■ Clinical vignette

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Complexities of frontal eye field seizure semiology

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Frontal eye field (FEF) is the area in the vicinity of the precentral sulcus and superior frontal sulcus that, on stimulation, produces eye movements [1]. It is well connected to other cortical areas of eye movements and functions as an integrator [1]. FEF seizures typically produce contralateral eye and head adversion [2]. We report a case of FEF seizures with eye blinking and visual perception impairment as prominent features.

A 33-year-old, right-handed female was evaluated for drug-resistant epilepsy from seven years of age. She had multiple daily seizures. EEG showed very frequent left frontal spikes (*figure 1A, B*). Video-EEG recorded focal aware seizures as eye blinks along with perception impairment as dysmorphic appearance of her surroundings, lasting for about 15-20 seconds. No eye deviation or head adversion were observed during these seizures (*video sequence 1*). Ictal EEG showed disappearance of epileptiform discharges with frequent eye blink artefacts (*figure 1C, D*). During drowsiness and sleep, she also had seizures manifesting as eye closure, followed by slow rolling of the eyes, progressing to right head and eye adversion, lasting for about 30 seconds. Postictally, she recovered immediately and at times placed her hand over her eyes (*video sequence 2*). The EEG showed an early left frontal evolving rhythm during these seizures. Her clinical examination was normal. Neuropsychology showed mild impairment in sustained attention and working memory. Brain MRI (3T) showed very focal 'bottom of sulcus dysplasia' (BOSD) with transmantle sign in the left anatomical FEF region with FDG-PET hypometabolism (*figure 1E-H*).

She underwent surgery whilst awake. A single depth electrode was placed stereotactically into the depth of the lesion prior to craniotomy for localisation. Intraoperative electrocorticography (ECoG) was performed combining grids and depth electrodes covering the lesion. Surprisingly, prolonged ECoG showed no abnormality. Recording was discontinued and stimulation studies were being prepared, when she reported her aura. Reverting back to ECoG settings revealed sequential spikes and polyspikes for several seconds, followed by a delta rhythm from the BOSD (*figure 1I, J*). The onset of the seizure could not be captured.

Cortical stimulation of the BOSD at 50 Hz and 0.5-1.0 mA showed an immediate and consistent response as bilateral eye closure with blinking. With an increase in intensity, at 2 mA and 3 mA, the initial eye blink was followed by prominent saccadic eye deviation to the right and upwards. She identified the low intensity stimulation as her habitual seizure (*video sequence 3*). These stimulation responses of the FEF were consistent with her recorded seizure types. Seizures with eye closure, blinking and visuospatial distortion corroborated with low intensity stimulation of the FEF. The other types of seizure semiology, such as eye closure, up rolling of the eyes, with adversive eye and head movement, were reproduced by

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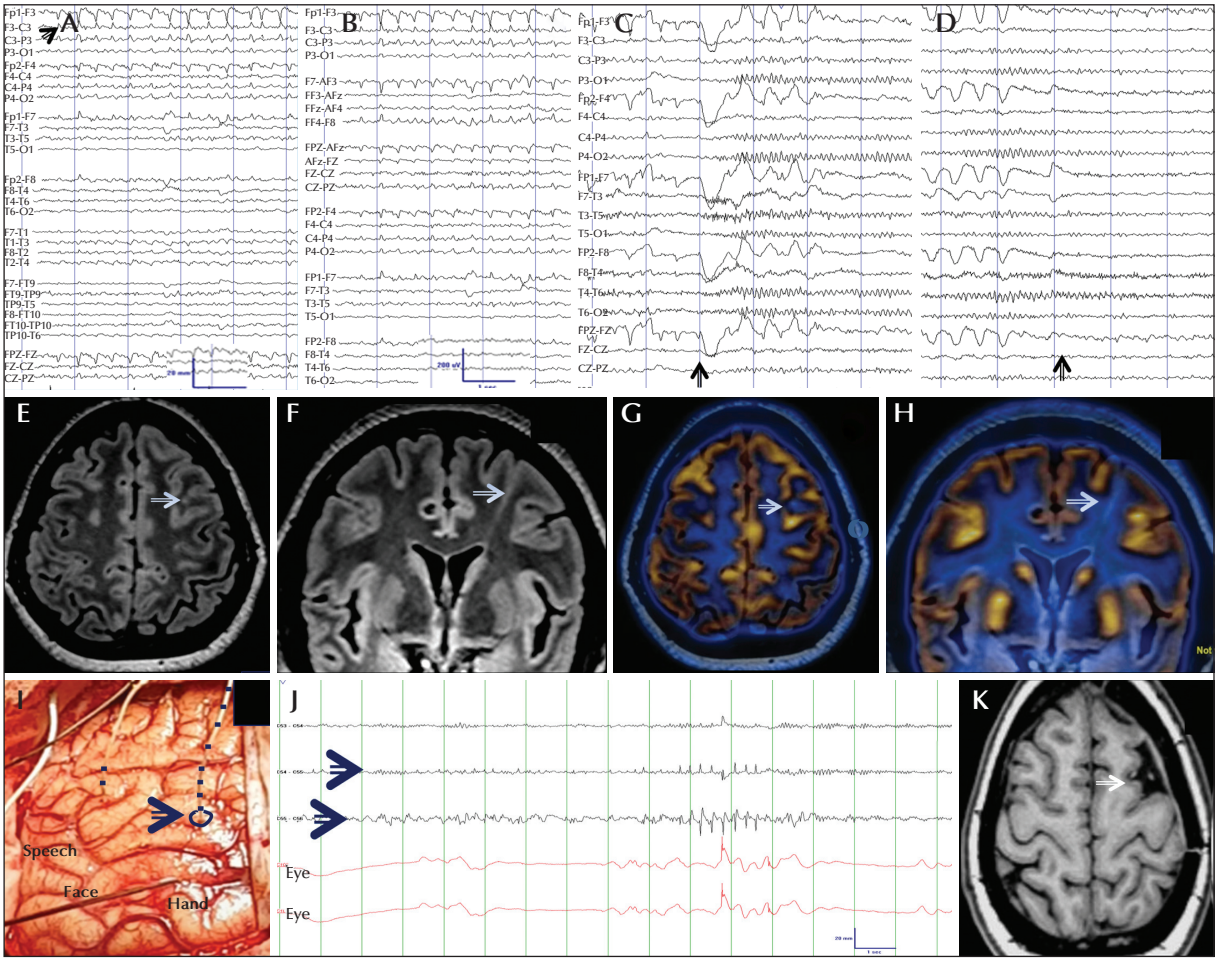

■ **Figure 1.** (A, B) Interictal EEG showing very frequent left frontal spikes in bipolar montage (A) and coronal montage (B) with spikes at F3, Fz, AF3, and AFz spreading to F4. (C, D) Ictal EEG showing disappearance of the left frontal spikes with posterior alphoid rhythm and prominent eye blink artefacts with reappearance of interictal spikes immediately after the seizure (two arrows: seizure epoch). (E-H) MRI (3T) FLAIR 3D showing very focal hyperintensity with transmantle sign in the left anatomical frontal eye field area suggestive of bottom of sulcus dysplasia with corresponding FDG PET hypometabolism. (I) Intraoperative image showing the left hand area, face area and speech area mapped by stimulation studies; the electrode marked with the arrow is within the depth of the FCD detected on MRI (anatomical frontal eye field).(J) EEG recording from the same electrode showing sequential spikes (arrow) during the aura described by the patient. (K) Postoperative MRI showing resection of the dysplasia.

higher-intensity stimulation of the FEF. These consistent time-locked responses to stimulation suggested that eye closure and blinking were due to FEF seizures and not a voluntary response. Functional mapping of motor hand and face areas and language was performed with 50-Hz stimulation. The patient underwent lesionectomy (*figure 1K*). Postoperatively, she had mild transient word finding difficulty. Histopathology confirmed type IIb FCD. She is currently classified as Engel Class 1a at three years of follow-up with no deficits.

The FEF plays an important role as part of the cortical oculomotor system. The FEF is located in the dorsolateral premotor cortex, in the vicinity of the posterior aspect of the middle or superior frontal gyrus at the intersection between the superior frontal sulcus and precentral sulcus or within the precentral sulcus [1]. Different sub-regions for saccadic and

pursuit eye movements within the FEF have been demonstrated using functional MRI studies [3].
Stimulation studies of the FEF by Penfield and Jasper many decades ago showed contralateral eye movements [4]. Godoy *et al*. demonstrated contiguity of the FEF with motor strip [5]. In their study, FEF stimulation produced contralateral conjugate eye movements (horizontal or oblique upwards) in all patients and was followed by head adversion in 58%. There are very few case reports of isolated focal FEF epilepsy [2].
The role of the FEF in eye blinks has not received much attention. A functional MRI study of blinking and winking showed that eye movements and unilateral winking strongly activated a bilateral fronto-parietal network while voluntary bilateral eye blinking activated the FEF but not the parietal or the supplementary eye fields [7]. In our patient, ictal eye closure mimicked blepharospasm rather than simple eye blinks. FEF stimulation produced a graded response, low-intensity 50-Hz stimulation produced bilateral eye closure and blinking, and progressively increasing intensity of stimulation produced contralateral and upward eye deviation. This suggests a possible somatotopic organization for eye blinking within the FEF. Eye blinking has been reported in occipital, occipito-temporal, mesial temporal, and insulo-opercular areas in a large cohort evaluated by stereo-EEG. It was also noted in patients with central and precentral epilepsy in this series. Rapid eye blinking was noted in insular opercular seizures. Associated nystagmus and tonic eye deviation localized the seizures to occipital lobe [8].
The impairment of visual perception in our patient is likely either due to FEF affection or propagation to the posterior visual network areas. FEFs are responsible for more complex visual functioning than simple eye movements, as conventionally considered [1]. Infrequent occurrence of this phenomenon during seizures is perhaps related to the extent of the lesion and seizure intensity. In this unique clinical situation, our patient had very focal bottom of sulcus dysplasia, allowing us to elucidate this phenomenon in relation to the FEF.
The FEF is often involved secondarily during seizure propagation. Very focal FEF seizures are rare. Our case demonstrates that FEF seizures may not be limited to saccadic eye movements but can present as more complex oculomotor and visual phenomena. ■

Disclosures.
None of the authors have any conflict of interest to disclose.

References

1. Vernet M, Quentin R, Chanes L, Mitsumasu A, Valero-Cabré A. Frontal eye field, where art thou? Anatomy, function, and non-invasive manipulation of frontal regions involved in eye movements and associated cognitive operations. *Front Integr Neurosci* 2014; 8: 66.

2. Bourdillon P, Guénot M, Beuriat PA, Ostrowsky-Coste K. The frontal eye field. *Neurology* 2018; 91: e398-9.

3. Rosano C, Krisky CM, Welling JS, Eddy WF, Luna B, Thulborn KR, *et al*. Pursuit and saccadic eye movement subregions in human frontal eye field: a high-resolution fMRI investigation. *Cereb Cortex* 2002; 12: 107-15.

4. Penfield W, Jasper H. *Epilepsy and the functional anatomy of human brain*. In: Functional localization in the cerebral cortex, ch. 3. Boston: Little, Brown, 1954. 41-155.

5. Godoy J, Lüders H, Dinner DS, Morris HH, Wyllie E. Versive eye movements elicited by cortical stimulation of the human brain. *Neurology* 1990; 40: Error: FPage (296) is higher than LPage (269)!.

6. van Koningsbruggen MG, Peelen MV, Davies E, Rafal RD. Neural control of voluntary eye closure: a case study and an fMRI investigation of blinking and winking. *Behav Neurol* 2012; 25: 103-9.

7. Lagarde S, Dirani M, Trebuchon A, Lepine A, Villeneuve N, Scavarda D, *et al*. Ictal blinking in focal seizures: Insights from SEEG recordings. *Seizure* 2020; 81: 21-8.

Legends for video sequences

Video sequence 1
Video-EEG recorded seizures during wakefulness as frequent eye blinks with retained consciousness. The patients describes her symptoms during the seizures as visual distortion.

Video sequence 2
During drowsiness and sleep, seizures as eye closure evolving to right head and eye versive seizures, lasting about 30 seconds, were captured. The EEG shows early left frontal evolving rhythm during these seizures.

Video sequence 3
Intraoperative functional stimulation shows eye closure, eye blinking at low-intensity 50-Hz stimulation and brief eye closure with saccadic eye deviation to the right and upwards during higher-intensity stimulation.

The patient could identify these stimulation responses as being similar to those associated with her habitual seizures.

Key words for video research on www.epilepticdisorders.com

Phenomenology: eye blinks and eye adversion
Localization: frontal eye field
Syndrome: focal non-idiopathic frontal (FLE)
Aetiology: focal cortical dysplasia

TEST YOURSELF

(1) The frontal eye field is located:
A. at the junction between the inferior frontal sulcus and precentral sulus
B. at the junction between the superior frontal sulcus and precentral sulcus
C. at the junction of the medial end of the precentral gyrus and the cingulate gyrus
D. at the junction of the inferior frontal gyrus and the lateral orbitofrontal gyrus

(2) Frontal eye field stimulation can result in all of the following except:
A. contralateral eye deviation
B. eye blinks
C. ipsilateral eye deviation
D. hands on eyes

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