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Eye closure sensitivity and epileptic syndromes: A retrospective study of 26 adult cases

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Summary

Purpose: The transient, mainly generalized, together with brief changes in EEG baseline immediately after eye closure, is called 'eye closure sensitivity' (ECS) which was first reported by Robinson in 1930 and there have been limited number of studies investigating ECS and epilepsy syndromes. Therefore, we aimed to reveal the possible relationship between ECS and the epilepsy syndromes in our adult patients.
Patients and methods: Adult patients monitored in Hacettepe University Hospitals EEG Laboratory, from January 1995 to December 2005, were screened retrospectively for the presence of ECS. During EEG recording, all patients were asked to open their eyes for at least for 10 s and close their eyes at the end of this period in six different montages. Hyperventilation and photic stimulation were performed according to the standard protocol of IPS.
Results: Twenty-six patients have had ECS during EEG recording. Nineteen (73%) were women, and mean age of the patients was 24 years. The mean ages were 12.3 ± 5.4 years for seizure onset and 18.5 ± 4.9 years for initial detection of ECS. Eleven had a history of febrile seizures. There was a family history for epilepsy in five patients. Photosensitivity in their EEG was noticed in 11 patients. ECS was established in five epilepsy syndromes: eyelid myoclonia with absences (EMA); (*n*: 6), juvenile myoclonic epilepsy (JME); (*n*: 6), idiopathic generalized epilepsy (IGE with tonic clonic seizure); (*n*: 4), juvenile absence epilepsy (JAE); (*n*: 1) and idiopathic occipital lobe epilepsy

Abbreviations: MRI, magnetic resonance imaging; CT, computerized tomography; MR, mental retardation; A, absence; GTC, generalized tonic clonic; SGTC, secondary generalized tonic clonic; EM, eyelid myoclonia; CP, complex partial; SP, simple partial; VPA, valproic acid; LTG, lamotrigine; ETX, ethosuxcimide; CBZ, carbamazepine; Prm, primidone; FC, febrile convulsion; FH, family history of seizure; IPS, intermittant photic stimulation

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(IOE) (*n*: 9). All patients were seizure free with or without anti-epileptic medication during follow up.
Conclusion: ECS is more common in females. It may overlap with photosensitivity but be independent from photosensitivity. It may be seen in different epilepsy syndromes including IOE which was not reported previously.

Introduction

Eye closure is a transient stage that immediately follows the closure of the eyes. It lasts less than 3 s and does not persist for the remaining time for which the eyes are closed[1] (Fig. 1). The baseline electrical activity and excitability of the brain is known to be altered with the closure of the eyes.[2] It has also been reported that the alpha rhythm is of higher frequency immediately after closing the eyes.[3]

Eye closures induced temporary epileptiform changes in EEG are mainly generalized, appearing within 2—4 s after closing the eyes and are brief, usually lasting 1—4 s.[1] This type of electrophysiological abnormality is known as eye closure sensitivity (ECS). The most-likely speculation about eye closure paroxysmal abnormalities is that, eye closure may be related to a mechanism of alpha rhythm augmentation.[2] The paroxysmal activity underlying this phenomenon, which could be arising in a number of cortical or subcortical locations, is usually unknown.[4]

Although the transient and brief change in the EEG baseline immediately after eye closure ECS was first reported by Robinson in 1930, there have been limited number of studies investigating ECS and epilepsy syndromes since then.[5—7] Therefore, we aimed to study the possibility of a relationship between ECS and epilepsy syndromes in our patients.

Patients and methods

Patients who had had routine EEG in Hacettepe University Hospitals EEG Laboratory for Adults between January 1995 and December 2005 were screened retrospectively for the presence of ECS. Patients who had ECS at least three times in one EEG were included in the study, otherwise excluded. The mean number of EEG recordings was three (1—17) per patient. During EEG recording in EEG laboratory, all patients were asked to open their eyes and recorded eyes-opened at least for 10 s and close their eyes at the end of this period in six different montages in a well illuminated room. All patients were asked to hyperventilate for 5 min. In all patients, intermittent photic stimulation (IPS) was investigated according to the standard protocol of IPS at the last montage. Diagnosis of photosensitivity was made if at least one EEG showed localized or generalized spike or spike and wave activities during IPS. EEGs were performed in the interictal state and interpreted by expert electroencephalographers (SS, AC).

The EEG stages of eyes-opened, eyes-closed and eye closure were examined in detail. ECS defined if closing of the eyes during EEG recordings repeatedly was followed within 2—4 s by spikes, multiple spikes or spike and slow waves lasting 1—4 s. EEG changes during ''IPS and closing the eyes'' are not considered as ECS. The hospital records of the patients were reviewed for detailed clinical data.

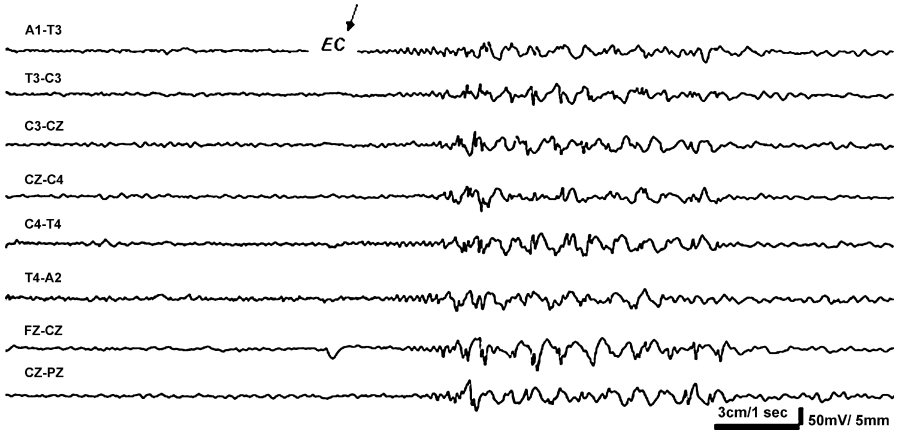

Figure 1 Generalized multiple spike waves after closing the eyes lasting 1—4 s in a patient with EMA.

Results

Twenty-seven patients were found to have ECS in their EEGs but one patient was excluded from the study because of insufficient clinical data. Nineteen (73%) were women; the mean age of the patients was 24 years, ranging between 18 and 38 years. The mean age of initial detection of ECS was 18.5 $\pm$ 4.9 years. Eleven had a history of febrile seizures. Family history was positive in five. Photosensitivity was noticed in 11. The neurological examinations were normal except one patient who had a mild mental retardation. Neuroimaging was normal in all patients.

Clinical and EEG features are summarized in Table 1.

ECS was found in five epilepsy syndromes, juvenile absence epilepsy (JAE), eyelid myoclonia with absences (EMA), juvenile myoclonic epilepsy (JME), idiopathic generalized epilepsy (IGE) with tonic clonic seizure, idiopathic occipital lobe epilepsy (IOE) (Table 1). Nine of the 26 patients were noted as IOE and 6 of 9 these exhibited idiopathic photosensitive occipital lobe epilepsy (IPOE).

During the follow-up, two were excluded because of insufficient follow-up data. An excellent outcome was observed in 24 patients during the follow-up (mean: 4.5 years). Twenty of them were seizure free with monotherapy. Two patients with combined therapy and two patients without medication were also seizure free. Valproate monotherapy was effective in 17 cases.

Table 1 Clinical and EEG features of the patients with ECS

Age, sex	Syndrome	FC	FH	Type of seizure	Type of ECS	Treatment	PS	Age of ECS	Prognosis
22 years, M	EMA	–	+	A + EM, GTC	Generalized	VPA	–	18	Seizure free
20 years, F	EMA	–	+	EM + A, GTC	Generalized	VPA, LTG, ETX	+	18	Seizure free
24 years, M	EMA	+	–	EM + A, GTC	Generalized	VPA	–	10	Seizure free
25 years, F	EMA	+	–	EM + A	Generalized	VPA	–	7	Seizure free
19 years, F	EMA	–	+	EM + A, GTC	Occipital	VPA	+	18	Seizure free
22 years, F	EMA	–	–	EM + A, GTC	Generalized	No medication	–	13	Seizure free
19 years, M	IGE	–	–	GTC	Posterior	VPA	–	19	Seizure free
33 years, F	IGE	–	–	GTC	Generalized	VPA	–	26	No follow-up data
29 years, F	IGE	–	–	GTC	Generalized	VPA	+	23	Seizure free
18 years, F	IGE	–	–	GTC	Generalized	VPA	–	16	Seizure free
38 years, F	JME	–	–	GTC, M	Generalized	Barbexaclone	+	32	Seizure free
22 years, M	JME	–	–	A, M	Generalized	VPA	–	23	Seizure free
24 years, F	JME	–	–	GTC, M	Generalized	VPA	–	22	Seizure free
25 years, F	JME	–	+	GTC, M	Generalized	VPA	–	17	Seizure free
25 years, F	JME	–	+	GTC, M	Generalized	VPA	–	17	Seizure free
21 years, F	JME	–	–	A, M, GTC	Generalized	VPA	+	16	No follow-up data
20 years, M	JAE	–	+	A, GTC	Generalized	LTG	–	20	Seizure free
21 years, F	OLE	+	+	SP, SGTC	Generalized	VPA	–	15	Seizure free
20 years, M	OLE	–	–	SP, SGTC	Generalized	VPA	–	18	Seizure free
33 years, F	OLE	–	–	SGTC	Generalized	LTG	–	22	Seizure free
27 years, F	OLE (IPOE)	–	–	SGTC	Generalized	CBZ, Prm	+	18	Seizure free
25 years, M	OLE (IPOE)	+	–	SGTC	Generalized	CBZ	+	14	Seizure free
21 years, F	OLE (IPOE)	–	+	SGTC	Posterior	VPA	+	18	Seizure free
24 years, F	OLE (IPOE)	–	+	CP, SGTC	Generalized	VPA	+	23	Seizure free
24 years, F	OLE (IPOE)	+	+	SGTC	Generalized	VPA	+	20	Seizure free
23 years, F	OLE (IPOE)	–	+	SP, SGTC	Occipital	VPA	+	18	Seizure free

A: absence, SP: simple partial, CP: complex partial, GTC: generalized tonic clonic, SGTC: secondary generalized tonic clonic, EM: eyelid myoclonia, FC: febrile convulsion, FH: family history for epilepsy, PS: photosensitivity, EMA: eyelid myoclonia with absence, IGE: idiopathic generalized epilepsy, OLE: occipital lobe epilepsy, IPOE: idiopathic occipital lobe epilepsy, JME: juvenile myoclonic epilepsy, JAS: juvenile absence epilepsy, ETX: ethosuxcimide, CBZ: carbamazepine, LTG: lamotrigine, Prm: primidone, VPA: valproic acid, posterior: temporooccipital region, and occipital: only occipital region.

Discussion

Abnormalities in EEG during the eye closure are to be found in a vast number of epilepsy syndromes. Although Duncan and Panayiotopoulos suggested that the ideal model for the study of ECS is EMA, other ECS related syndromes are reported as JAE, JME, IGE, EMA, Epilepsy with Grand Mal on Awakening and Childhood Absence Epilepsy (CAE).[1,7]

Brigas et al. reported 11 of the 335 patients (3.1%) with ECS, and they had a relation to IGE which include five patients with CAE; two patients, JAE; three patients, JME; and one patient, Epilepsy with Grand Mal on awakening.[6] Kurt et al. reported 10 patients with ECS and investigated the relationship of ECS with epilepsy syndromes and clinical features.[7] They found five JME, three EMA, one JAE, and one CAE.

In our patients, we found a high rate of ECS in IOE in addition to the other epilepsy syndromes related with ECS such as EMA, JME, IGE and JAE. IOE has never been reported to be associated with ECS. In the literature, there is one other study, probably, but not clearly reported that paroxysmal abnormalities were enhanced both with eye closure and with the eyes closed state in three patients with IOE.[8] There are three forms of IOE, early onset childhood epilepsy with occipital spikes, late on set childhood epilepsy with occipital spikes and IPOE.[9] In our patients 9 of the 26 patients were noted as IOE and 6 of these 9 patients exhibited IPOE. In our patients, ECS was found to be mainly generalized or limited to the posterior or occipital region. The pattern of ECS was not associated with the type of syndrome.

Panayiotopoulos reported that eye-closure transient EEG paroxysmal abnormalities occur mainly in photosensitive patients.[10,11] The prevalence of eye closure discharges in patients with photosensitivity is supposed to be 20—36%.[10,12] Kohno et al. and Gobbi et al. have reported the presence of photosensitivity in 72.2% and 63.6% of patients with ECS, respectively.[13,14] Although photosensitivity was noted in 42.3% of our patients with ECS, we did not find a strong relationship between photosensitivity and the presence of ECS in all syndromes in our series.

In the longitudinal study, Fabian and Wolf suggested that both ECS and photosensitivity may be age related.[15] Gobbi et al. concluded that the presence of ECS without photosensitivity could be explained in various ways: a different reflex mechanism, the anti-epileptic medication or age.[14] Fabian and Wolf reported 13 patients with ECS who were followed up for at least 5 years. They revealed that ECS is more common in females, and develops at a later age and lasts longer than photosensitivity.[15] The results for female sex predominance, age dependency and the association of photosensitivity and ECS in our study were consistent with these studies.

Kohno reported the high rate of family history for epilepsy in first and second-degree relatives in 33% patients.[13] As with the other studies, we found a high rate of family history for epilepsy (42.3%) and five patients' parents were second-degree relatives. Taylor et al. demonstrated an electro-clinical overlap between JME and IPOE, and claimed that this overlap may be due to shared genetic determinants.[16] This mechanism may explain why ECS was found in IOE patients in our series. Concerning the family histories reported in the literature and demonstrated in our study, genetic studies are foreseen to be extremely helpful in the near future for this phenomenon.

We would like to emphasize the importance of the eye closing test in routine EEG examination with repetitive eye closure in the illuminated room in order to establish photosensitivity associated with eye closure abnormalities which are eliminated in darkness.[1] While recording the routine EEG, patients should be asked to repeat eye closure in every montage in order to elicit the presence of ECS.

As a conclusion, ECS is more common in females; it may overlap with photosensitivity, but is independent from photosensitivity. It may be seen in different epilepsy syndromes including JAE, CAE, JME, IGE, EMA, and IOE. In patients with ECS, prognosis of epilepsy is excellent and seizures cease after anti-epileptic therapy, implying that it is responsive to drugs.

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