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Self-perception of factors that precipitate or inhibit seizures in juvenile myoclonic epilepsy

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KEYWORDS
Juvenile myoclonic epilepsy;
Seizure precipitants;
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Questionnaire;
Patient education

Summary

Purpose: To assess self-perception of factors that precipitate or inhibit seizures in patients with juvenile myoclonic epilepsy (JME).
Patients and methods: Thirty-six males and 39 females with JME and mean age of 25.8 ± 8.7 years were analysed. All patients completed a standardized questionnaire to assess for the presence or absence of precipitant or inhibitory factors for their seizures in a face-to-face interview. These data were statistically analysed through logistic and linear regression models and Phi coefficient.
Results: Ninety-two percent of the patients identified at least one precipitating factor (PF). In order of frequency the following PFs were recorded: stress (83%), sleep deprivation (77%), specific thoughts/mental concentration (23%), performance of hand activities and complex finger movements (20%), flashing lights and playing games (15%), speaking out in public (11%) and alcohol intake (11%), reading (7%), calculating and writing (5%), playing musical instruments (4%), drawing (3%), and specific types of music (1%). Menstrual cycle was the third most important PF in the women (33%). Although PFs were easily recognized, 77% of the patients stated that they were unable to avoid the occurrence of the seizures.
Conclusions: Structured questionnaire is useful in stimulating patients to self-report seizure precipitants. Patients with higher education and uncontrolled seizures identified them more easily. The presence of a significant number of uncommon PFs, such as mental and motor hand tasks, considered uncommon for other epileptic syndromes, suggests that the role of these factors may be under-recognized in JME.
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Introduction

Previously neglected and restricted to reflex forms of seizures and epileptic syndromes, precipitant factors (PFs) have been object of renewed interest during recent decades. Characterization of factors involved in triggering or inhibiting epileptic seizures as well as their prevalence in distinct epileptic syndromes might lead to a better understanding of their physiopathological mechanisms.[1]

Defined as any endogenous or exogenous factors that promote the occurrence of seizures,[1] PFs have already been well defined for juvenile myoclonic epilepsy (JME).[2–10] Several factors are known to be effective in precipitating seizures in this epileptic syndrome. Janz and Christian[2] initially recognized sleep deprivation, excess of alcohol intake, premature awakening, menstruation, psychological stress, physical exhaustion and photic stimulation as triggering factors. Emotions, surprises, fatigue in evening hours and prolonged fasting were subsequently recognized.[3] With the renewed interest in JME during the 1980s, photic stimulation, menstruation and fatigue were confirmed as PFs,[4] and new factors, such as auditory precipitation, were additionally identified.[5] Inoue et al.[6] later characterized in a group of 21 patients with JME, reflex seizures related to calculating or performing mathematics, constructing or drawing, writing, playing cards or chess, performing complex finger tasks, reading and speaking. Mental precipitants such as concentrating and thinking, television or video games were further described.[7,8] More recently, a structured questionnaire survey in JME patients included other PFs considered unusual, such as praxis, reading, writing, calculating, making decision, speaking and playing musical instruments.[10] Other series[11–14] and case reports[15,16] have confirmed these factors. Praxis induction was observed in 31% of 62 German patients[10] and in 12.6% of 213 Japanese individuals.[9]

The aim of this study was to evaluate the self-perception of precipitant and inhibitory factors in 75 Brazilian JME patients.

Patients and methods

In this study we included 75 JME patients followed between January 1st, 2000, and June 1st, 2004 at Hospital São Paulo Epilepsy Outpatient Clinic, Federal University of São Paulo, São Paulo, Brazil.

Inclusion criteria were: (a) unequivocal diagnosis of JME based on criteria defined in the revised Classification of Epilepsies and Epileptic Syndromes[17]; (b) age over 12 years old; (c) no evidence of neurological or intellectual deficits and (d) being able to read and write. We excluded those patients with intellectual, psychiatric or emotional disturbances that could affect the reliability of their responses.

Written consent was obtained from all participants prior to the interview. During one of their regular outpatient visits all patients then underwent a face-to-face semi-structured interview answering a questionnaire applied by one of the investigators (P.S.S.). Each patient included had been followed up regularly at the Epilepsy Outpatient Clinic where socio-demographic data were recorded. Epilepsy characteristics (seizure types, onset, antecedents, medication and therapeutic response) were obtained directly from the patients. The questionnaire was prepared based on the format adopted by Antebi and Bird[18] and Spector et al.,[19] and included three questions: (a) Have you noticed any situations or states which will cause you to have more seizures? (b) Can you identify these PFs on this list: stress, sleep deprivation, specific thoughts/concentration, flashing lights, performing hand activities and complicated finger manipulation, playing games, calculating, speaking in public, drinking alcohol, playing musical instruments, listening to music, reading, writing, drawing, menstrual cycle and others? And finally, (c) Can you identify some factors or situations that would stop or inhibit your seizures?

In order to compare our data with previously published articles, we performed a bibliographic survey through Medline that identified 18 publications referring to the prevalence of each PF in series of patients with JME.

Statistical methods

For data analysis five variables were considered: number of PFs, stress, sleep deprivation, specific thoughts/concentration and motor activity. The number of PFs was analysed through a multiple linear regression model. Each one of the others was examined using a logistic regression model. In both models we considered the following clinical factors: age, gender, schooling and seizure control.

The association among all PFs mentioned by the patients was analysed using Phi coefficient. We considered significant $p < 0.05$.

Data were evaluated using the SPPS for Windows, version 10.0, statistical software.

Results

A total of 75 patients (39 women, 36 men) were interviewed. The mean age at the time of interview was 25.8 ± 8.7 (13–54 years). See Table 1 for

Table 1 Clinical and demographic data of juvenile myoclonic epilepsy patients.

	Total	Males	Females
JME patients (*n*)	75	36	39
Mean age (years)[a]	25.8 ± 8.7 (13—54)	26.7 ± 8.6 (13—53)	24.9 ± 8.9 (14—54)
Age at onset (years)[a]	13.3 ± 4.3 (1—31)	13.3 ± 4.9 (3—31)	13.3 ± 3.8 (1—23)
Age of diagnosis (years)[a]	23.2 ± 8.0 (11—51)	23.6 ± 7.8 (12—50)	22.7 ± 8.3 (11—51)
Duration of epilepsy (years)[a]	12.5 ± 9.6 (1—43)	13.4 ± 9.7 (2—43)	11.6 ± 9.6 (1—39)
Positive family history (%)	51 (68.0)	24 (66.7)	27 (69.2)

[a] Expressed as mean ± S.D. (range).

detailed clinical data. Despite appropriate doses of valproate, topiramate, phenobarbital, clonazepam and lamotrigine, 43 continued presenting infrequent seizures while 32 were seizure free.

Overall 92% of the participants could identify at least one PF, including in order of frequency: stress (83%), sleep deprivation (77%), specific thoughts/concentration (23%), performing hand activities and complicated finger manipulation (20%), flashing lights and playing games (15%), speaking in public and alcohol intake (11%), reading (7%), calculating and writing (5%), playing musical instruments (4%), drawing (3%), and listening to specific types of music (1%). Menstrual cycle was the third most important precipitant in women (33%). In relation to gender these numbers are shown in Fig. 1.

Although most patients reported at least one PF, when asked whether they could avoid seizures, 77% of them said there was nothing they were aware of, 22% reported keeping calm and 1% said that practicing sport and sleeping were the best strategies. Ten percent of women and 6% of men could not identify any PF.

Patients often mentioned multiple factors, up to 9 (mean 2.9 ± 1.7). There was no significant statistical association between the number of PFs perceived and age, gender, schooling and seizure control. The final model is shown in Table 2.

Stress was the most common PF (83%) and female patients were the most likely to identify it. This factor was cited more commonly in patients older than 30 years (94%), than in those who were younger than 30 (79%). Age was the only statistically significant variable ($\alpha = 0.05$, $p = 0.03$), and the chances of citing stress increased on average 1.14 times each year.

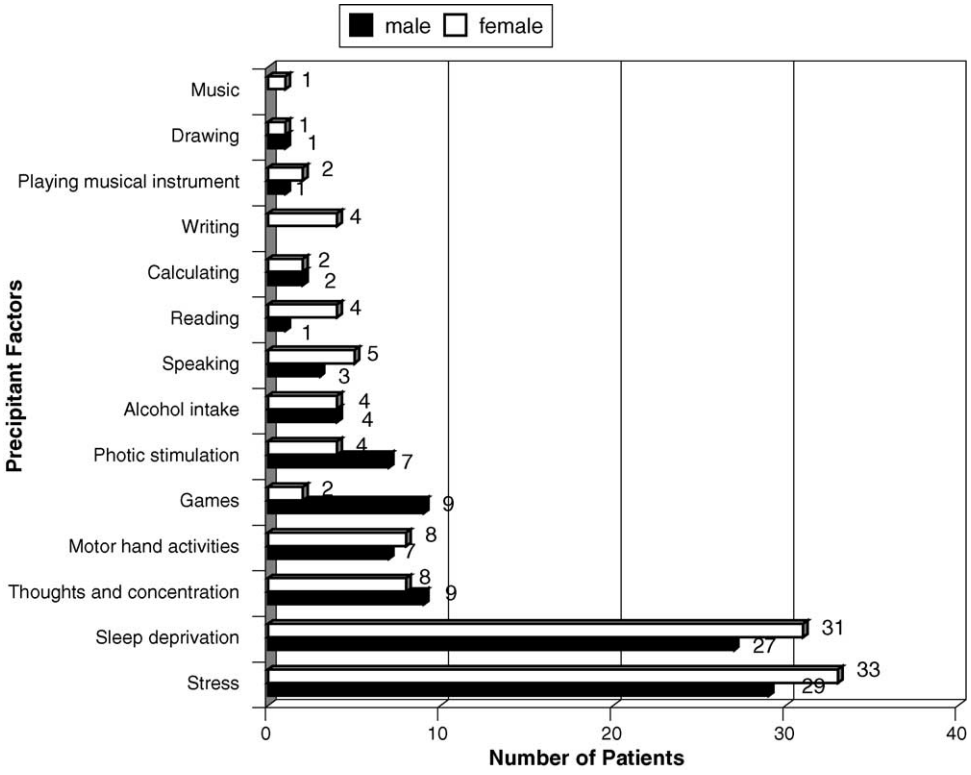

Figure 1 Distribution of precipitant factors according to gender.

Table 2 Multiple linear regression model for the number of precipitant factors ($\alpha = 0.05$).

Factors	Coefficients	S.E.	*p*
Constant	2.108	0.848	0.015
Gender[a]	0.153	0.415	0.714
Age	0.012	0.023	0.599
Secondary education	0.612	0.426	0.155
University level	1.008	0.650	0.126
Seizure control	−0.066	0.411	0.872

[a] Male = 0, female = 1.

Sleep deprivation was the second most common PF (77%). Younger patients frequently reported this precipitant (31/36, 86%). However, the inferential analysis showed no statistically significant correlation between sleep deprivation and age, gender, schooling and seizure control ($\alpha = 0.05$).

Men and women recognized different factors. Specific thoughts/concentration, especially when they were older (60% > 30 and 11% < 30), were perceived as most important to men, while the menstrual cycle, especially the premenstrual phase (33%) in women. These factors were followed by performing motor hand activities, particularly among younger male patients (25% up to 30 years of age versus 6% above). Overall, 15 (20%) patients recognized praxis induction but there was no statistical difference ($p = 0.91$) between those with controlled (7/32, 22%) or uncontrolled seizures (8/43, 19%).

Statistical analysis failed to identify significant association among the five variables above mentioned. However, in spite of the *p*-value of 0.08 for seizure control and specific thoughts/concentration, the odds ratio showed that patients with uncontrolled seizures (35% male; 27% women) had 3.23 times greater chance of self-reporting this PF than those seizure free (Table 3).

There was statistically significant association among the following PFs: sleep deprivation and stress (Phi = 0.425), motor hand activities and playing games (Phi = 0.452), motor hand activities and calculating (Phi = 0.475), and finally, reading and speaking (Phi = 0.427) (Table 4).

Table 4 Phi coefficient statistically significant for association between precipitant factors.

Factor 1	Factor 2	Correlation	
		Phi	*p*
Sleep deprivation	Stress	0.425	<0.001
Motor activity	Games	0.452	<0.001
Motor activity	Calculating	0.475	<0.001
Reading	Speaking	0.427	<0.001

Discussion

In this study we investigated the self-perception of seizure precipitant and inhibitory factors in 75 patients with JME comparing them to the data regarding PFs of all the 18 series surveyed (Table 5). The results showed that 92% of the participants could clearly describe and identify at least one PF compared to 61−100% reported in other series.[7,8,20,21] Several PFs clustered together, suggesting a common mechanism for triggering seizures. Although the recognition of these factors was possible for most of the patients, only 23% of them were able to use this knowledge in their favour setting up strategies to avoid them.

Among all PFs, stress (62/75; 83%) was the most frequently reported. Often cited although not quantified[4,10,12] this rate is much higher than the 7−46.5% reported in the 18 series of JME surveyed. This difference might be attributable to regional genetic and environmental differences with the lowest figures observed in countries like India, 7%[14] and 7.6%,[8] an intermediate range in Germany, 10.6%,[2] Saudi Arabia, 12.3%[7] and Turkey, 18.4%,[20] and the highest prevalence in those such as Italy, 45%[22] and Norway, 46.5%.[23] Older patients recognized stress more frequently. Although this associa-

Table 3 Logistic regression for the precipitating factor specific thoughts/concentration ($\alpha = 0.05$).

Factor	*B*	S.E.	*p*	Odds ratio	95.0% C.I. for odds ratio	
					Lower	Upper
Gender[a]	−0.34	0.62	0.58	0.71	0.21	2.40
Age	0.03	0.03	0.30	1.03	0.97	1.10
Education level			0.48			
Secondary education	−0.57	0.64	0.38	0.57	0.16	1.99
University level	0.41	0.91	0.65	1.50	0.26	8.86
Seizure control[b]	−1.17	0.67	0.08	0.31	0.08	1.16

B, regression coefficient and S.E., standard error.
[a] Male = 0, female = 1.
[b] Controlled = 1, uncontrolled = 0.

Table 5 Results of all the series surveyed.

First author (reference number)	Year	Country	Precipitant factors	Patients
Janz[2]	1957	Germany	Lack of sleep (85.1%), menses (42.1%), excessive alcohol intake (40.4%), sudden/provoked awakening (38.3%), psychological stress (10.6%), physical exhaustion (6.4%), intermittent light stimulation (2.1%)	47
Castells[3]	1958	Uruguay	Menstruation (51.4%), awakening (47.1%), stress (17.1%), sleep deprivation (12.8%), emotion (11.4%), alcohol intake (8.6%)	70
Asconapé[5]	1984	USA	Photic stimulation (33%), auditory stimuli, loud noise with elements of surprise (8.3%)	12
Panayiotopoulos[7]	1994	Saudi Arabia	Sleep deprivation (89.5%), fatigue (73.7%), photosensitivity (36.8%), menstruation (24.1%), thinking and concentration (22.8%), stress, expectation, frustration (12.3%), television or video-games (8.8%)	66
Atakli[20]	1998	Turkey	Sleep deprivation (85.5%), photic stimulation (25%), stress (18.5%), fatigue (11.8%), menstruation (2.6%)	76
Kleveland[23]	1998	Norway	Sleep deprivation (83.7%), stress (46.5%), alcohol intake (39.5%), flickering light (37.2%), changed sleeping habits (30.2%), menstruation (28.1%), intense light (23.2%), physical activity (20.9%), being anxious (16.3%), being expectant (11.6%)	43
Murthy[8]	1998	India	Sleep deprivation (54.2%), menstruation (20%), fatigue (9.2%), stress (7.6%), concentration (6.9%), photic stimulation (1.5%), TV/video (1.5%)	131
Pedersen[21]	1998	Denmark	Lack of sleep (83.7%), alcohol intake (51.2%), flashing light stimuli (37.2%)	43
Canevini[22]	1992	Italy	Lack of sleep (60%), stressful situations (45%), sudden awakening (35%), menstrual cycle (10%), relaxed evening and TV-watching (1.6%)	60
Wolf[10]	2000	Germany	Praxis (31%), talking/reading (23%), thinking (12.9%), writing (11.3%), intermittent light stimuli (11%), decision-making (6.4%), computer tasks and video-games (9.7%), calculation/playing piano (1.6%)	62
Inoue[9]	2000	Japan	Sleep deprivation (61%), praxis activity (12.7%), photosensitivity (10.8%), writing/typing (9.4%), playing cards or chess (7.5%), calculating (7%), construction/drawing/complicated finger manipulation (5.2%), playing video-games (2.8%), reading/speaking (0.9%)	213

Montalenti[11]	2000	Italy	Sleep deprivation (52.4%), menses (47.4%), photic stimulation (14.3%), early awakening (9.5%), alcohol intake (7.9%), complex mental tasks-arithmetic or playing piano (1.6%)	63
Gunatilake[13]	2000	Sri Lanka	Sleep deprivation (68%), menstruation (4.8%), stress arithmetic (2.5%), alcohol intake (2.5%)	20
Dhanuka[24]	2001	India	Sleep deprivation (73.3%), fatigue (13.3%)	24
Jha[25]	2002	India	Inadequate sleep (73.8%)	84
Mehndiratta[26]	2002	India	Premature awakening (73.9%), sleep deprivation (58.2%)	103
Jain[14]	2003	India	Awakening (86%), sleep deprivation (79%), stress of examination/menstrual cycle/excitement/being on an empty stomach/fatigue (7%)	500
Vijai[27]	2003	India	Sleep deprivation (78.3%), poor drug compliance (20.9%), menstruation (7.9%), watching television (3.3%), alcohol intake (1.6%)	183

tion has not been previously mentioned in series of patients with JME, it has already been described in other forms of epilepsy.[1,18]

Sleep deprivation was the most frequently reported PF in past series, varying from 52.4 to 89.5%,[2,3,7–9,11,13,14,20–27] but it was the second most common PF in the present study (58/75; 77%). Sleep deprivation was more frequently reported by patients who had also reported stress. There was a strong correlation between sleep deprivation and stress. There has been some speculation that stress might lead to physiological changes in the corticosteroid levels as well as in the cerebral blood flow facilitating seizure occurrence.[19]

Factors such as specific thoughts/concentration, not commonly mentioned in other publications, occupied the third place in our series, being reported by 23% of the patients. It was quantified in only three other series of patients: in India, 6.9%,[8] Germany, 12.9%[10] and Saudi Arabia, 22.8%[7] and additionally in two case reports, where it was suggested that the presence of this PF could be related to difficulty in treatment and seizure persistence.[15,16] Our data appear to confirm this association, since most of the patients (76% of those with uncontrolled seizures versus 52% of those seizure free) self-reporting this PF continued presenting seizures.

There has been much discussion about the importance of proprioceptive factors in triggering seizures in JME.[9,10] Praxis induction was observed in 20% of our patients, compared with 31% of the German[10] and 12.6% of the Japanese cases.[9] It has been suggested that these factors could precipitate seizures.[6,15] However, we were unable to assess this adequately because of the small number of cases. Young male patients were more prone to report this PF. This might have been because older Brazilian patients with a lower level of education, most of them coming from rural areas, had not been exposed as much as the younger generation to activities that demand fine finger movements such as game playing and computer manipulation.

Specific thoughts/concentration had no significant correlation with other PF and socio-demographic and anamnestic variables. Some PFs appeared more frequently together: sleep deprivation and stress, motor hand activities and playing games, motor hand activities and calculating, reading and speaking. The recognition of these associations could probably be of considerable therapeutic importance in JME, a syndrome in which drug therapy should necessarily be accompanied by PFs prevention.

Although this study was based on a self-perception basis and did not have a control group, it shows that the use of structured questionnaire is useful in stimulating patients to self-report seizure precipi-

tants and inhibitors. Confirming previous data, stress and sleep deprivation were the most encountered PFs. Non-habitual precipitants such as mental and complex motor tasks were also reported. Furthermore, this study shows that there are factors, which cluster together.

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References

1. Frucht MM, Quigg M, Schwaner C, Fountain NB. Distribution of seizure precipitant among epilepsy syndromes. *Epilepsia* 2000;**41**(12):1530—9.
2. Janz D, Christian W. Impulsive petit mal. *Deutsche Zeitschrift Nervenheilkunde* 1957;**176**:346—86.
3. Castells C, Mendilaharsu C. La epilepsia mioclónica bilateral y consciente (Considerações clínicas y fisiopatológicas). *Acta Neurol Latinoam* 1958;**4**:23—48.
4. Delgado-Escueta AV, Enrile-Bacsal F. Juvenile myoclonic epilepsy of Janz. *Neurology* 1984;**34**:285—94.
5. Asconapé J, Penry JK. Some clinical and EEG aspects of benign juvenile myoclonic epilepsy. *Epilepsia* 1984;**25**(1):108—14.
6. Inoue Y, Seino M, Tanaka M, et al. Epilepsy with praxis-induced epilepsy. In: Wolf P, editor. *Epileptic seizures and syndromes*. London: John Libbey; 1994. p. 81—91.
7. Panayiotopoulos CP, Obeid T, Tahan AR. Juvenile myoclonic epilepsy: a 5-year prospective study. *Epilepsia* 1994;**35**:285—96.
8. Murthy JMK, Rao CM, Meena AK. Clinical observations of juvenile myoclonic epilepsy in 131 patients: a study in South India. *Seizure* 1998;**7**:43—7.
9. Inoue Y, Kubota H. Juvenile myoclonic epilepsy with praxis-induced seizures. In: Schmitz B, Sander T, editors. *Juvenile myoclonic epilepsy: the Janz syndrome*. Petersfield: Wrightson; 2000. p. 73—81.
10. Wolf P, Mayer T. Juvenile myoclonic epilepsy: a syndrome challenging syndromic concepts? In: Schmitz B, Sander T, editors. *Juvenile myoclonic epilepsy: the Janz syndrome*. Petersfield: Wrightson; 2000. p. 33—9.
11. Montalenti E, Imperiale D, Rovera A, et al. Clinical features, EEG findings and diagnostic pitfalls in juvenile myoclonc epilepsy: a series of 63 patients. *J Neurol Sci* 2000;**184**: 65—70.
12. Matsuoka H, Takahashi T, Sasaki M, et al. Neuropsychological EEG activation in patients with epilepsy. *Brain* 2000;**123**: 318—30.
13. Gunatilake SB, Seneviratne SL. Juvenile myoclonic epilepsy: a study in Sri Lanka. *Seizure* 2000;**9**:221—3.
14. Jain S, Tripathi M, Srivastava AK, Narula A. Phenotypic analysis of juvenile myoclonic epilepsy in Indian families. *Acta Neurol Scand* 2003;**107**:356—62.
15. Matsuoka H, Takahashi T, Sasaki M, et al. The long-term course of seizure susceptibility in two patients with juvenile myoclonic epilepsy. *Seizure* 2002;**11**:126—30.
16. Chiafari R, Piazzini A, Turner K, et al. Reflex writing seizures in two siblings with juvenile myoclonic epilepsy. *Acta Neurol Scand* 2004;**109**:232—5.
17. Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989;**30**:389—99.
18. Antebi D, Bird J. The facilitation and evocation of seizures. A questionnaire study of awareness and control. *Br J Psychiatry* 1993;**162**:759—64.
19. Spector S, Cull C, Goldstein L. Seizure precipitants and perceived self-control of seizures in adults with poorly-controlled epilepsy. *Epilepsy Res* 2000;**38**:207—16.
20. Atakli D, Sözüer D, Atay T, et al. Misdiagnosis and treatment in juvenile myoclonic epilepsy. *Seizure* 1998;**7**:63—6.
21. Pedersen SB, Petersen KA. Juvenile myoclonic epilepsy: clinical and EEG features. *Acta Neurol Scand* 1998;**97**:160—3.
22. Canevini MP, Mai R, Di Marco C, et al. Juvenile myoclonic epilepsy of Janz: clinical observation in 60 patients. *Seizure* 1992;**1**:291—8.
23. Kleveland G, Engelsen BA. Juvenile myoclonic epilepsy: clinical characteristics, treatment and prognosis in a Norwegian population of patients. *Seizure* 1998;**7**:31—8.
24. Dhanuka AK, Jain BK, Daljit S, Maheshwari D. Juvenile myoclonic epilepsy: a clinical and sleep EEG study. *Seizure* 2001;**10**:374—8.
25. Jha S, Mathur VN, Mishra VN. Pitfalls in diagnosis of epilepsy of Janz and its implications. *Neurol India* 2002;**50**:467—9.
26. Mehndiratta MM, Aggarwal P. Clinical expression and EEG features of patients with juvenile myoclonic epilepsy (JME) from North India. *Seizure* 2002;**11**:431—6.
27. Vijai J, Cherian PJ, Sylaja PN, et al. Clinical characteristics of South Indian cohort of juvenile myoclonic epilepsy probands. *Seizure* 2003;**12**:490—6.