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Epileptic ictal strabismus: a case report and review of the literature

Francesco Brigo [1,2], Franco Alessandrini [3], Giammario Ragnedda [2], Piera Canu [2], Veronica Tavernelli [2], Arianna Bratti [2], Raffaele Nardone [2,4]

[1] Department of Neurosciences, Biomedicine, and Movement Sciences, University of Verona
[2] Division of Neurology, Franz Tappeiner Hospital, Merano
[3] University Hospital Verona, Department of Neuroradiology, Verona, Italy
[4] Department of Neurology, Christian Doppler Medical Centre, Paracelsus Medical University, Salzburg, Austria

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ABSTRACT – Ictal strabismus, sometimes associated with epileptic nystagmus, is an extremely rare epileptic phenomenon, suggestive of cortical involvement in monocular eye movement control. We describe a patient with ictal disconjugate contraversive horizontal eye deviation of cortical origin as the main clinical feature of a focal seizure. A 17-year-old, previously healthy woman had a seizure characterized by initial rightward conjugate eye deviation, followed by convergent strabismus due to adduction of the right eye towards the nose without conjugate left eye abduction (esotropia), forced leftward head deviation with impaired awareness, and subsequent evolution into a bilateral tonic-clonic seizure. Postictal and interictal neurological status were unremarkable; more specifically, neuro-ophthalmological examination revealed no nystagmus or altered eye motility. Ictal EEG showed a rhythmic theta activity over the right posterior temporal region, involving fronto-central regions when strabismus appeared. MRI showed cortical dysplasia in the right temporal lobe. Due to the low spatial resolution of scalp EEG, we could not identify with precision the symptomatogenic zone underlying ictal strabismus. However, the concomitant appearance of rhythmic theta activity over the right fronto-central region and the leftward head version with MRI perfusion sequences, showing cerebral blood flow increase in the right frontal eye field area, suggest involvement of the right frontal lobe. [*Published with video sequence on www.epilepticdisorders.com*].

Key words: ictal strabismus, eye movement, seizure, MRI, EEG, frontal lobe

VIDEO ONLINE

Correspondence:
Francesco Brigo
Department of Neurosciences, Biomedicine, and Movement Sciences, University of Verona,
Piazzale L.A. Scuro,
10 - 37134 Verona, Italy
<dr.francescobrigo@gmail.com>

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Ictal strabismus, sometimes associated with epileptic nystagmus, is an extremely rare epileptic phenomenon, suggestive of cortical involvement in monocular eye movement control (Galimberti *et al*., 1998; Thurtell *et al*., 2009; Schulz *et al*., 2013). We describe a patient with ictal disconjugate contraversive horizontal eye deviation of cortical origin as the main clinical feature of a focal seizure. We also review the extant literature on this intriguing ictal phenomenon.

Case study

A 17-year-old, previously healthy, right-handed woman was referred to our centre for diagnostic evaluation. Four days earlier, at around 7.00 a.m., the sister, who was sleeping in a nearby room, had heard the patient crying and when entering the patient's room she had found her unable to react, with foaming of the mouth. The patient was brought to the emergency department, where brain MRI and routine blood examinations were performed yielding normal results. During video-EEG recording, performed during the following days, the patient had a seizure characterized by initial rightward conjugate deviation of the eyes, followed by convergent strabismus due to adduction of the right eye towards the nose without conjugate left eye abduction (esotropia) (*figure 1, video sequence*). When the strabismus appeared, the patient blinked. Tachycardia was also detected immediately after the blink. Strabismus was not accompanied by nystagmus. Afterwards, she did not react to external stimulation, had leftward deviation (version) of the head, and then a bilateral tonic-clonic seizure. Postictal and interictal status were unremarkable; more specifically, neuro-ophthalmological examination revealed neither nystagmus nor altered eye motility. After the seizure, she did not report having experienced any double vision or visual disturbance. Ictal EEG showed a

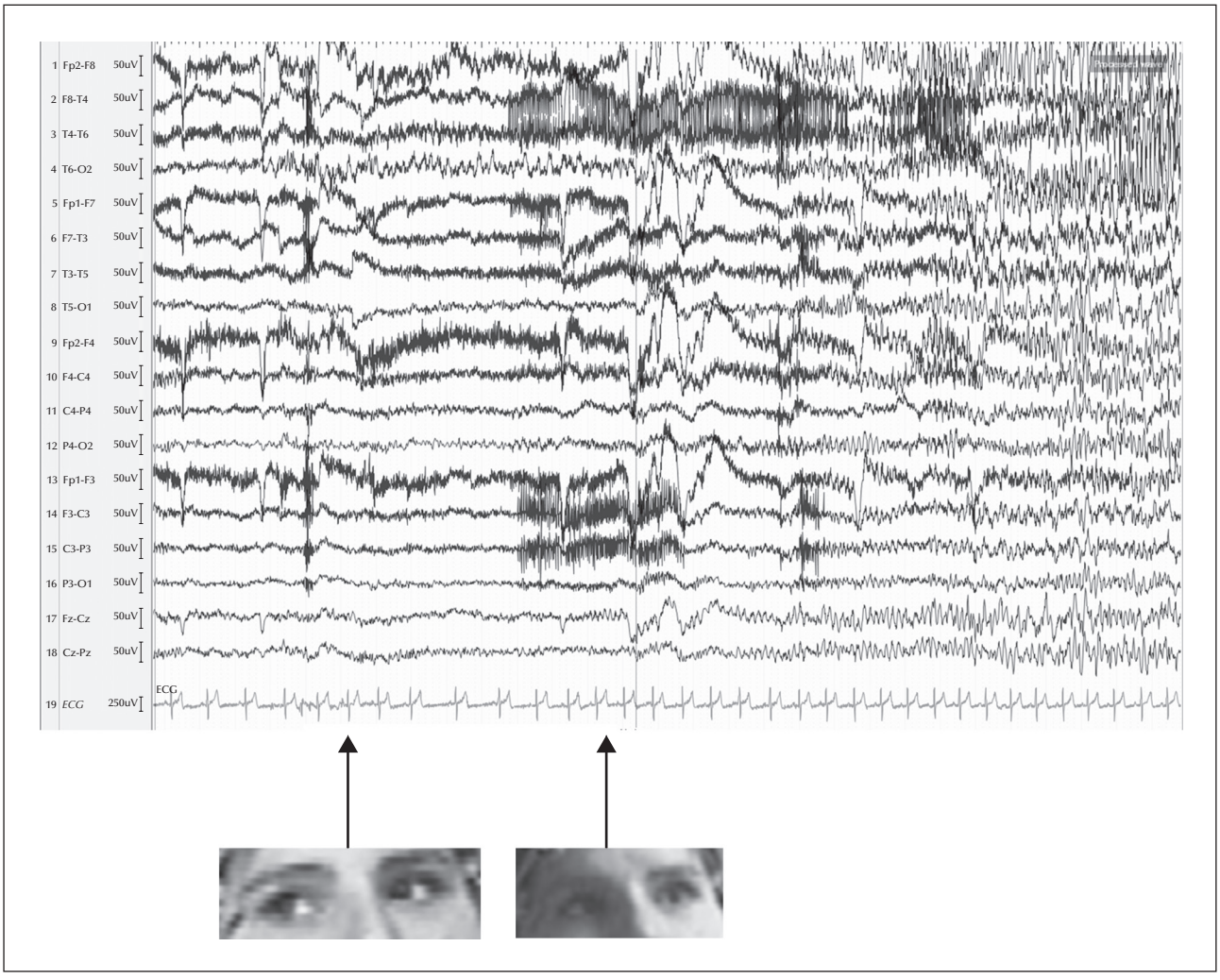

Figure 1. At seizure onset (left arrow), the patient has a rightward horizontal conjugate eye deviation; the EEG shows rhythmic theta activity over the right posterior temporal region and rhythmic epileptic activity from the right temporal to right fronto-central regions, concomitant with the appearance of convergent strabismus due to adduction of the right eye without conjugate left eye abduction (right arrow). The patient's blinking (see blink artefact over frontal regions indicated by the right arrow) could be a semiconscious reaction to the sudden onset of diplopia due to ictal strabismus (when questioned postictally, the patient did not recall any symptom of double vision occurring immediately before loss of consciousness). Ictal tachycardia starts just after the blink.
Sensitivity: 7 μV; LF: 0.53 Hz; HF: 70 Hz; speed: 30 sec/page.

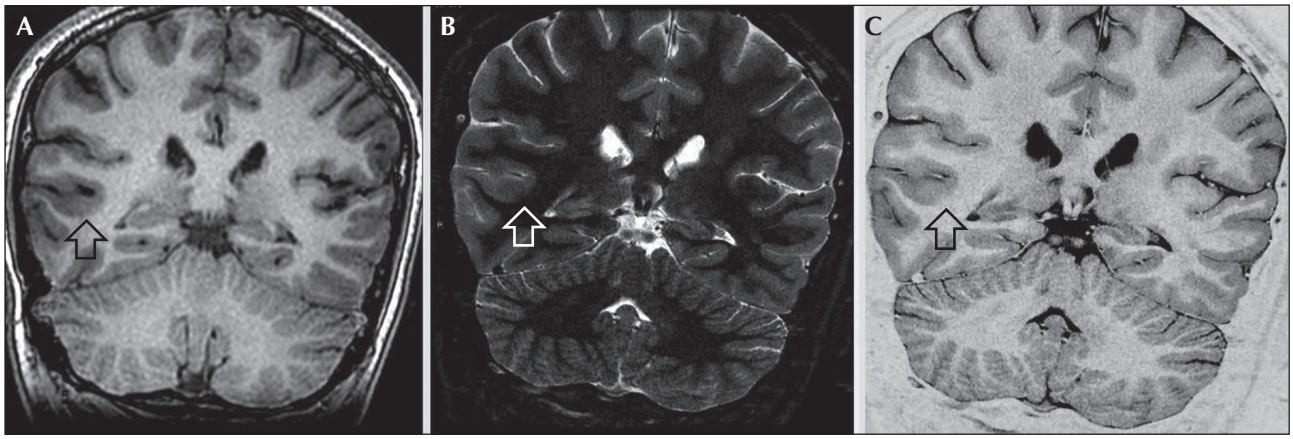

Figure 2. (A) Coronal T1-weighted peri-ictal MRI multiplanar (MPR) reconstruction, (B) coronal thin-slice inversion recovery (IR), and (C) coronal thin-slice FSE T2 image of the patient whose previous MRI had been considered normal. Note the focal area of slightly thickened cortex and blurred cortical-subcortical junction in the posterior section of the right temporal lobe; 1-mm thin sections are suggestive of cortical dysplasia.

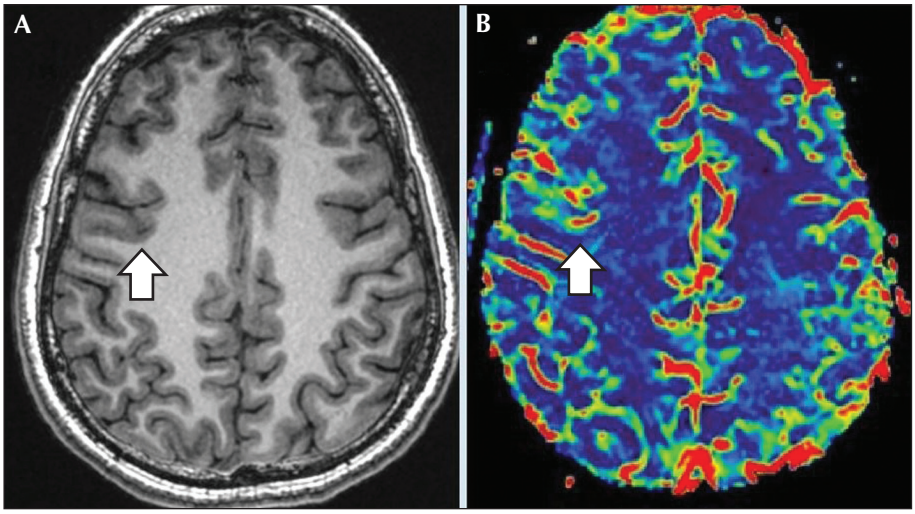

Figure 3. (A) Peri-ictal axial T1-weighted MRI multiplanar (MPR) reconstruction, and (B) axial DSC PWI image. Perfusion-weighted imaging clearly shows focal cortical-subcortical cerebral blood flow increase in the right frontal eye field area, correlating with the ictal epileptic activity.

rhythmic theta activity over the right posterior temporal region (related to rightward conjugate deviation of the eyes), spreading to ipsilateral fronto-central regions when strabismus appeared. Treatment with levetiracetam up to 1,000 mg/day was started. Two months after the seizure described above, the patient experienced a further epileptic seizure which was unwitnessed. The dosage of levetiracetam was therefore increased to 1,500 mg/day without further seizures (overall length of follow-up was 10 months). 3.0 Tesla MRI was performed peri-ictally, and images were acquired with a 3.0 Tesla MRI scanner (Signa Architect, GE Healthcare, Milwaukee, WI). The protocol included a 3D MPR T1-weighted sequence (BRAVO), a 3D FLAIR (CUBE) sequence, a thin-slice (3.5-mm) axial DWI sequence, a thin-slice axial (3-mm) FSE T2-weighted sequence, coronal T2 and inversion recovery (IR) thin-section (1-mm) images, as well as a dynamic susceptibility contrast (DSC) MR perfusion sequence and a 3D MPR T1-weighted sequence after contrast media administration. 3.0 Tesla MRI showed a focal area of slightly thickened cortex and blurred cortical-subcortical junction in the posterior section of the right temporal lobe, suggestive of cortical dysplasia (*figure 2*). Perfusion-weighted imaging showed focal cortical-subcortical cerebral blood flow increase in the right frontal eye field area, correlating with the ictal epileptic activity (*figure 3*).

Discussion

We describe a patient with ictal strabismus due to adduction of the right eye without conjugate left eye abduction (esotropia) as the main clinical feature of a focal seizure. Ictal strabismus is an epileptic phenomenon which has been very rarely reported in the medical literature.

Intermittent esotropia associated with attacks of dizziness has been interpreted as an equivalent of absences in a three-year girl, with an EEG showing generalized symmetric and synchronous 3/s spike-wave discharges; squinting resolved completely after therapy with ethosuximide (Gusek-Schneider *et al*., 2000). Other reports have described strabismus as a clinical expression of focal seizures.

Tischler and colleagues described a nine-year-old girl with strabismus due to in-turning of the right eye and jerk nystagmus on lateral gaze with preserved consciousness, associated with spike discharges in the left parietal-occipital region (Tischler *et al*., 1996). Authors attributed this clinical phenomenon to epileptic activation of a smooth pursuit pathway.

Galimberti and co-workers described a patient with epileptic skew deviation, diplopia, and oscillopsia associated with a right-beating nystagmus (Galimberti *et al*., 1998). The EEG recording showed epileptic activity over left parieto-occipital regions. The authors suggested that these ocular motor signs were "derived from an ictal activation of the vestibular cortex, which in turn activated descending projections to the vestibular nuclei, leading to both a dynamic (right-beating nystagmus) and a static (skew deviation) vestibular imbalance" (Galimberti *et al*., 1998).

Thurtell and colleagues described two epilepsy patients with ictal strabismus occurring during electrical stimulation of the frontal eye fields or during focal seizures spreading from the supero-posterior Sylvian bank to the ipsilateral frontal lobe (Thurtell *et al*., 2009). As in the patient we describe, the interictal neuro-ophthalmological findings were normal, and neuroimaging did not show any abnormality in the brainstem. Hence, the authors concluded that the cortical frontal eye field plays a role in both contralateral version and vergence eye movements. In this regards, Rasmussen and Penfield had already observed that stimulation of the precentral gyrus immediately anterior to the central sulcus (Area 8) resulted in contralateral eye deviation (Rasmussen and Penfield, 1948), although less often it could also result in convergence (Smith, 1944). Subsequently, Jampel (1960) reported that stimulation of the frontal lobe of the macaque brain could elicit vergence eye movements, and a further animal study has demonstrated that the frontal eye field is a cortical area involved in the generation of disconjugate eye movements (Ferraina *et al*., 2000).

Subsequently, Schulz and co-workers described a patient with ictal nystagmus affecting only one eye, associated with ictal diplopia; symptoms disappeared after resection of right frontal focal cortical dysplasia (Schulz *et al*., 2013). Whereas this finding could support the hypothesis of an exclusively cortical involvement in monocular eye movement control, as previously suggested (Thurtell *et al*., 2009), the presence of monocular nystagmus and spasm of the contralateral eye observed on interictal neuro-ophthalmological examination "argue for an irregular activation of both the cortical frontal eye field and the brainstem" (Schulz *et al*., 2013).

Our patient had an initial rightward conjugate eye deviation associated with a right posterior temporal discharge, followed by ictal disconjugate contraversive (leftward) horizontal eye deviation with convergent strabismus resulting from adduction of the right eye without conjugate left eye abduction. It was difficult to ascertain the presence of impaired awareness at the very onset of ictal strabismus in our patient. However, when the strabismus appeared, she blinked, as if she was initially aware of and disturbed by diplopia (but when questioned postictally, the patient did not recall any symptom of double vision occurring immediately before loss of consciousness). Immediately after the appearance of strabismus, she was not able to react to external stimuli. The ictal tachycardia, starting immediately after the blink, could simply be the consequence of emotional stress and heightened adrenergic drive, but may also represent a symptom of early involvement of the temporal and orbito-frontal cortex at seizure onset (Stefanidou *et al*., 2015).

No baseline alterations in eye motility or brainstem abnormality were found. It is therefore reasonable to conclude that in our patient, the ictal strabismus had an exclusive cortical origin.

The initial rightward conjugate eye deviation associated with right posterior temporal rhythmic theta activity (ipsiversive eye deviation) is likely to be the clinical manifestation of a seizure originating from the inferio-posterior temporal lobe (seizure onset zone) (Zhang *et al*., 2017). MRI confirmed the presence of an epileptogenic lesion (Lüders *et al*., 2006) in that region, showing cortical dysplasia in the posterior section of the right temporal lobe. Due to the low spatial resolution of scalp EEG, we could not identify with precision the symptomatogenic zone underlying ictal strabismus. Ictal activity was not recorded invasively, hence it is impossible to draw definitive conclusions regarding possible propagation of epileptic activity from the right inferio-posterior temporal to ipsilateral frontal lobe. It is possible that the epileptic activity remained initially confined to the right temporal lobe and cortical regions nearby. If so, cortical regions involved in controlling versive and vergence eye movements,

such as the parietal eye field and dorsolateral prefrontal cortex (Coubard and Kapoula, 2006), or the involvement of middle temporal and medial superior temporal areas, which control normal smooth pursuit movement (Tijssen *et al*., 1992), may have contributed to the ictal strabismus.

However, the patient eventually had a leftward head version, indicating epileptic activation of the frontal eye field (inferior/medial frontal gyrus) (Bonelli *et al*., 2007; Noachtar and Arnold, 2008). Hence, the ictal strabismus might have been the clinical expression of epileptic activity involving the right frontal eye field (symptomatogenic zone) (Thurtell *et al*., 2009; Schulz *et al*., 2013), as further supported by the concomitant appearance of rhythmic theta activity over the right fronto-central region and by the perfusion sequences showing focal cortical-subcortical cerebral blood flow increase in the right frontal eye field area, correlating with the ictal epileptic activity. □

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Legend for video sequence

00:09. The patient has a rightward horizontal conjugate eye deviation; the EEG shows rhythmic theta activity over the right posterior temporal region.
00:14. Appearance of convergent strabismus due to adduction of the right eye without conjugate left eye abduction; the EEG shows rhythmic epileptic activity over the right fronto-central regions.
00:15. The patient blinks (see blink artefact over frontal regions).
00:32. Leftward deviation (version) of the head and subsequent bilateral tonic-clonic seizure (not shown).
Sensitivity: 10 μV; LF: 0.53 Hz; HF: 70 Hz; speed: 20 sec/page.

Key words for video research on www.epilepticdisorders.com

Phenomenology: eye deviation
Localization: frontal eye field
Syndrome: focal non-idiopathic frontal (FLE)
Aetiology: dysplasia (architectural)

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TEST YOURSELF

(1) What does ictal strabismus suggest?
A. Subcortical involvement in monocular eye movement control
B. Cortical involvement in monocular eye movement control
C. Involvement of the cerebellum in monocular eye movement control

(2) Ictal strabismus:
A. always originates from parieto-occipital regions
B. is an exclusively subcortical phenomenon
C. is a heterogeneous epileptic phenomenon, which may arise from activity involving the frontal eye field or other cortical regions involved in controlling versive and vergence eye movements

(3) Ipsiversive conjugate eye deviation
A. has been reported in seizures originating from the inferio-posterior temporal lobe
B. is the consequence of epileptic activity involving the frontal eye field
C. is constantly associated with good response to antiepileptic drugs

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