Two types of isolated epileptic nystagmus: case report

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Abstract: Epileptic nystagmus (EN) is a quick, repetitive jerky movement of the eyeball caused by seizure activity, unaccompanied by other ictal phenomena rare. Here, we described two cases, one characterized by binocular and the other by monocular isolated epileptic nystagmus (IEN), and we identified the characteristics of the etiology, clinical manifestations, electroencephalogram, imaging, treatment and prognosis in epileptic nystagmus through reviewing literature. We found IEN occurs more frequently in children than in adults. Etiological factors included trauma, cerebral vascular disease, tumor, and anoxia. The frequency of IEN was high, which varied from several to hundreds of times per day, and the duration of it was usually less than 1 minute. EN and its subtypes, such as epileptic monocular nystagmus, vertical epileptic nystagmus, epileptic skew deviation, periodic alternating nystagmus, and partial oculo-clonic status, are rare. The fast phase of the nystagmus was contralateral to the epileptogenic zone in most cases. Periodic lateralized epileptiform discharges (PLEDs) is a distinct EEG pattern in EN. Our findings suggested that the occipital lobe may plays a key role in the origin of EN.

Keywords: Epilepsy, nystagmus, electroencephalogram, etiology, clinical manifestations

Introduction

Nystagmus is an involuntary, to-and-fro movement of the eyes that may reduce visual acuity and cause oscillopsia [1]. The condition can be congenital or acquired. Acquired nystagmus may be caused by diseases of the eye or inner ear, multiple sclerosis, stroke, anti-seizure medication such as phenytoin [2], alcohol intoxication, deficiency of B12 or thiamine, and brain tumors. Moreover, nystagmus can be caused by seizure activity, that is, a type of epilepsy.

Epileptic nystagmus (EN) is a quick, repetitive jerky movement of the eyeball caused by seizure activity [3]. Féré was credited with the first description of EN [4]. Nystagmus (the only sign) caused by epilepsy and nystagmus occurring during the course of epilepsy (with symptoms including other seizure types) may differ. EN unaccompanied by other ictal phenomena is rare. Von proposed the term “isolated epileptic nystagmus” (IEN) to distinguish between nystagmus caused by epilepsy and that occurring during an epileptic attack [5]. A total of 62 cases of EN have been reported in the literature between 1890 and 2014. Of those, 10 were classified as IEN and 2 cases were monocular epileptic nystagmus, 1 of which was triggered by photic stimulation [6]. Here, we describe two cases, one characterized by binocular and the other by monocular IEN. Then we reviewed the literature about epileptic nystagmus.

Methods

Two patients presented to our epilepsy clinic complaining of episodes of oscillopsia and diplopia. Both patients provided informed written consent for the publication of their data. The study protocol was approved by our Institutional Ethics Committee. We reviewed most of the cases of EN reported since 1890 to determine the clinical characteristics of the condition. Clinical information was obtained from the history of the patients and their relatives and from medical records.

Case 1

A right-handed 14-year-old male complained of episodic vibratory sensations in both eyes for
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The patient had a horizontal, left-beating nystagmus in which the eyes did not cross the midline of the orbit during the slow phase. Seizures occurred during the day and evening, and the patient had dozens of seizures daily. He had no history of dystocia or head trauma, but had a febrile seizure at the age of 1 year. The family medical history was not remarkable. No abnormalities were found in the routine ophthalmological examination, electronystagmogram, or vestibular function test completed at another hospital before the patient visited our neurological clinic. Electroencephalograms (EEG) were recorded digitally; electrodes were attached according to the International 10-20 system. The background EEG was normal. The interictal EEG showed periodic spike-slow wave complexes with a frequency of 1.5-2.5 Hz and amplitude of 150-330 mV over the parietal, occipital, and post-temporal regions (right lateral predominant) lasting 10 s during sleep. The ictal discharges manifested as intermittent discharges abruptly shifted to a fast rhythm over the parietal and occipital regions and varied to spike-slow.

Figure 1. EEG data of case one: A. Periodic lateral epileptic discharge (PLED) like intermittent discharge over the posterior of head in sleep; B. Intermittent discharge disappeared and revolved into fast rhythm; C. Then, periodic slow waves over all leads; D. Fast rhythm appeared again; E. Fast rhythm evolved into spike and slow waves mainly over the posterior region; F. Spike and slow waves and followed by electric resting. We cannot define the exact origin of seizure.
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wave complexes with a frequency of 4.5-5.5 Hz and amplitude of 100-175 µV and spreading to other regions lasting 45 s (Figure 1). Magnetic resonance imaging (MRI) was performed using a 1.5 Tesla scanner (T1-, T2-, diffusion-weighted images) and was normal. Oxcarbazepine 600 mg twice daily (b. i. d.) did not completely control the seizures; thus, her regimen was supplemented with levetiracetam 0.5 g b. i. d. The patient had no seizures during the following year.

Case 2

A right-handed 57-year-old female presented complaining of episodes of left eye subsultus and diplopia accompanied by dizziness from the age of 7 years. She was diagnosed with viral hepatitis type C in her 40 s. The patient had no history of asphyxia, febrile seizures, or head trauma, and her growth and development were normal. During the seizures she felt the line on the ceiling separated gradually and had diplopia and did not experience loss of consciousness, hallucinations, rotation of the head, or secondary generalized tonic-clonic seizures (GTCS). During the seizures, her left eye had a horizontal left-beating nystagmus in which the eye did not cross the midline of the orbit during the slow phase. Her seizures occurred dozens to hundreds of times daily persisting for several seconds, but no longer than

Figure 2. EEG data of case two: A. The background showed α waves deceased and its amplitude lower in right occipital region than that of left side; B, C. Periodic lateral epileptic discharge (PLEDs) notable in both occipital regions; D, E. PLEDs evolved into fast rhythm in all regions; F. Spike and slow waves over the both occipital-temporal regions, at last electric resting.
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Table 1. The feature of the patient's age

<table>
<thead>
<tr>
<th>Age group</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>71~80y</td>
<td>3.60%</td>
</tr>
<tr>
<td>61~70y</td>
<td>8.90%</td>
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<tr>
<td>51~60y</td>
<td>17.90%</td>
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<tr>
<td>41~50y</td>
<td>7.10%</td>
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<tr>
<td>31~40y</td>
<td>7.10%</td>
</tr>
<tr>
<td>21~30y</td>
<td>14.30%</td>
</tr>
<tr>
<td>11~20y</td>
<td>14.30%</td>
</tr>
<tr>
<td>≤10y</td>
<td>26.80%</td>
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</tbody>
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Note: the axis of ordinate was age (years), the axis of abscissas was percentage of patients.

1 min. The seizures occurred during the day and night and awakened her from sleep. Episodes could be triggered by certain visual stimuli such as reading a book or watching television. Her neurological and ophthalmological examinations were normal. The background EEG revealed decreased α-wave amplitude over the right occipital region lower than that of the left side. The intermittent discharge was long time course periodic spike-slow wave with a frequency of 1.5-3 Hz and amplitude of 55-115 μV over the occipital and post-temporal regions lasting for 110 s. Ictal discharges manifested that periodic discharges which continued 70 seconds evolved into a fast rhythm (about 20 s) over the occipital regions and propagated to other regions and then varied to spike-slow wave complexes with frequency of 3-6 Hz and amplitude of 35-75 μV (Figure 2). Her brain MRI scan was normal. Following the administration of carbamazepine 0.1 gram b. i. d., her seizures decreased markedly. She refused anti-epileptic drugs (AEDs) owing to concerns about potential side effects to her liver and the minimal impact of seizures on her daily life.

Literature review

We found a total of 62 patients from several countries diagnosed with EN between 1890 and 2014. Of those, 27 were male, 26 were female, and the sex of the remaining 9 patients had not been noted (Table 1). The youngest patient was 10 days old, and the oldest was 75 years of age. The signs and symptoms of EN (Table 3). The fast phase of the nystagmus was contralateral to the epileptogenic zone in 83% of the cases. The remaining 17% included cases with deviations ipsilateral to the epileptogenic zone, upbeat nystagmus, generalized ictal discharges on the EEG, or the direction of the fast phase was not recorded. The treatment outcome was recorded in 22 cases and of those, 12 were seizure-free following treatment. Phenytoin sodium and carbamazepine were the most frequently administered AEDs.

Results

IEN is a rare condition that affects children more often than adults. The etiological factors include trauma, cerebral vascular diseases, tumors, and anoxia. IEN seizures occurred frequently (from several to hundreds of episodes daily) and the duration was short, typically lasting less than 1 min. In most cases, the fast phase of the nystagmus was contralateral to the epileptogenic zone. Our findings suggest that the occipital lobe plays a key role in the origin of EN.

Discussion

Nystagmus

Nystagmus is a common sign of central nervous system disease and is frequently encountered in clinical practice; however, binocular EN is rare in patients without brain lesions. Monocular nystagmus (MN) is an uncommon, yet heterogeneous phenomenon associated
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with anterior visual pathway lesions, monocular blindness [7], spasmus nutans [8], brainstem infarction, and multiple sclerosis. Epileptic monocular nystagmus (EMN) triggered by photic stimulation has been reported in a patient with mental retardation, severe uniocular visual loss, and generalized seizures [6]. However, Grant et al. described a case of EMN in a cognitively normal adult with normal vision, similar to our patient [9]. They found focal seizures originating in the occipital lobe contralateral to the involved eye and an associated structural lesion thought to represent a forme fruste of Sturge-Weber syndrome. The primary difference between our patient and that of Grant et al. was that our patient had a normal MRI. Grant and colleagues hypothesized that the seizure discharge activated a cortical saccade region causing simultaneous supranuclear inhibition of the ipsilateral eye movement or triggered monocular eye movement commands. Other types of EN have been described, such as vertical epileptic nystagmus [10], epileptic skew deviation [11], periodic alternating nystagmus [12], and partial oculo-clonic status [13].

Of the 62 EN cases reported previously, 58 were associated with partial seizures. We found that horizontal EN was most often associated with seizure activity involving the occipital cortex (32 cases), although adjoining portions of the parietal and temporal cortices may be involved.

Mechanisms underlying epileptic nystagmus

EN has been classified into three pathogenic types according to the clinical features of the nystagmus [13]:

EN caused by epileptic activation of a cortical saccade region. The nystagmus is limited to the opposite side of the focus with quick, contraversive phases and slow phases with diminishing speed, which do not cross the midline of the orbit. The quick phase is caused by activation of the cortical saccade region, and the slow phase is due to a defect in the gaze-fixing mechanism ("leaky neural integrator" or "velocity storage mechanism"), possibly after antiepileptic medication or coma, although this mechanism has been questioned [14].

EN caused by epileptic activation of a cortical pursuit region. Here, the nystagmus has wide amplitude, the epileptic activation of the cortical pursuit region triggers a slow, ipsiversive saccade that crosses the midline and presents linear velocity. The quick (contraversive) phase is generated reflexively.

EN caused by epileptic activation of a cortical optokinetic region. This involves seizure-induced, ipsiversive slow phases associated with reflexive quick phases. They also lead to vertigo because of the connection with the vestibular nucleus in the brain stem.
Despite the fact that EN is a unique phenomenon, it has been increasingly associated with cryptogenic or symptomatic occipital epilepsy (or that from adjacent areas). In a recent study, Gire et al. reported the case of an 8-year-old child who presented with EN as a manifestation of (idiopathic) non-lesional benign epilepsy [15].

Most previous studies have not provided sufficient detail to determine the patients’ pathogenic type; however, the pathogenic type was identified in 15 of the patients in our literature review. Of those, 11 were type 1 and four were type 2. Both of our patients were type 1.

Epileptic activation of the frontal areas is not thought to be essential to trigger conjugate eye deviations or EN [4, 16]. In fact, the posterior cortical areas may control oculor saccades. Recent mapping studies have revealed three small saccade eye fields that elicit contraversive saccades: an area in the posterior portion of area 8 (frontal eye field), an area in the dorsal portion of area 6, and a region in area 7 within the intraparietal sulcus [17, 18].

In the monkey, two small eye fields that support smooth pursuit eye movements have been shown to elicit ipsiversive slow-phase eye movements or an increase in eye velocity during ongoing ipsiversive slow phases when stimulated. These areas are located in the inferiormost portion of the frontal eye field and a region in the superior temporal sulcus within the temporoparietal cortex [19, 20]. A small optokinetic cortical area within the temporoparietal cortex projects to the nucleus of the optic tract (NOT), which in turn projects to the vestibular nucleus. Stimulation of the NOT induces ipsiversive slow phases followed by a resetting quick phase [21].

Furthermore, Kaplan and Tusa attributed the rarity of EN to the infrequency of the underlying conditions: an ictal focus in the temporoparieto-occipital (TPO) junction, an ictal discharge of at least 10 Hz, and a leaky neural integrator [22].

The intermittent and ictal EEGs revealed periodic lateralized epileptiform discharges (PLEDs) in our patients. Two cases of EN with PLEDs have been reported previously [23]. Chatrian et al. argued that although PLEDs generally occur in structural brain diseases of vascular origin, severe metabolic disorders may contribute by lowering the seizure threshold and upsetting the recovery process of the neurons after they discharge [24]. However, our patients did not have brain lesions. The MRI findings revealed no lesions in our patient with EMN. The ictal EEG originated from the occipital lobe, suggesting that the occipital lobe, but not the TPO area, may be the source of EN.

EN characteristics

EN may occur at any age; however, we observed two peaks: prior to the teenage years and among adults in their 50 s. The fast phase of the nystagmus was contralateral to the epileptogenic zone in all but one patient. Seizure frequency was high, ranging from several to hundreds daily, and the duration was short, persisting less than 1 min. Symptoms reported before, after or during EN included dizziness, hallucinations, head rotated to one side, cortical blindness, automatism, secondary GTCS, and loss of consciousness. The etiology included head trauma (22%), brain cerebral vascular disease (22%), anoxia (13%), tumor (10%), abnormal blood glucose (8%), intracranial infection, and unknown (17%). Our primary goal was to characterize EN and identify its underlying mechanisms. The data were obtained from scalp EEGs, which is not a precise method for localizing seizures; thus, our findings are an approximation of the seizure origin among the five cerebral lobes.

Most of the ictal EEG data revealed involvement of more than one lobe during EN, such as the temporal-occipital, forehead-temporal, parietal-occipital or temporal-parietal-occipital; however, the involvement of only one lobe was observed in the occipital (eight cases), parietal (three cases), frontal (five cases), and temporal (three cases) lobes. Overall, the occipital lobe was the most frequently involved lobe (32 cases). Four patients had a generalized ictal EEG, two of which had 3-Hz spike-slow waves [25].

Diagnostic procedure for patient complaining of oscillopsia or diplopia

Patients complaining of oscillopsia or diplopia should first be assessed to determine whether the nystagmus is caused by peripheral or central nervous system disease. Peripheral nystagmus may be caused by dysfunction of the
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1. Introduction

Epileptic nystagmus may be caused by brainstem, cerebellar, or cerebral cortex lesions. In cases where the etiology is difficult to determine, diagnostic tools, such as the vestibular function test, electronystagmogram, electrooculogram, brain MRI, video EEG, and SPECT may be useful [26]. The shortcoming of our cases is lack of electronystagmogram meanwhile with EEG. If abnormal findings are not revealed, we initiate tentative treatment with AEDs according to the patient's condition. Voluntary nystagmus can be a component of a nonepileptic seizure. In our patient, an EEG during a nonepileptic seizure showed normal resting background activity at 9 Hz with infrequent sharp and spike discharges arising from the temporal regions independently (clearly not an ictal pattern), and occasional delta and theta slow waves arising independently from both temporal regions. The presence of volitional nystagmus during an apparent seizure should prompt the evaluation of possible nonepileptic events, including attempts to record an episode on EEG. Physicians should strive to accurately document the nature of the nystagmus, whether by history or on examination and should not assume that the presence of nystagmus is an objective sign of a physiological epileptic event [27].

2. EN treatment and prognosis

The outcome of treatment and follow-up was reported for 21 of 62 patients in our study. Perhaps because of time issue, most patients were treated with phenytoin sodium (nine cases), and the remaining patients were treated with carbamazepine, lamotrigine, sodium valproate, or other AEDs. Of the 21 patients, 12 (57%) were seizure-free throughout treatment; thus, the prognosis was good.

3. Conclusion

EN is a rare condition, particularly types such as EMN, vertical epileptic nystagmus, epileptic skew deviation, periodic alternating nystagmus, and partial oculo-clonic status. When the etiology of the nystagmus is not known, epilepsy should consider when the seizure frequency is high and the nystagmus duration is short. The fast phase of the nystagmus was mostly contralateral to the epileptogenic zone. Our findings suggest that the occipital lobe plays a key role in the origin of EN.

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Disclosure of conflict of interest

None.

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References

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