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Electroclinical characteristics and syndromic associations of "eye-condition" related visual sensitive epilepsies—A cross-sectional study

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ABSTRACT

Purpose: The systematic study of visual phenomena such as eye closure (ECLS), eye-closed/fixation-off sensitivity (FOS) [terminology proposed as eye-condition sensitive (ECS) epilepsy] distinct from photosensitivity is rarely explored in literature.
Methods: Clinical, electroencephalographic (EEG) and imaging records of patients attending an epilepsy clinic were screened. Inclusion criterion was demonstrable electrographic visual sensitivitiy in the form of ECS parameters with/without photosensitivity. Subsequently, detailed analysis of their data was undertaken.
Results: Fifty two patients had one or more ECS parameters. Mean age of onset of epilepsy of the cohort was 10.26 ± 7.79 yrs. A family history of seizures was noted in 17% of the cohort. ECLS, FOS, combination of both, co-existent scotosensitivity and photosensitivity were noted in 32.6%, 48.1%, 19.2%, 23.1% and 30.8% respectively. Epilepsy syndromes included late-onset childhood occipital epilepsy-Gastaut variant (23.1%), reflex occipital lobe epilepsy with ECS without photosensitivity (21.2%), idiopathic photosensitive occipital epilepsy (13.5%), genetic generalized epilepsy (13.5%) and symptomatic epilepsy (28.7%) predominated by patients with posterior cortex gliosis or who were imaging negative. The idiopathic group also had lower seizure score and marked sleep activation of epileptiform abnormalities. Co-existent phostosensitivity was associated with a significantly higher predisposition for female gender, ECLS, generalized seizures and spikes with lower prevalence of FOS and extra-occipital spikes. Parieto-occipital spikes were noted in 88.4% patients.
Conclusion: Syndromic heterogeneity is evident in ECS epilepsies. These form a unique subset of visual-sensitive epilepsy syndromes with focal or generalized seizure subtypes of idiopathic or symptomatic etiologies, with and without associated photosensitivity.

1. Introduction

Visual sensitive epilepsy is the most common type of reflex epilepsy, yet not a distinctively recognized homogenous entity [1–3]. Visual sensitivity is defined as the susceptibility towards seizures which are triggered by physical characteristics of visual stimuli and not by their perceptual properties [4]. Some of the well known triggers for visual sensitivity include sunlight, flicker and patterns such as stripes [5]. Visual sensitivity in an epilepsy cohort can either be evident on directed questioning, following inciting stimuli such as video game or television viewing or manifest as apparent unprovoked seizures including generalized onset with motor, (myoclonic) and non-motor seizures (absence). Focal-onset seizures triggered by visual stimuli associated with visual auras are uncommon but these may be under-diagnosed. Apart from intermittent photic stimulation, different eye-conditions such as eye-closure, interruption of fixation and eye open/closed states in darkness and bright light have also been reported to induce interictal epileptiform discharges (IED) in electroencephalography (EEG) [6,7]. However, the combined prevalence and electro-clinical correlates of these specific parameters of visual sensitivity has

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been rarely studied in detail [1,8] or is lost in discussions on light characteristics such as photo- or scotosensitivity. This study was aimed to ascertain the phenotypic characteristics of what may be termed as "eye-condition" sensitivity (ECS) [8] such as eye-closure, eye-closed/fixation-off sensitivity in a cohort of epilepsy patients attending the outpatient and inpatient care in a tertiary referral centre and to categorize the electro-clinical characteristics in this cohort of reflex ECS epilepsy patients.

2. Methods

This was a descriptive study based on the prospectively maintained database of electronic records of patients who attended at the comprehensive epilepsy care centre at a tertiary referral hospital situated in the city of Trivandrum, Kerala, south India over 5 years.

2.1. Inclusion criteria

Those patients who demonstrated visual sensitivity as captured in any single EEG record, which was available for review, by any one or more of the following parameters were included-

1) Eye-closure 2) Eye-closed/Fixation-off sensitivity with and without scotosensitivity. Definitions of each of these parameters considered for inclusion are as below.

i) Eye closure sensitivity (ECLS): Eye closure was defined as the period immediately after eye closure and lasting for 3 s or less. IED on EEG induced by eye-closure was referred to as ECLS, characterized by generalized and transient abnormalities appearing within 3 s after closing the eyes and lasting for 1–3 s
ii) Eye closed/fixation-off sensitivity (FOS): The period lasting for more than 3 s and persisting as long as the eyes remain closed or when fixation was interrupted. Since prolonged eye closure leads to interruption of fixation, these terms were used together in this study. EEG abnormalities related to this condition constituted eye-closed sensitivity (ECLDS), which may be continuous or repetitive, generalized or focal, unilateral or bilateral and persisting as long as the eyes are closed. FOS was additionally tested by placing a sheet of white paper, 20 cm in front of the subject, with the eyes open without fixating as Frenzel lenses were not available at our centre.
iii) Scotosensitivity (SS): Elimination of retinal light stimulation by complete darkness in the room and presence of epileptiform abnormalities irrespective of eyes open and closed states under this condition was considered as SS.

2.1. Exclusion criteria

Isolated photosensitivity on EEG without atleast one demonstrable ECS parameter mentioned above, or normal EEG were considered exclusionary. Photosensitivity (PS) was defined by reproducible Grade III/IV photoparoxysmal discharges, photoconvulsive responses on photic stimulation at standard frequencies of 1Hz–30 Hz.

Being a retrospective study, any default of the EEG protocol as detailed below could not be corrected and in case inadequate testing or non availability of tests was discovered during the review, such records were marked for exclusion from the study. This was done to maintain uniformity in data acquisition and to avoid sampling bias.

2.2.1. Standard protocol for EEG acquisition

EEG was performed with a standard arrangement of 10–20 international electrode placement. EEG was recorded for a minimum duration of 30 min and sleep record was obtained for at least 15 min. Duration of recording was extended with prolonged sleep period (1–2 h) and longer period of awakening from sleep on case based criteria (e.g., JME). Patients undergoing EEG recording were sleep deprived the prior night and at least an overnight record was available in those patients who underwent video EEG (VEEG) for apparent refractoriness of seizures or for exclusion of non-epileptic events. EEG interpretations were done independently by 2 certified epileptologists with atleast 5 years experience in EEG (RM & AR) and in case of disagreement the interpretation was finalized after a joint meeting. During the awake state, all patients underwent testing in eye-open and eye-closed (the duration of eye-closure lasted more than 10 s) states for activations as discussed above, at least thrice during one EEG recording along with hyperventilation and intermittent photic stimulation tests.

2.2.2. Definition of parameters

The definition of ECS parameters and EEG response was defined as per standard definitions proposed in literature as mentioned in the inclusion criteria and are depicted in Fig. 1 [9].

2.2.3. Clinical details

Demographic factors, seizure type and frequency, etiology, family history, pharmacotherapy and clinical history of visual sensitivity, if available, were noted. Details with regard to episodes of visual auras, eyelid blinking on exposure to light, self induction phenomenon, pulling sensation of eyes, behavior arrest or confusion, tonic head and eye deviation and generalized-onset seizures (motor/non-motor) were recorded. EEG data analyzed included presence of focal or generalized spikes with additional focus on posterior cortex IED (posterior temporo-parieto-occipital), symmetry of discharges, activation during sleep, presence of visual sensitivity parameters (ECLS, ECLDS/FOS) and documentation of seizures recorded, if any. Radiological data if available was also noted. Categorization of the patients in to idiopathic and symptomatic groups was based on history, the presence of neurological co-morbidities, focal or generalized background slowing, IED, seizure frequency and/or radiologically demonstrable epileptogenic lesion as mentioned in the ILAE 1989 classification system. This was preferred over the current ILAE 2010 classification schema so as to achieve a pragmatic classification of the epilepsy syndromes in the cohort into these two groups for comparison purposes. Seizure frequency was graded by utilizing modified Engel seizure score based on seizure status at the time of evaluation [10].

2.3. Statistics

Data was tabulated in and statistical analysis was done by using Statistical Package for the Social Science Statistics for Windows version 21 (Armonk, NY: IBM Corp). Fisher's Exact Test was used to compare qualitative variables for test of independence between groups and for test of goodness of fit when appropriate and the non-parametric Mann Whitney U Test to compare quantiative variables; statistical significance was accepted at $p < 0.05$. Relative risk (RR) was computed when the probability of an event occurring between two groups was needed.

3. Results

3.1. Demographic data

Out of 10,529 EEG and 3012 vEEG records, 52 patients who met the inclusion criteria of objectively documented ECS namely,