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Case Report

Ictal unilateral eye blinking and contralateral blink inhibition – A video-EEG study and review of the literature [☆]



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ABSTRACT

Introduction: There is limited information on ictal unilateral eye blinking (UEB) as a lateralizing sign in focal seizures. We identified two patients with UEB and propose a novel mechanism of UEB based on a review of the literature.

Materials and methods: We report on two patients with intractable focal epilepsy showing UEB among 269 consecutive patients undergoing noninvasive video-EEG monitoring from October 2011 to May 2013.

Results: Unilateral eye blinking was observed in 0.7% (two of 269) of our patients. Patient one had four focal seizures. Semiological signs in all of her seizures were impaired consciousness, bilateral eye blinking (BEB), and UEB on the right. During one seizure, BEB recurred after UEB with a higher blink frequency on the right. Patient two had ten focal seizures. Among them were one electrographic seizure and nine focal seizures with BEB (in 3/10) and UEB on the left (in 1/10 seizures, respectively). Both patients did not display any clonic activity of the face. In seizures with UEB, ictal EEG onset was observed over the ipsilateral frontotemporal region in both of the patients (over F8 in 2/4, Fp2-F8 in 1/4, Sp2-T2 in 1/4, and F7 in 1/1 seizures, respectively). Ictal pattern during UEB showed bilateral ictal activity (in 4/4) and ictal discharges over the ipsilateral frontal region (maximum over F3 in 1/1 seizure). Interictal EEG showed sharp waves over the same regions.

Discussion: Unilateral eye blinking was ipsilateral to the frontotemporal ictal EEG pattern in both patients. The asymmetric blink frequency during BEB in patient one leads to the hypothesis that ictal UEB is caused by contralateral blink inhibition due to activation in frontotemporal cortical areas and mediated by trigeminal fibers.

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1. Introduction

The clinical semiology of focal epileptic seizures may help in localizing the seizure onset zone during presurgical evaluation and can provide valuable information on functional organization of the human brain. Unilateral eye blinking (UEB) can be observed in 0.8 to 1.5% of patients undergoing video-EEG monitoring [1,2] with a positive predictive value of 83% against EEG localization [1]. The mechanisms and pathways involved in UEB are not understood. Ipsilateral precentral, postcentral, temporal, and cerebellar regions as well as trigeminal fibers are regarded as key structures for UEB [1–8]. Because of the rare

occurrence of UEB, further information on its possible lateralizing value is needed. We report on two patients with UEB during focal seizures and review the literature on UEB and its functional anatomy.

2. Materials and methods

We report on two patients with drug-resistant focal epilepsies, who underwent prolonged (96 h) noninvasive video-EEG monitoring for presurgical evaluation at the Department of Neurology at Salzburg Paracelsus Medical University between October 2011 and May 2013. The patients gave written informed consent for the investigation and possible unmasked publication of its results. A detailed clinical history and analysis of interictal and ictal EEG as well as clinical seizure semiology were performed. Electrodes were placed according to the international 10–20 system with additional temporomesial electrodes (Sp2/Sp1, T2/T1). Antiepileptic medication was continuously reduced to half the dose of the preceding day and eventually stopped.

Unilateral eye blinking was defined as smooth blinking of one eye, without any clonic activity of the face or any mouth deviation as proposed previously [1].

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Fig. 1. Changes in ictal EEG pattern after switching from BEB to UEB on the right: First ictal EEG pattern shows rhythmic sharp waves over both frontotemporal areas. After switching from BEB to UEB on the right, EEG shows decrease of sharp waves over both frontal areas and over the left temporal region, whereas sharp waves are predominantly documented over the right temporal region (maxima Sp2-T2). A. Longitudinal bipolar montage. B. Cz reference montage.

3. Results

During the study period, a total of 269 patients with epilepsy underwent video-EEG monitoring. Unilateral eye blinking was observed in 2 of them (0.7%).

3.1. Case reports

3.1.1. Patient one

Patient one is a 38-year-old, right-handed woman with drug-resistant right-sided focal epilepsy. The patient was on carbamazepine 1200 mg/day and topiramate 175 mg/day at the time of investigation. Seizure history included focal seizures with retained consciousness, abdominal aura, and déjà vu, eventually preceding focal seizures with impairment of consciousness and evolving into bilateral, convulsive seizures. After gradual withdrawal of the antiepileptic medication, four seizures with UEB on the right were recorded. Semiological signs in all of the seizures were bilateral eye blinking (BEB) 29 seconds (s) after EEG onset in median (range: 18–37 s, median duration: 9 s, range: 6–11 s), followed by UEB on the right, starting 51 s after EEG onset in median (range: 30–71 s, median duration: 17 s, range: 10–34 s). Unilateral eye blinking did not evolve into any clonic activity of the face. During one seizure, BEB recurred asymmetrically with a higher blink frequency on the right after UEB on the right (which began 59 s after EEG onset, lasting 17 s) (see Video 1). Further lateralizing seizure phenomena were head-turning to the right (in 2/4 seizures), eye deviation to the left (in 3/4), postictal aphasia (in 2/4), postictal impaired figural memory (in 1/4), and postictal nose wiping (in 2/4). Ictal EEG showed the seizure onset over F8 (in 2/4 seizures), Fp2-F8 (in 1/4), or Sp2-T2 (in 1/4) after placement of additional temporomesial electrodes, which quickly spread to the contralateral hemisphere. During UEB, her EEG showed bilateral widespread ictal activity (in 4/4 seizures). During the focal seizure with a second period of (asymmetric) BEB, ictal EEG discharges decreased over both frontal areas and in the left temporal region (maximum ictal discharges over Sp2-T2) after the switch from BEB to UEB on the right (see Fig. 1). Interictal EEG showed sharp waves over F8, F8-T4, F8-Sp2, or T2 and frontal intermittent rhythmic delta activity (FIRDA) with a frequency of 2–3/s.

3.1.2. Patient two

Patient two is a 36-year-old, left-handed man with drug-resistant left-sided frontal lobe epilepsy (FLE) due to a perinatal ischemic stroke. Clinical feature is a mild spastic hemiparesis on the right. The patient was treated with lamotrigine (LTG) 600 mg/day, levetiracetam (LEV) 4000 mg/day, and lacosamide (LCM) 400 mg/day at the time of the investigation. He had a history of focal seizures with retained consciousness, vegetative symptoms, motor and sensory symptoms in the right arm, and nonconvulsive status epilepticus. Under gradual tapering of the antiepileptic drugs down to LTG 400 mg/day, LEV 3000 mg/day, and LCM 0 mg/day, the patient developed ten focal seizures. Among them were one electrographic seizure and nine focal seizures with vegetative symptoms (in 3/10 seizures), tonic limb posturing of the right arm (in 6/10), UEB on the left (in 1/10), and BEB (in 3/10). During one focal seizure with BEB, the patient showed impairment of consciousness. Unilateral eye blinking on the left was observed 28 s after EEG onset over the left anterior temporal area (F7), with a duration of 15 s. Bilateral eye blinking was observed 7 s after EEG onset in median (range: 0–9 s, median duration: 6 s, range: 5–30 s). Ictal EEG showed the seizure onset over F7 (in 5/10 seizures), Fp1 (in 2/10), Sp1 (in 1/10), or absence of ictal EEG pattern (in 2/10), which rapidly spread to the ipsilateral hemisphere. Ictal EEG pattern during UEB was ipsilateral (maximum over F3) in this patient. Interictal EEG showed sharp waves over F7, F7-T3, or Sp1-T1 and focal slowing over the left frontotemporal region.

4. Discussion

4.1. Review of the literature of ictal UEB

The prevalence of UEB in our population (0.7%) was similar to that of earlier studies (0.8% by Henkel [2] and 1.5% by Benbadis [1]). Unilateral eye blinking is most often associated with fronto- and/or temporal seizure onset on the left side [1,5,8] and was caused by cortical or direct trigeminal stimulation [3,5,9] during spontaneous seizures [1,2,4,7,8]. In both of our patients, UEB was ipsilateral to the seizure onset zone documented by EEG. This is consistent with previous literature on UEB where a positive predictive value of 83% against EEG localization was reported [1] (see Table 1).

The first descriptions of UEB date back to 1874 when Bartholow [3] stimulated the “posterior lobe” in a woman who then showed movements in the contralateral limbs with pain in the contralateral hemibody, as well as ipsilateral UEB with retained consciousness. In 1954, Penfield [10] reported that the motor control of the upper part of the facial motor function depends on both the contralateral and ipsilateral motor cortices, mainly originating from the lower precentral gyri.

Both early reports suggest that the ipsilateral precentral cortex may mediate UEB. This hypothesis was supported by studies reporting UEB in temporal lobe epilepsy (TLE) and FLE [1,2,4,7] as well as UEB in association with a frontotemporal EEG pattern [8].

Only one study group [2] reported UEB followed by ipsilateral clonic activity of the face or mouth deviation. Mesiwala and colleagues [6] reported on one case of ipsilateral UEB in association with a cerebellar ganglioglioma in an infant. Lesions of the cerebellum may abolish the conditioned Pavlovian eye blink response of the ipsilateral eye not affecting the corneal reflex [11–13]. Thus, it is plausible that this mechanism plays a role in UEB associated with infratentorial lesions.

4.2. Trigeminal stimulation and blinking

Unilateral eye blinking during cortical stimulation may, however, be evoked by yet another mechanism: In 1873, Ferrier [14] was the first to recognize the potential current-conducting ability of dura mater while experimenting on cats. He described motor movements evoked by currents conducted by dura mater. In 1957, Livingston and Phillips [15] applied electrical impulses to the dura mater lateral to the frontal sinus in cats, which resulted in ipsilateral eyelid and whisker movements.

Three decades later, Lesser [5] was the first to hypothesize that trigeminal fibers in the meninges via the corneal reflex pathway may convey UEB in humans, as this was occasionally observed after electrical stimulation of temporobasal and precentral subdural electrodes. This hypothesis was supported by the findings of Sindou [9] who reported that direct intracranial stimulation of the trigeminal nerve occasionally caused ipsilateral blinking response in humans.

When Bartholow [3] produced ipsilateral UEB in his investigation in 1874, he placed the second electrode on the dura mater, which was the most likely explanation for UEB in his report. Furthermore, trigeminal pathways can convey epileptic activity, which was registered by foramen ovale electrodes during ictal UEB in patients with TLE [4]. This strongly suggests the involvement of trigeminal fibers in the generation of UEB.

4.3. Functional anatomy of blinking and blink reflexes

The corneal reflex is conducted via trigeminal fibers to the pons, and corneal pain is further cortically represented in the contralateral superior-inferior extent of the postcentral gyrus [16]. However, it seems unlikely that UEB could be mediated through this pathway as corneal stimulation exclusively elicits a late bilateral blinking response (R2) [17]. Furthermore, UEB was never described in pontine lesions,

Table 1
Unilateral eye blinking and its lateralizing value in focal epilepsy.

Authors	Number		f (%)	EEG localization					Hemisphere			Lateralization		Seizure type	
	Pts.	UEB		F	T	P	C	nr	R	L	nr	Ipsi	Contra	CFS	SFS
Bartholow R (1874) [3]		1				1			1	1		1			1
Wada JA (1980) [4]		5			5							5			5
Lesser RP et al. (1985) [5]				•	•						•	•			
Benbadis SR et al. (1996) [1]	914	14	1.5	5	6			1	3	9	2	10	2	10	4
Henkel A et al. (1999) [2]	239	2	0.8		2				2			2		1	1
Mesiwala AH et al. (2002) [6]		1					1			1		1			
Bonelli SB et al. (2007) [7]	31	1	3.2*	1									1	1	
Pestana EM et al. (2007) [8]		1		1					1			1		1	
Kalss G et al. (2013)	269	2	0.7	2					1	1		2		1	1

Abbreviations and explanations: Numbers indicate the number of patients in whom the described attribute was documented in each study. Only column “f (%)” counts the percentage of patients with UEB in the epilepsy monitoring unit, “*” indicates that the number of patients in whom the pattern was described was not documented, “number of UEB” indicates the number of patients with UEB, “number of pts.” indicates the number of patients in the epilepsy monitoring unit, “*” indicates the UEB percentage in patients with FLE, “F” means frontal lobe, “T” means temporal lobe, the numbers between “F” and “T” indicate the frontotemporal EEG pattern, “P” means parietal lobe, “C” means cerebellum, “nr” means not rated, “R” means right, “L” means left, “Ipsi” indicates UEB ipsilateral to the epileptogenic zone, “Contra” indicates UEB contralateral to the epileptogenic zone, “CFS” indicates focal seizure with impairment of consciousness, and “SFS” indicates focal seizure with retained consciousness.

and an impact on corneal reflex latency occurs only in postcentral lesions [18]. The blink reflex circuit via trigeminal roots to the pons may also be involved as it elicits an early short ipsilateral (R1) and an R2 response [17]. Distant from the pontomedullary level of the reflex, lesions in postcentral regions or large unilateral vascular hemispheric lesions may alter R2 [19,20]. However, this hypothesis also appears unlikely as ictal UEB is neither localizing to the pons nor predominantly localizing postcentrally.

Alternatively, the trigeminal roots, which are involved in several physiological blink conditions, may be altered during focal seizure activity. Spontaneous blinking is mediated via trigeminal afferents in order to maintain a corneal tear film [21]. Parahippocampal regions, the visual cortex, the inferior frontal gyrus (Broca's area), and the frontal eye field are active during blink inhibition and voluntary and spontaneous blinking [22–25]. The fusiform, superior temporal, and cingulate gyri are active exclusively during blink inhibition [23–25] (see Table 2). Blinking was assessed as active blinking with a high frequency while looking at the word “blink”, whereas blink inhibition was trying not to perform spontaneous blinks while looking at the word “open”. In this fMRI paradigm, additional activation of Broca's area was most likely caused by the test procedure itself [23–25]. We assume that afferent trigeminal impulses mediating blink inhibition are most likely similar to those mediating spontaneous blinking.

4.4. Conclusion

We hypothesize that the eye that is not blinking (contralateral to the seizure activity) is the pathologically inhibited one during ictal UEB. We

Table 2
Eye blinking and its neuroanatomical correlation based on fMRI studies.

Location	Blink inhibition	Voluntary blinking	Spontaneous blinking
Superior frontal gyrus	[24]	[22,24]	
Medial frontal gyrus	[24]	[22]	[25]
Inferior frontal gyrus	[23]	[23]	
Precentral gyrus	[24,25]	[22,24]	
Cingulate gyrus	[24]		
Superior temporal gyrus	[24]		
Fusiform gyrus	[24]		
Parahippocampal gyrus	[25]	[24]	[25]
Precuneus	[24]	[22]	
Inferior occipital gyrus	[25]		[25]
Medial occipital gyrus	[23]		[25]
Superior occipital gyrus		[22,23]	

Brain regions activated during spontaneous blinking, voluntary blinking, or blink inhibition shown by fMRI.

postulate that ictal ipsilateral UEB is a result of cortical blink inhibition of the contralateral eye due to seizure activity in the frontotemporal region.

The most important limiting factor is the low number of cases reporting UEB. Second, the absence of studies using intracranial electrodes to localize the eloquent anatomical area for UEB is a further limitation.

However, this is the first study to hypothesize contralateral blink inhibition to be the functional anatomic correlate of ictal UEB. As a future approach to clarify the hypothesis, it is necessary to perform invasive video-EEG monitoring with intracranial electrodes in patients showing ictal UEB.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.ebcr.2013.10.001>.

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