1.68. (P < 0.001).

JME patients performed significantly worse on number letter (NL) task (P = 0.002), word fluency (P = 0.002), design fluency (p = <0.001), memory distraction task (P = 0.002), finger nose finger task (P = 0.022), GNG task (P =0.017), echopraxia 1 (P = 0.008), Luria sequence 2 (P = 0.002), serial order reversal task (P = 0.018), and counting task (p = <0.001).

Parietal lobe function assessment

Clock drawing and Cube copying test

JME patients were less successful on the CDT with a mean score of 4.72 ± 0.86 (P = 0.023) when compared to controls with a mean score of 5.00. Similarly, in the CCT, JME patients had a mean score of 2.42 ± 0.81; vs mean score of 2.86 ± 0.40 in controls. This difference was also found to be statistically significant with a P value of 0.001.

Nahor Benson test

Though the JME patients were less successful on the Nahor Benson test when raw scores were compared (mean score of JME patients 1.84 ± 1.49, P = 0.001) but there was no significant difference when dysfunction score were taken into account (P = 0.906).

Association of risk factors with cognitive dysfunction in JME patients

Age

Negative correlation of age at the time of testing was seen with serial order reversal task (r = 0-.292, P = 0.040), no. of designs per minute (r = -0.408, P value =0.003) and retention of similar pairs (r = -0.42, P = 0.002) whereas a positive correlation was seen with NL task (r = 0.295, P =0.038), design fluency (r = 0.300, P =.034), thematic perception (r = 0.297, P =.036), and interference task (r =.298, P =.035).

Age of onset

Negative correlation with conflicting instructions (r = -0.276, P = 0.052) and positive correlation with thematic perception (r = 0.357, P = 0.011) was seen when correlated with the age of onset.

Duration of epilepsy

Positive correlation was seen with the interference task (r = 0.373, P =0.012), design fluency (r = 0.287, P = 0.055), whereas a negative correlation was found with the number of designs made per minute (r = 0.301, P = 0.044) [Figure 2].

EEG abnormalities

Abnormal EEG displayed a negative correlation with NL task (r = -0.286, *P* = 0.044) and echopraxia (r = -.274, *P* =0.054). A positive correlation was found with GNG test (r = 0.324, *P* = 0.022).

Education level

Education level correlated positively with FAB (r = 0.307, *P* = 0.03), Cube copying test (r = 0.282, *P* = 0.047), similarities (r = 0.443, *P* =0.001), immediate recall (r = 0.362, *P* = 0.010), digit backward span (r = 0.388, *P* = 0.005), recognition (r = 0.394, *P* =0.005), whereas a negative correlation was seen with EXIT (r = -0.350, *P* = 0.013) [Figure 3] and the following individual components of EXIT scale i.e. GNG (r = -0.287, *P* = 0.043), serial order reversal task (r = -0.474, *P* = 0.001) and Luria sequence II (r = 0-.294, *P* =.038).

Type of therapy and seizure frequency

No significant correlation was seen with these two variables.

Discussion

Cognitive impairments in epilepsy have been attributed to interactions among genetics, ongoing seizures, different epilepsy syndromes, subclinical epileptiform discharges, psychosocial issues, underlying causes of symptomatic epilepsy, and treatment with antiepileptic drugs.[13,14]

Idiopathic epilepsies do not show any apparent cognitive impairment. Sophisticated neuropsychological tests can bring out subclinical cognitive dysfunction in them. Cognitive functions in JME patients have been studied previously and the results of these studies have been summarized in Table 2.

At the outset in our study there was no significant difference between the controls and cases in terms of age, gender, and education levels. Age and level of education which could have confounded our study were appropriately matched.

Our study revealed that JME patients performed significantly worse on MMSE. This indicates general cognitive dysfunction. Most patients lost points on attention, calculation and recall. Though the average MMSE score was normal when compared to the normative value of the population. Different studies have used different sets of tests for assessment of cognitive dysfunction. Sonmez *et al*.[15] who had also employed MMSE did not report any difference in the scores between JME and controls.

On comparison of results of cases and controls in relation to PGI Memory scale, it was found that JME patients had significantly lower score in the following tasks i.e. mental balance, digit span forward, digit span backward, delayed recall, immediate recall, retention similar pairs, retention dissimilar pairs and visual retention. Significantly lower digit span forward and backward scores for the JME patients suggested global attention impairment. These results positively correlated with the education level but did not show any association with the other factors such as seizure frequency, duration of epilepsy and AEDs used. The attentional deficits have been postulated to be related to epileptiform discharges which may have been the case in our study too.[18] We could not prove the association as in our study the patients didn't underwent a simultaneous 24-hour VEEG recording.

Impaired memory functions, both verbal and visual memory, were indicated by the PGI memory scale battery which was consistent with the previous studies.[15,16] In addition the patients also displayed constructional deficits which have not been studied extensively in the previous studies. However, these variables did not show any correlation with clinical or electrographic parameters of the patients.

JME patients performed poorly on the clock drawing and cube copying test when compared to controls which suggested executive and visuospatial dysfunction as well. These results were similar to those seen in Sonmez *et al*. study.[17] Majority of studies assessing cognitive dysfunction in JME have focused on frontal lobe dysfunction, in our study we tried to assess other cognitive domains especially

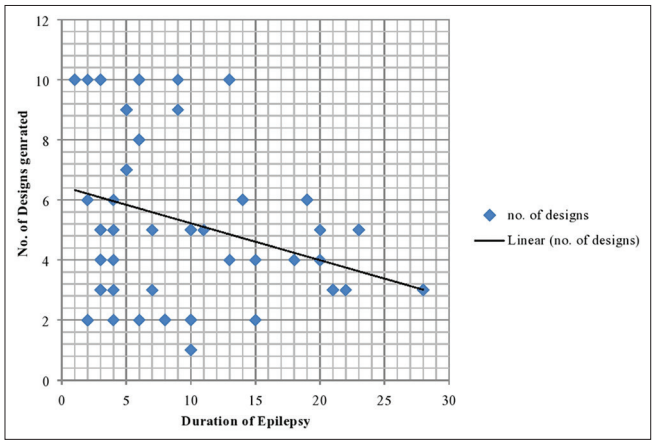

Figure 2: Correlation of number of designs generated per minute to education level

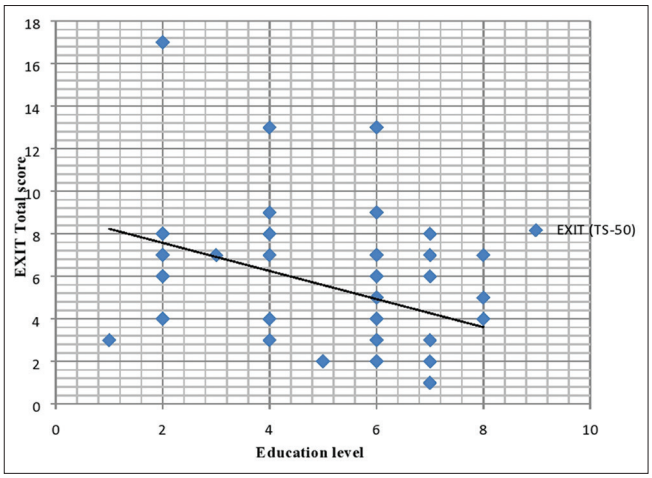

Figure 3: Graph showing Negative correlation between EXIT total score and education level

Table 2: Studies assessing cognitive dysfunction in JME

Study name	Sample size	Tests in which JME patients performed poorly	Correlation analysis
Devinsky *et al*.1997[6]	15 JME vs 15 TLE	Wisconsin Card Sorting Test Trail making test	Not done
Sonmez *et al*. 2004[15]	35 JME vs 35 controls	Clock drawing test Cube copying test Word generation score Total recall Verbal memory - total learning score Stroop test Comprehension	Education level Seizure type Age Family history
Sun Kim *et al*. 2007 [7]	27 JME vs 27 controls	List learning Digit span forward and backward Trail making test A Trail making test B Verbal fluency	Age of onset Duration of disease
Pascalicchio *et al*. 2007[16]	50 JME vs controls	Tests for IQ Vocabulary Digital symbol Arithmetic Digit span Trail making and stroop test Comprehension Boston naming test Symbol search FAS and Animal naming Visual reproduction Logical memory	School years Duration of epilepsy
Piazzini *et al*. 2008[8]	50 JME, 40 FLE, 40 TLE, and 40 controls	Wisconsin Card Sorting Test Word fluency	Did not show any significant correlation with family history, duration, frequency of seizures or therapy type
Motamedi *et al*. 2014[17]	32 JME vs 32 controls	Mental control Forward digit span Total digit span IQ	Age Education level Duration of epilepsy Medication

involving visuospatial dysfunction and found impairment in the visuospatial function in the JME patients, which either implies a more widespread dysfunction or may be related to the duration of epilepsy which was 14.58 years, quite higher than that found in other studies.[7]

JME patients reported lower scores on FAB and when the individual components of the FAB were compared it was noted that JME patients had impaired conceptualization, verbal fluency, mental flexibility, and set shifting, indicating executive dysfunction thus pointing towards dorsolateral prefrontal dysfunction.

Similarly, JME patients demonstrated significant impairment on the EXIT interview which is also a test for frontal lobe function assessment. Further analysis suggested that JME patients were more impaired in abstract thinking, task planning and sequencing, lexical fluency, design fluency, response inhibition, memory distraction tasks.

The results pertaining to both FAB and EXIT were in agreement with the previous studies reiterating the significant executive dysfunction in JME patients.[6-9,17]

Executive dysfunction leads to maladaptive behavior with significant social consequences in the form of disturbances in organization and self-regulation behavior. Disorders of social integration and personality have been frequently reported in JME.

Studies utilizing sensitive imaging studies have demonstrated frontothalamic network dysfunction in JME patients. Other studies have indicated cerebellum and basal ganglia dysfunction as well which have a role in modulating the EEG discharges. Extra frontal structures may also be involved as indicated by Kim *et al*.[19] Table 3 summarizes the results of the imaging studies in JME.

Longitudinal studies combining neuropsychological assessment with imaging studies can help us determine the underlying pathogenesis of various motor manifestations and cognitive dysfunction in JME.

Association of risk factors with the clinical and electroencephalographic variables

Cognitive dysfunction in JME may be associated with various disease and treatment-related factors. Different studies have

Table 3: Imaging studies indicating structural and functional abnormalities of brain in JME

Study	Sample Size	Techniques	Results
Tae *et al*. 2008 [20]	19 JME vs 18 controls	Cortical thickness measurement	cortical thicknesses of superior/middle/medial frontal gyri, and superior/middle/inferior temporal gyri were decreased
Roebling *et al*. 2009[21]	19 JME 20 controls	Neuropsychological tests, fMRI	No difference on fMRI or VBM
Pulsipher *et al*. 2009 [10]	20 JME, 12 BECTS, 51 controls	Quantitative MRI	smaller thalamic volumes and increased frontal CSF on comparison to both controls and BECTS
Saini *et al*. 2013 [22]	40 JME vs 19 controls	MRI T1-3D TFE (Turbo Field Echo) image	focal thalamic alterations in the anteromedial aspect of the thalamus Reduced volume of both thalami.
O'Muircheartaigh J *et al*. 2012 [11]	28 JME	Diffusion tensor imaging	task-modulated connectivity alteration in a region of frontal cortex connected to the thalamus via the same anatomical bundle, and overlapping with the supplementary motor area.
Kim *et al*. 2017 [19]	64 JME vs 58 controls	Volumetric MRI and Diffusion Tensor Imaging	Reduced volume of left pallidum and bilateral putamen and thalamus MD increases in left pallidum and bilateral hippocampus, putamen, and thalamus
Lin *et al*. 2009[23]	60 JME vs 30 controls	Multi voxel-based proton spectroscopy	The NAA/Cr ratio reduced in PMC, MPC, and thalamus Reduced GLX/Cr ratio PMC, MPC, and Posterior Cingulate Gyrus and increased ratio in insula and striatum.
Vollmar *et al*. 2011 [24]	30 JME vs 26 controls	Functional MRI SPM 5	Functional connectivity between the Motor system and frontoparietal cognitive networks.

BECTS- Benign partial epilepsy of childhood with centrotemporal spikes, Cr- creatine, FLE- Frontal Lobe epilepsy, fMRI- functional magnetic resonance imaging, GLX- Glutamate, GMV- Grey matter volume, MD- mean diffusivity, MPC- Medial prefrontal cortex, NAA- N acetyl aspartate, PMC - Primary motor cortex, rs-fMRI- resting state functional Magnetic Resonance Imaging, SPM - Statistical Parametric Mapping, VBM- voxel based morphometry

indicated different factors to be associated with the cognitive dysfunction.

In our study longer, duration of epilepsy and abnormal EEG was related with more cognitive dysfunction. This finding was in agreement with the other studies.[7,16,17]

Cases with longer duration of epilepsy performed worse on Interference task and design fluency task. Long-lasting epilepsy causes neuronal loss, metabolic dysfunctions, and MRI-detectable morphological changes which can explain these findings.[25]

JME patients with EEG abnormalities did not do well on NL task, echopraxia, and GNG test.

There is some evidence that interictal or at least subclinical discharges can lead to transient cognitive impairment. Lavandier *et al*.[26] found that patients who presented with epileptiform discharges during rest were significantly more impaired on tests of abstract reasoning, concept formation, and mental flexibility than patients without paroxysmal EEG changes while executive function tests were performed simultaneously with 24-hour EEG monitoring.

Studies have indicated that such mild effects may accumulate over time (when frequent epileptiform EEG discharges persist over years) and consequently result in effects on stable aspects of cognitive function such as educational achievement and intelligence.[27] Hence, the clinical relevance is that early detection of cognitive effects of epileptiform EEG discharges and subsequent treatment may prevent a definite impact on cognitive and educational development.

Patients with higher education level performed better on the tests for cognition including FAB, Cube copying test, similarities, immediate recall, digit backward span, recognition, EXIT total, GNG, serial order reversal task and Luria sequence II emphasizing the importance of education in the overall development of JME patients. Pascalicchio *et al*.[16] found patients with greater number of years of education (>11 years of formal education) demonstrated less progression of cognitive deficits. This result confirms the importance of a "cognitive reserve" of greater education and schooling in JME.

Patients with higher age at presentation as well as higher age of onset had more impaired cognition which was not in congruence with previous studies result. The high variation in age of presentation and age of onset in comparison to the sample size may have resulted in such results.

In our study, cognitive impairment did not show any significant correlation with the type of therapy i.e. drug naïve patient vs patients on monotherapy vs those on polytherapy ($P > 0.05$). Majority of our patients were on either valproate or levetiracetam. A few patients in our study were taking carbamazepine, phenytoin and phenobarbitone prior to coming to us. Only one patient of our study was taking topiramate. Sstudies revealed valproate can both positively and negatively influence the cognition.[28] Levetiracetam use has consistently shown either neutral or a positive effect on cognition.[29] Cognitive dysfunction with use of topiramate has been unequivocally proven.[30] Hence, the effect of drugs can be variable and our study population was vastly inhomogeneous in terms of treatment patients were taking. In fact it has been postulated that the AEDs may actually have

a beneficial effect on cognition by following mechanisms—first, by reducing the clinical as well as electrographic seizure activity; second, by modulation of neurotransmitters, for instance, phenytoin antagonizes glutamate induced excitotoxicity and carbamazepine increases the levels of acetylcholine; third, by inhibition of Ca2+-mediated cellular functions (protein phosphorylation and neurotransmitter release) and Ca2+-dependent depolarization as seen with phenytoin and levetiracetam; fourth, by acting as free radicle scavengers and lastly due to their psychotrophic effect.[31]

Higher seizure frequency is associated with neuronal loss in hippocampus and progressive memory dysfunction. Though in our study seizure frequency did not show any significant correlation with cognitive impairment ($P > 0.05$). The possible explanation could be that the median duration of the epileptic disorder of our study population was 8 years which may suggest that the maximum extent of hippocampal neuronal loss, consequently memory dysfunction, may have already set in.

Limitations of the study

1. Cognitive testing along with 24-hour EEG monitoring should be performed to assess the transitory cognitive deficits associated with EEG abnormalities.
2. We did not rule out depression using a formal questionnaire which could be a confounding factor as some cognitive abilities may be associated with depression.

Conclusion

JME patients in our study exhibited poor performance on tests of mental flexibility, task planning, sequencing, set shifting, verbal memory, visual memory, tests for attention, mental balance, response inhibition, and visuospatial function tests, thus suggesting a dysfunction of frontal, prefrontal, memory and visuospatial domains. The results also demonstrated that the cognitive impairment is related duration of the disease, EEG abnormalities and education level.

Such studies can help us to determine the cognitive domains affected and underlying pathophysiology of the cognitive impairment in JME. Further will help us develop a better understanding of the disease and promote development of better management strategies focusing on the neuropsychological development of the patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

No competing interests to declare.

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Annexure 1

COGNITIVE EVALUATION

1. ***General cognitive evaluation- Mini Mental State Examination***
2. ***Memory and Learning – PGI Memory Scale***
   - Remote memory
   - Recent memory
   - Mental Balance
   - Attention and Concentration
   - Delayed Recall
   - Immediate Recall
   - Retention of similar objects
   - Retention of dissimilar objects
   - Visual retention
   - Recognition
3. ***Frontal lobe Function Assessment***

   → ***Frontal Assessment Battery***- *which includes*
   - Similarities (Conceptualization)
   - Lexical fluency (Mental flexibility)
   - Motor series "Luria" test (Programming)
   - Conflicting instructions (Sensitivity to interference)
   - Go–No Go (Inhibitory control)
   - Prehension behaviour (Environmental autonomy).

   → ***The Executive Interview (EXIT)***
   - Number-Letter Task
   - Word Fluency
   - Design Fluency
   - Anomalous Sentence Repetition
   - Thematic Perception
   - Memory/Distraction Task
   - Interference Task
   - Automatic Behavior I
   - Automatic Behavior II
   - Grasp Reflex
   - Social Habit
   - Motor Impersistence
   - Snout Reflex
   - Finger-Nose-Finger Task
   - Go/No-Go Task
   - Echopraxia
   - Luria Hand Sequence I
   - Luria Hand Sequence II
   - Grip Task
   - Echopraxia II
   - Complex Command Task
   - Serial Order
4. ***Parietoccipital Lobe Function Assessment***
   - Clock drawing Test
   - Cube copying test

- Nahor Benson Test

Annexure 2

Normative values of the neuropsychological tests

1. MMSE

Score

Education	21	Abnormal for 8th grade education
	<23	Abnormal for high school education
	<24	Abnormal for college education
Severity	24-30	No cognitive impairment
	18-23	Mild cognitive impairment
	0-17	Severe cognitive impairment

2. PGI MEMORY SCALE

Conversion of Raw Score of Memory Subtests in Quintile for 0-V, VI-IX and X and above Educational Levels

Converted Score	Sub-tests and Raw Scores									
	I	II	III	IV	V	VI	VII	VII	IX	X
Subjects having Education upto V Class										
5+	6	5	3–9	7–15	7–10	6–12	4–5	8–15	5–13	8–10
3–4	5	4	2	6	6	5	3	5–7	4	7
0–2	0–4	0–3	0–1	0–5	0–5	0–4	0–2	0–4	0–3	0–6
Subjects having Education upto VI-IX Class										
5+	6	5	7–9	8–15	8–10	7–12	5	12–15	8–13	9–10
3–4	5	4	5–6	7	7	6	4	10–11	6–7	8
0–2	0–4	0–3	0–4	0–6	0–6	0–5	0–3	0–9	0–5	0–7
Subjects having Education of X and Above										
5+	6	5	8–9	10–15	9–10	9–12	5	13–14	10–13	9–10
3–4	5	4	7	9	8	7–8	4	10–11	8–9	8
0–2	0–4	0–3	0–6	0–8	0–7	0–6	0–3	0–9	0–7	0–7

Adapted from Pershad (1977) and Pershad and Wig (1988)

Rating of Converted Score for Dysfunction Score

Converted Score of	be given a Dysfunction Rating
0–2	3
3–4	2
5+	0

Maximum Dysfunction Rating Score for each subtest is 3 and there are 10 sub-tests, so total Dysfunction Rating Score on PGIMS would be 3 × 10 = 30.

3. FAB

Score

16-18 – Normal
13-15 – Mild impairment
7-12 – Moderate impairment
0-6-Severe impairment

4. EXIT Interview

Score≥15 indicates executive impairment.

5. Clock Drawing test

Score<4 is abnormal

6. Cube Drawing Test

Score

0- Poor
1- Fair
2- Good
3- Excellent

7. Nahor Benson Test

Score

Educational	Error Score	Dysfunction Rating
Those who can read with considerable difficulty	0–3	0
	4–5	2
	6–8	3
Those who can read fluently	0–2	0
	3–4	2
	5–8	3