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■ Clinical commentary

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Localisation and stimulation of the parietal eye field*

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ABSTRACT

Localisation of the human parietal eye fields (PEF) has not been as well studied as the human frontal eye fields (FEF). Stimulation studies in rhesus monkeys have suggested the localisation of the PEF to be within the intraparietal sulcus. Functional MRI studies have demonstrated this region to be highly active and potentially connected in saccadic and gaze shifting tasks. Here, we present a case of a patient with left versive seizures evaluated with SEEG, in whom electrical stimulation within the right intraparietal sulcus resulted in horizontal and downward conjugate eye movements contralateral to stimulation. We illustrate clinical differences between the FEF and PEF on cortical stimulation. In addition to the frontal eye field, it is important to recognise other cortical regions involved in eye movement which can cause conjugate contralateral eye movement.

Key words: frontal eye field, parietal eye field, ictal semiology, SEEG, cortical stimulation

VIDEO ONLINE

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In humans, various gaze control systems have been postulated for eye movement including the frontal eye field (FEF), dorsolateral prefrontal cortex (dlPFC), supplementary eye field (SEF), cingulate eye field (CEF), middle superior temporal area (MST) and parietal eye field (PEF) [1]. The human FEF has been shown to be located below the intersection of the precentral sulcus and superior frontal sulcus within the middle frontal gyrus based on cortical stimulation [2-4] and functional neuroimaging studies [5, 6]. Few studies have explored the localisation of the human PEF. In stimulation studies on monkeys, it has been shown that the posterior intraparietal sulcus (pIPS) and adjacent inferior parietal lobule play a role in visually guided saccadic movements [7]. The PEF appears to be located within the intraparietal sulcus in its posterior half, adjacent laterally to the anterior part of the angular gyrus (Brodmann area 39) and medially to the superior parietal lobule (Brodmann area 7) [8, 9]. In macaque monkeys, the PEF has independent connections to the FEF and superior colliculus, both sharing similar distinct cytoarchitectural features [10, 11]. Studies looking at lesions damaging the parieto-collicular tract suggest that the PEF is crucial for reflexive saccade generation, which is triggered by the appearance of peripheral stimuli or the disappearance of fixation stimuli. PEF are not thought to be involved in intentional saccade generation, which is mainly dependent on the FEF, SEF and dlPFC. Diffusion

tensor imaging has been used to trace, using deterministic methods, the first branch of the superior longitudinal fasciculus (SLF-I). The SLF I is the dorsal-most white matter pathway linking the superior parietal lobule encompassing the intraparietal sulcus (IPS) with the middle and superior frontal gyrus, where the FEF is located [12, 13].

Case study

A 38-year-old, right-handed male was referred for epilepsy pre-surgical evaluation. Perinatal, birth, developmental and family history were unremarkable including no history of intracranial infections or febrile convulsions. There was a history of head injury from a motorbike accident with associated loss of consciousness at age nine. The onset of seizures occurred following this with semiology consisting of a sustained and forceful turning of the eyes and head to the left, accompanied by retained awareness; a focal aware motor seizure or versive seizure. Preceding the motor seizure, the patient would describe an initial aura of a pressure behind the eyes. The patient was on a medication regime including levetiracetam at 2 g BD, lamotrigine at 400 mg BD and primidone at 500 mg BD. Whilst on medication, versive seizures occurred daily and only from sleep. Progression to bilateral tonic-clonic seizures were rare. Previous medication trials included carbamazepine, topiramate, valproate, phenytoin, and phenobarbitone. Initial MRI had suggested possible cortical malformation in the right inferior portion of the precuneus with scalp evaluation demonstrating ictal and interictal right parieto-central changes. The patient proceeded with subdural grid evaluation demonstrating interictal and ictal EEG changes in the right subsplenial region. Following subdural grid evaluation, the patient had a right-sided resection involving the inferior portion of the precuneus and posterior cingulate gyrus. The resection margins involved the junction of the calcarine sulcus and parieto-occipital sulcus posteriorly, the interhemispheric fissure mesially, and the occipital horn anteriorly. The patient unfortunately continued to have seizures and was re-evaluated in our epilepsy unit 12 years later. Typical left versive seizures were captured in the re-evaluation with preserved awareness demonstrated during ictal examination. Scalp EEG demonstrated an ictal onset arising from the right centro-parietal electrodes (C4-P4).. Following the scalp evaluation, investigations including repeat volumetric MRI, brain PET and neuropsychological assessment. No lateralising or localising features were found on neuropsychological assessment. Repeat volumetric brain MRI revealed a subtle high T2/FLAIR signal in the superior frontal gyrus with a linear signal extending to the bottom of the sulcus with associated PET hypometabolism on co-registered brain FDG-PET (*figure 1*).

SEEG data

Pre-surgical evaluation data was reviewed in our multidisciplinary meeting. The primary hypothesis was of seizures arising from the right FEF secondary to

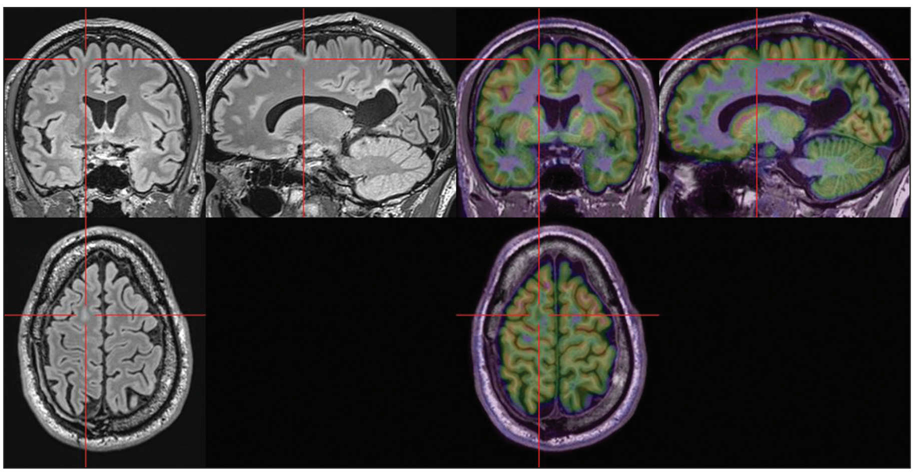
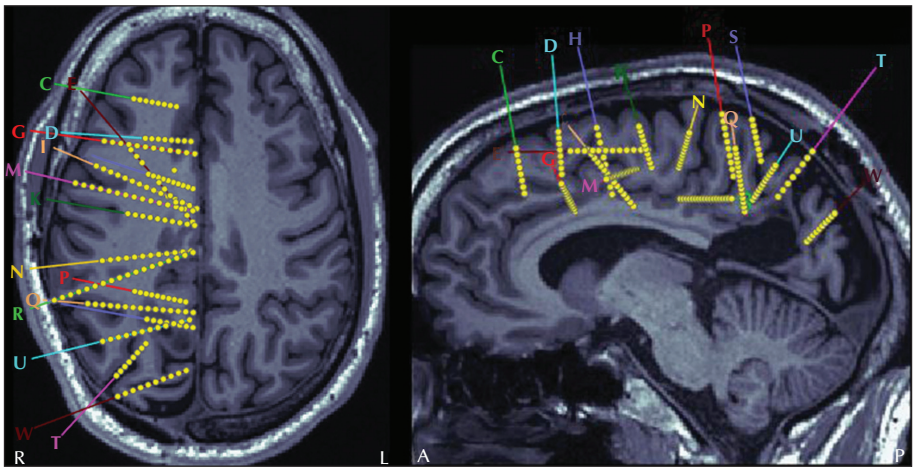


Figure 1. Co-registered volumetric MRI FLAIR (left) and FDG-PET overlayed over volumetric MRI T1 (right).



■ **Figure 2.** Electrode map overlayed over volumetric MRI T1 (left: superior view; right: lateral view).

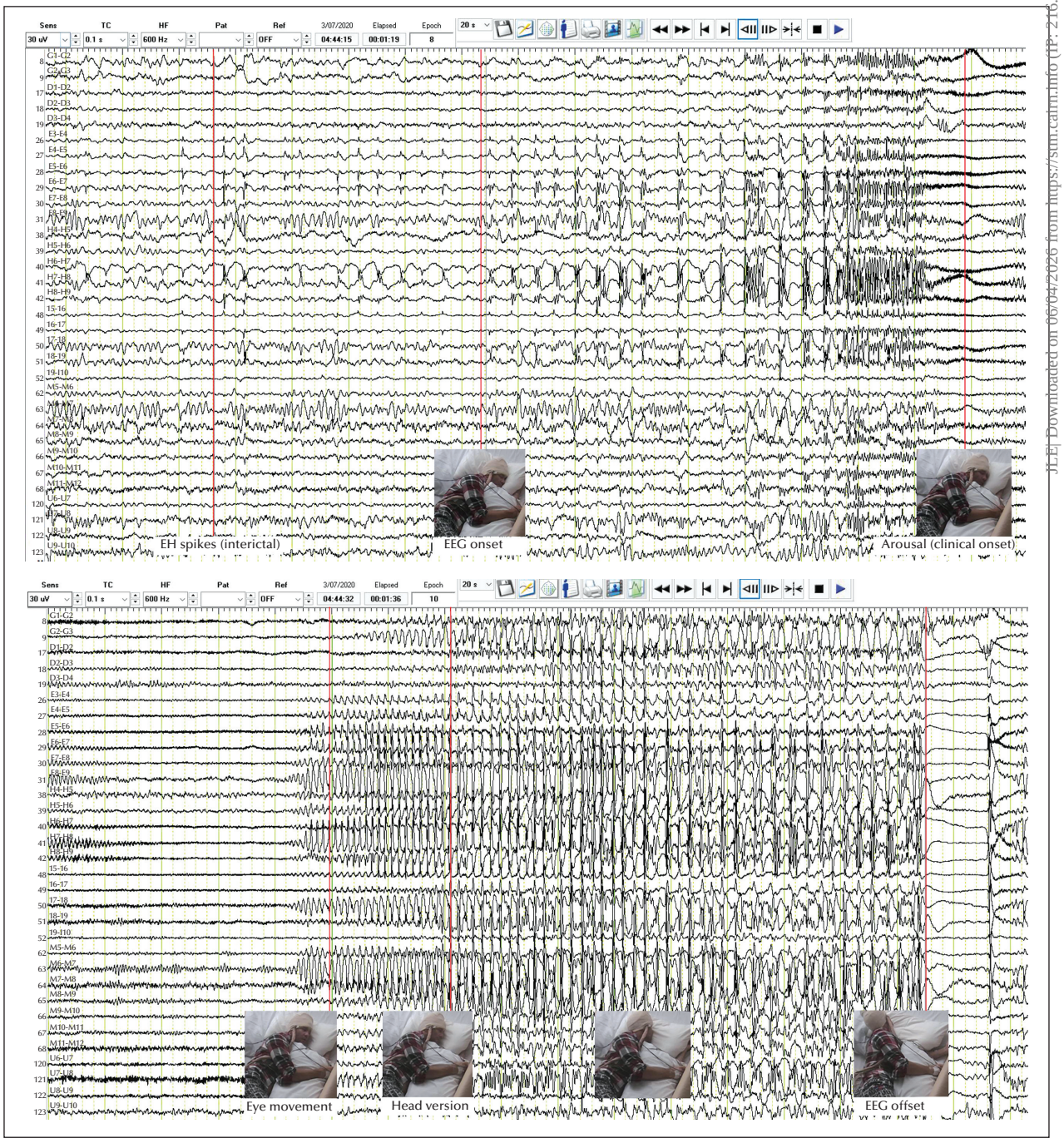
this possible lesion. The secondary hypothesis considered was a parietal-occipital onset based on previous resection and scalp EEG. A decision was made to proceed to SEEG. Sixteen intracerebral electrodes (Dixi medical, Besancon France, 8-18 contacts, 2 mm length, and 0.8 mm diameter) were implanted with a unilateral approach of the right hemisphere covering the suspected cortical dysplasia, right FEF, right parietal region covering the intraparietal sulcus and around the previous resection site (*figure 2*).

Frequent interictal spike-wave discharges were seen over the right frontocentral region. Three populations were recorded. The most frequent interictal population consisted of runs of spike and wave discharges recorded by electrodes in the caudal aspect of the right superior frontal gyrus (E3-8 and H6-8), traversing the suspected lesion. The second interictal population included a wider field involving electrodes in the right anterior cingulate (G1-2) and right superior frontal sulcus (I5-9). The third interictal population would additionally involve electrodes in the right precentral sulcus (M6-12) and distant right intraparietal sulcus (U7-8).

High-frequency oscillations (HFO) were seen within the right superior frontal gyrus electrodes (E3-8, H6-8). Following reduction of medication, multiple typical auras were recorded with associated electrographic seizures originating from the right superior frontal electrodes. These auras could also progress into left versive seizures. The EEG seizure onset preceded clinical onset in all events and was marked by an increase in amplitude of discharges occurring maximally at E6 and H7, before propagation to electrodes E3-8, H6-8, G1-2, I5-9, M6-12, and U7-8 (*figure 3*). There were no differences in ictal patterns between auras and versive seizures. Following recording of spontaneous seizures, medications were restarted. Cortical stimulation was performed between two contiguous electrode contacts with a biphasic current at maximum charge density of 60 µC/cm^2. Stimulation frequency was performed with 5 and 20-Hz stimulation runs and a train duration of 5-10 seconds, with gradually increasing stimulation intensity with 0.5-mA increments up to 10 mA.

Electrical stimulation produced eye version at I7-8 electrodes where we postulated the right FEF to be (*figure 4*). Electrodes E6-10 and H5-7, located around the lesion, caused conjugate contralateral eye movement, suggesting a potential network with the right FEF. Stimulation of electrodes U7-8 located in the right intraparietal sulcus triggered conjugate contralateral movement of the eyes, horizontally and with a slightly inferior angle. In all the stimulations which caused eye movement, the patient would describe an "aura" of pressure behind the eyes before eye version. The signs produced in the stimulation replicated the ictal clinical expression recorded from the spontaneous seizures without accompanying ictal EEG changes, suggesting the electrodes were likely to be within the symptomatogenic zone. The patient could not distinguish between the sensations arising from stimulating either frontal electrode I7-8 or parietal electrode U7-8. However, review of the video revealed that stimulation of the U7-U8 electrodes would cause slightly inferior eye movement compared to stimulation of the right FEF electrodes.

The SEEG evaluation captured habitual seizures localising the seizure onset zone in the right superior frontal gyrus within the vicinity of the right FEF

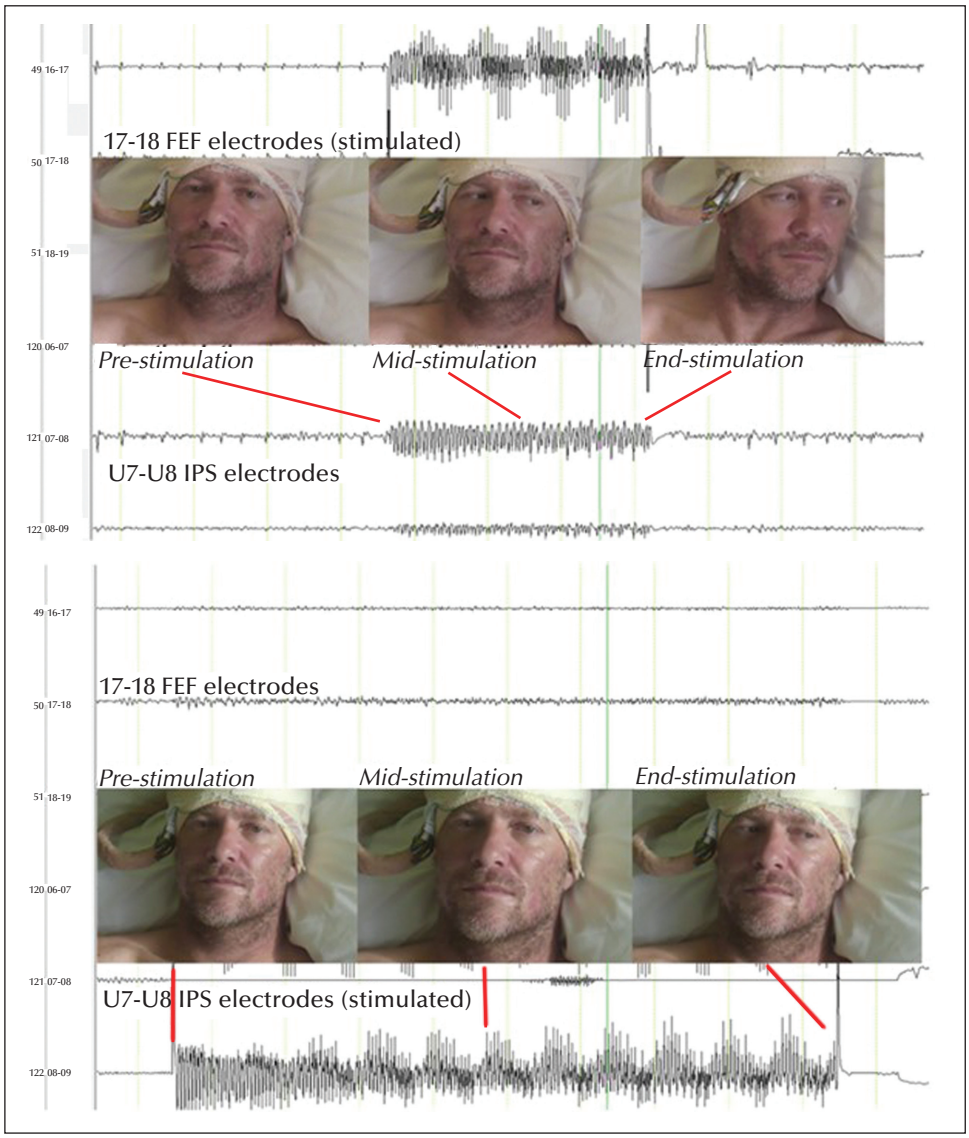


■ **Figure 3.** Ictal onset pattern. (A) EEG onset; (B) EEG offset.

(*figure 5*). The patient underwent focal resection of the suspected frontal lesion and histopathology showed focal cortical dysplasia type 2B. He remained seizure-free at two years of follow-up.

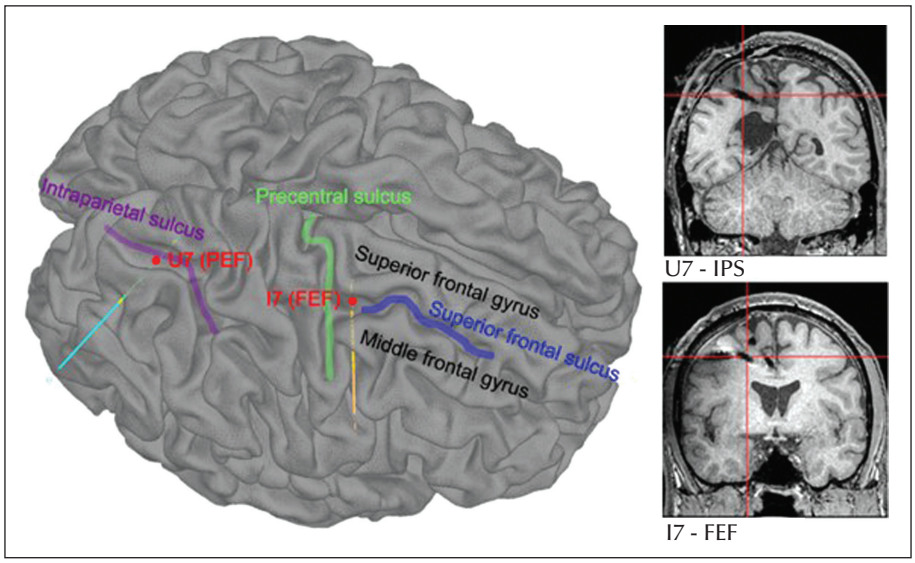
Conclusion

In this study, we demonstrate that stimulation within the right intraparietal sulcus can produce conjugate



■ **Figure 4.** (A) FEF stimulation at I7 to I8; intraparietal sulcus electrodes (PEF) U7-U8 are consistently recruited with stimulation. (B) Intraparietal sulcus stimulation (PEF) at U7 to U8; FEF electrodes are not recruited with intraparietal sulcus electrode stimulation.

contralateral eye movement that is horizontal and slightly inferior. The right intraparietal sulcus likely represents the location of the human PEF. Stimulation from the right intraparietal sulcus could be activating the parieto-collicular pathway for eye movement as all the surrounding right FEF electrodes were not recruited.
Stimulation of the right FEF electrodes consistently triggered conjugate and contralateral eye movement, followed by a smooth head turn in the same direction. Stimulation of the right intraparietal sulcus electrode caused a head turn following sustained and prolonged stimulation, although this finding was inconsistently reproducible. This study demonstrates the existence of a human PEF and its intimate relationship with the FEF. In addition to the FEF, it is important to recognise other cortical regions involved in eye movement which can cause conjugate contralateral eye movement. ■



■ **Figure 5.** Left: 3D reconstruction with co-registered electrodes, U and I. Right: coronal view of U7 electrode (upper panel) and coronal view of I7 electrode (lower panel).

Supplementary material.
Summary slides accompanying the manuscript are available at www.epilepticdisorders.com.

Disclosures.
The authors have no conflict of interest to declare.

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Legend for video sequence

This video demonstrates conjugate contralateral horizontal eye movement induced by electrical stimulation of the frontal eye field. The second part of the video demonstrates conjugate contralateral eye movement horizontally and inferiorly with electrical stimulation of the parietal eye field.

Key words for video research on www.epilepticdisorders.com

Phenomenology: versive seizure (controlateral), eye deviation
Localization: parietal eye field and frontal eye field
Syndrome: focal non-idiopathic (localization not specified)
Etiology: focal cortical dysplasia (type II)

TEST YOURSELF

(1) What symptoms does electrical stimulation of the frontal eye fields usually produce?
A. Ipsilateral eye deviation followed by ipsilateral head version
B. Contralateral eye deviation followed by contralateral head version
C. Ipsilateral blinking
D. Contralateral blinking
E. Contralateral head version with ipsilateral eye deviation

(2) Where is the parietal eye field located?
A. Superior parietal lobule
B. Inferior parietal lobule
C. Post central gyrus
D. Intraparietal sulcus
E. Parieto-occipital sulcus

(3) What is the role of cortical stimulation using stereoelectroencephalography (SEEG)?
A. Reproduce ictal clinical expression
B. Seizure induction
C. Determination of functional cortex
D. Prognostication of surgical outcome
E. All of the above

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com.