Epilepsy & Behavior xxx (2011) xxx–xxx

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Benign temporo-parieto-occipital junction epilepsy with vestibular disturbance: An underrecognized form of epilepsy?

Russell Hewett [a,b], Maxime Guye [a], Martine Gavaret [a], Fabrice Bartolomei [a,b,*]

[a] CHU Timone, Service de Neurophysiologie Clinique, Assistance Publique des Hôpitaux de Marseille, Marseille, France
[b] Hôpital Henri Gastaut/CINAPSE, Marseille, France

ARTICLE INFO

Article history:
Received 14 February 2011
Revised 13 May 2011
Accepted 14 May 2011
Available online xxxx

Keywords:
Parietal lobe
Epilepsy
Vertigo
Dizziness
Vestibular syndrome
Syncope

ABSTRACT

We describe a series of adolescents and adults who share the electroclinical characteristics of a nonlesional, pharmacoresponsive epilepsy manifesting as prominent vestibular disturbances, suggesting a temporo-parieto-occipital (TPO) junction origin. We retrospectively reviewed a database of consecutive patients referred to the epilepsy clinic over a 10-year period with respect to the following criteria: recurrent episodes of paroxysmal vestibular symptoms, normal MRI, and interictal EEG changes over the posterior regions. Fourteen patients were finally selected (10 males, 4 females). Mean age at onset was 26.5 (range: 12–59). The diagnosis of epilepsy was usually delayed until after cardiology and/or otorhinolaryngology workup. The predominant features on interictal scalp EEGs were abnormalities over the posterior areas. All patients responded well to antiepileptic medication. We propose that although further characterization is needed to label it a syndrome, this underdiagnosed form of epilepsy merits recognition.

1. Introduction

Epileptic seizures manifesting as prominent "vestibular" symptoms have been described in the past and attributed mainly to epileptic foci or lesions surrounding the superior temporal gyrus and the temporo-parietal cortex [1–4]. Other epileptic foci have been reported more recently, in particular in frontal lobe seizures [5,6]. This probably reflects the large number of regions of human cortex that have been shown to receive vestibular information, including the temporo-parietal junction, the somatosensory cortex, the posterior parietal cortex, the insula, and the lateral and medial frontal cortices [reviewed in 7].

Despite a large literature dedicated to "epileptic vertigo," a diverse set of etiologies are currently held to account for vestibular disturbances (peripheral vestibular lesions, brainstem lesions, migraine), and an epileptic origin is believed to be rare [8,9]. In the past some attempt has been made to individualize patients with vestibular disturbances as the main clinical picture of their epilepsy [1,4,10,11]. However, these epilepsies are generally not recognized as clinical syndromes in adults, but are regarded as a heterogeneous group of partial seizures [12].

In this study we describe a series of adolescents and adults who share the electroclinical characteristics of a nonlesional, pharmacoresponsive epilepsy manifesting as prominent vestibular disturbances. The diagnosis of epilepsy was usually delayed until after cardiology and/or otorhinolaryngology workup. We propose that although further characterization is required to label this a syndrome, it is an underdiagnosed form of epilepsy that merits recognition.

2. Methods

We retrospectively reviewed a database of consecutive patients (~1000) referred to the epilepsy clinic over a 10-year period with respect to the following criteria: (1) recurrent episodes of paroxysmal vestibular symptoms, including true vertigo and loss of balance; (2) normal MRI scan; (3) interictal EEG changes over the parietal or temporo-parieto-occipital (TPO) regions.

Extensive clinical examinations (patient history and neurological examination) were carried out in all cases. MRI brain scans were obtained in all cases following a previously described protocol [13]. EEG evaluation consisted of at least one standard 21-channel awake EEG recording and, in many cases, included further EEG evaluation such as sleep EEG monitoring. All files contained complete information on medical treatment.

3. Results

Clinical information is summarized in Table 1. Fourteen patients were finally selected (10 males, 4 females). Mean age at onset was 26.5 (range: 12–59) and average age at diagnosis was 30.5 (range: 14–59). Four patients had a family history of epilepsy, though none with a first-degree relative. No other risk factors for epilepsy

* Corresponding author at: Service de Neurophysiologie Clinique, CHU Timone-264 Rue st Pierre. F-13005-Marseille, France. Fax: +33 491385826.
E-mail address: fabrice.bartolomei@ap-hm.fr (F. Bartolomei).

1525-5050/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.yebeh.2011.05.017

Table 1
Clinical and EEG data of patients.

Patient			Age		Family history	Semiology (subjective and objective)		
No.	Hand.[a]	Sex	Onset	Diagnosis		Vestibular	Visual	Other
1	L	M	43	44	No	Rotational vertigo	Object transposition	Nausea, malaise, fatigue
2	R	M	15	26	Cousin with epilepsy	Disequilibrium	No	No
3	R	M	20	22	No	Rotational vertigo	Flashing lights	Nausea, limb paresthesia, bursts of body heat, headaches
4	R	F	31	32	Sister with narcolepsy	Disequilibrium	Color images	Premonition, body tingling, anxiety, heat in chest
5	R	M	29	33	No	Rotational vertigo	No	Whistling and flowing sound L ear?, nausea
6	L	M	17	24	No	Rotational vertigo	No	Body paresthesia
7	R	M	42	48	No	Rotational vertigo	No	Sensation of levitation, derealization
8	R	M	59	59	No	Rotational vertigo	No	Ascending heat
9	R	M	10	14	No	Rotational vertigo	Visual changes	Nausea and headache
10	R	F	25	29	Aunt with psychosis/ epilepsy	Rotational vertigo	No	No
11	R	M	18	19	Cousin IGE, 2nd degree cousin (?)	Disequilibrium	Blue colors, autoscopy	Palpitations, thoracic heaviness, throat, facial paresthesia
12	R	F	12	17	Uncle with adolescent epilepsy	Disequilibrium	Micro/macropsia, occipital complex illusions	Malaise
13	R	M	17	21	No	Disequilibrium	No	Malaise, heat
14	R	F	34	39	No	Rotational vertigo	No	Heat, malaise, nausea

S, spike; SW, sharp wave; SAW, spike and wave.
[a] Hand., handedness (R = right, L = left); LOC, loss of consciousness; GTCS, generalized tonic–clonic seizure; IGE, idiopathic generalized epilepsy; ORL, otorhinolaryngology; CBZ, carbamazepine; PGB, pregabalin; LTG, lamotrigine; OXC: Oxcarbamazepine; LEV: Levetiracetam; VPA: Sodium Valproate.

were reported. All patients had normal intellectual development and normal neurological examinations.

Three patients had been initially reviewed by otorhinolaryngology, and 9 patients had a cardiology workup, which consisted of more detailed investigation than electrocardiography, such as Holter monitoring or echocardiography. Treatment was initiated in 2 patients following a single short burst of atrial fibrillation. One patient had a positive tilt-table test. The initial diagnosis in 3 patients was vagal syncope.

The predominant features on interictal scalp EEGs were abnormalities over the parietal or TPO areas (Figs. 1 and 2, Table 1). Six patients had spikes or sharp wave changes in the parietal or centro-

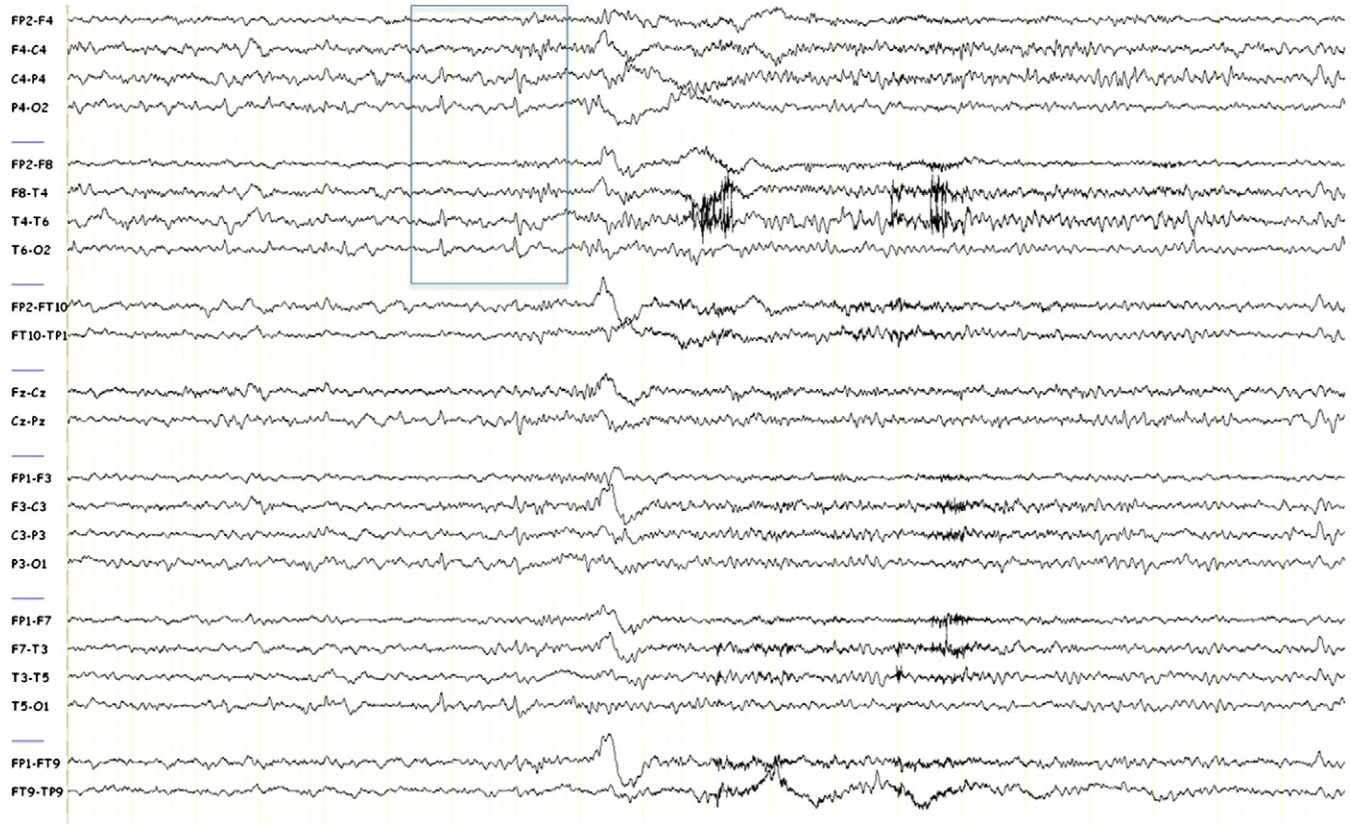

Fig. 1. Interictal EEG recorded during drowsiness showing interictal biphasic spikes over the right TPO junction.

Please cite this article as: Hewett R, et al, Benign temporo-parieto-occipital junction epilepsy with vestibular disturbance: An underrecognized form of epilepsy? Epilepsy Behav (2011), doi:10.1016/j.yebeh.2011.05.017

Objective				Seizure frequency	Previous workup	EEG	Treatment
Fall	LOC	GTCS	Other				
No	No	No	Vomiting, pallor	Every 2–12 wk	Cardiac, ORL	Right SW and S (T6, P4, 02)	CBZ
Yes	Yes	No	No	Every 2 mo	No	Right S (P4, T4)	PGB
No	No	No	Pallor, vomiting, trembling	1/y	Cardiac	Left SW (C3, P3)	Nil
Yes	Yes	No	Vomiting	2/y	Cardiac	Right S (T6, P4, O2).	CBZ, now LMT
No	No	No	No	3/y	ORL, cardiac	3 seizures in right (C4,P4,T4,T6); asystole for 10–15 s	OXC + LEV
Yes	Yes	Yes	No	1/mo	Cardiac	Right SW (T6, P4, 02)	VLP + LMT
No	No	No	Ataxia	2/y	ORL, Cardiac	Bilateral SW (T6, P4, O2, T5, P3)	CBZ
Yes	Yes	No	Vomiting	Once	Cardiac	Right and left SW (P4, P3)	LEV
Yes	Freq.	No	No	4 or 5/mo	No	Left SAW (T5, P3, 01)	VLP + CBZ
Yes	Yes	Yes	Fixed stare, vocalization, incontinence	3 in 5 y	No	Right SW and rhythmic theta (P4)	Nil
Once	Once	No	Vomiting	2/mo	No	Right S (P4)	LEV
Yes	Yes	Only first	Hyper-ventilation	Every 2 mo	No	Right S (C4, P4)	LMT + VLP
Yes	3/ 4	3/4	No	4 in 4 y	Cardiac	Right S (P4)	CBZ
Occ	Occ	No	No	1/wk	Cardiac	Right S (P4, T6, 02)	CBZ

parietal region (maximal over C3P3 or/and C4P4). Eight patients had spikes or sharp waves at the TPO junction. EEG anomalies were prominent on the right side in 11 patients and on the left side in 2. Bilateral anomalies were observed in 1 patient. Seizure activity was localized over the right TPO junction in 1 patient; this patient also experienced associated asystole for some seconds during the seizure.

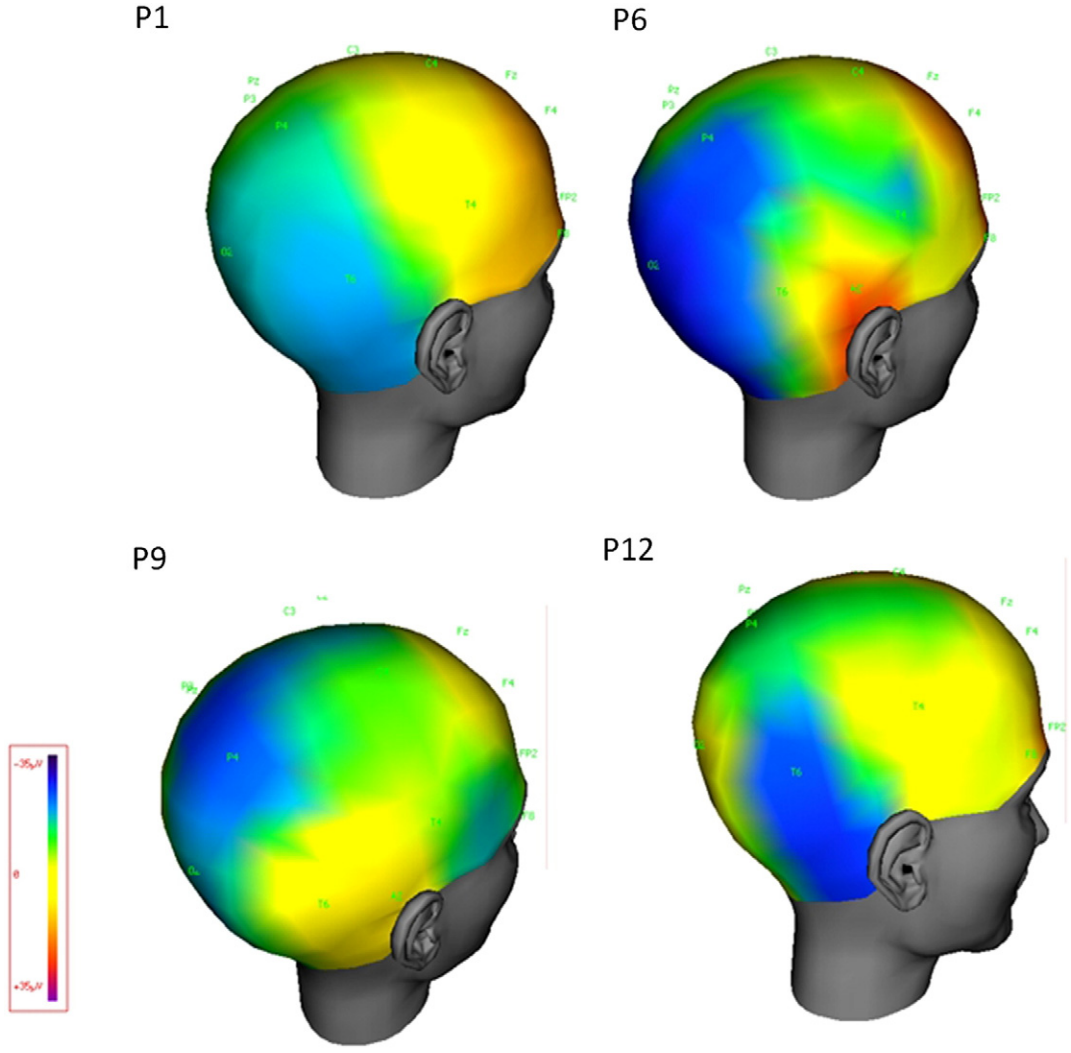

Fig. 2. Amplitude cartography using Coherence (Detltamed-Natus) software. Average reference. One representative single interictal spike is shown. Note the negative distribution (in blue) over the TPO region, maximal in T6, P4, and O2 in the four patients. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Please cite this article as: Hewett R, et al, Benign temporo-parieto-occipital junction epilepsy with vestibular disturbance: An underrecognized form of epilepsy? Epilepsy Behav (2011), doi:10.1016/j.yebeh.2011.05.017

All except two abnormalities that appeared to be activated by sleep were observed during awake EEGs.

Two patients refused treatment; seizures in 8 patients are currently controlled on monotherapy and in 4 patients on dual therapy. Follow-up has ranged from 1 to 11 years (mean follow-up = 3.9 years); all patients remain seizure free including the 6 patients followed up for more than 3 years.

4. Discussion

This study was aimed at describing a group of patients with a form of nonlesional partial epilepsy with the following characteristics: age at onset during adolescence or adulthood; predominant symptom of vestibular disturbance; normal MRI scan and neurological examination; interictal spikes over the parietal and TPO regions; and a generally good response to medical therapy. We believe that the electroclinical characteristics describe an underdiagnosed form of late-onset focal epilepsy that merits recognition and further study.

Apart from the benign childhood epilepsies, nonlesional epilepsies involving the parietal lobe or TPO junction have come under the umbrella of poorly described and differentiated epilepsies that have been occasionally characterized by simple localization of interictal spikes, such as "cryptogenic parietal lobe epilepsy" [14]. However, the characteristics of our patients are comparable to those of a form of epilepsy reported in the past as "vestibular epilepsy" [1] or "epileptic dizziness" [11]. Patients experience sudden disequilibrium with pronounced rotational or linear vertigo. Kogeorgos et al. [11] reported 30 patients exhibiting a form of epilepsy very similar to that described in the present series. All patients were reported to have seizures in which the prominent symptom was a "vestibular" sensation consisting mainly of a feeling of rotation and/or disequilibrium. EEG features were not detailed, but these patients had normal neuroimaging (CT scan) and most responded well to antiepileptic drugs. Similarly, the main subjective aura in our patients was vestibular disturbance in the form of vertigo or disequilibrium. Although recognized as an ictal epileptic phenomenon, these symptoms are considered to be relatively rare [9] by modern physicians.

This series of patients reflects the recent trend toward alternative etiologies for vestibular disturbances and the subjective overlap with vagal presyncopal symptoms. Although 11 of the 14 patients

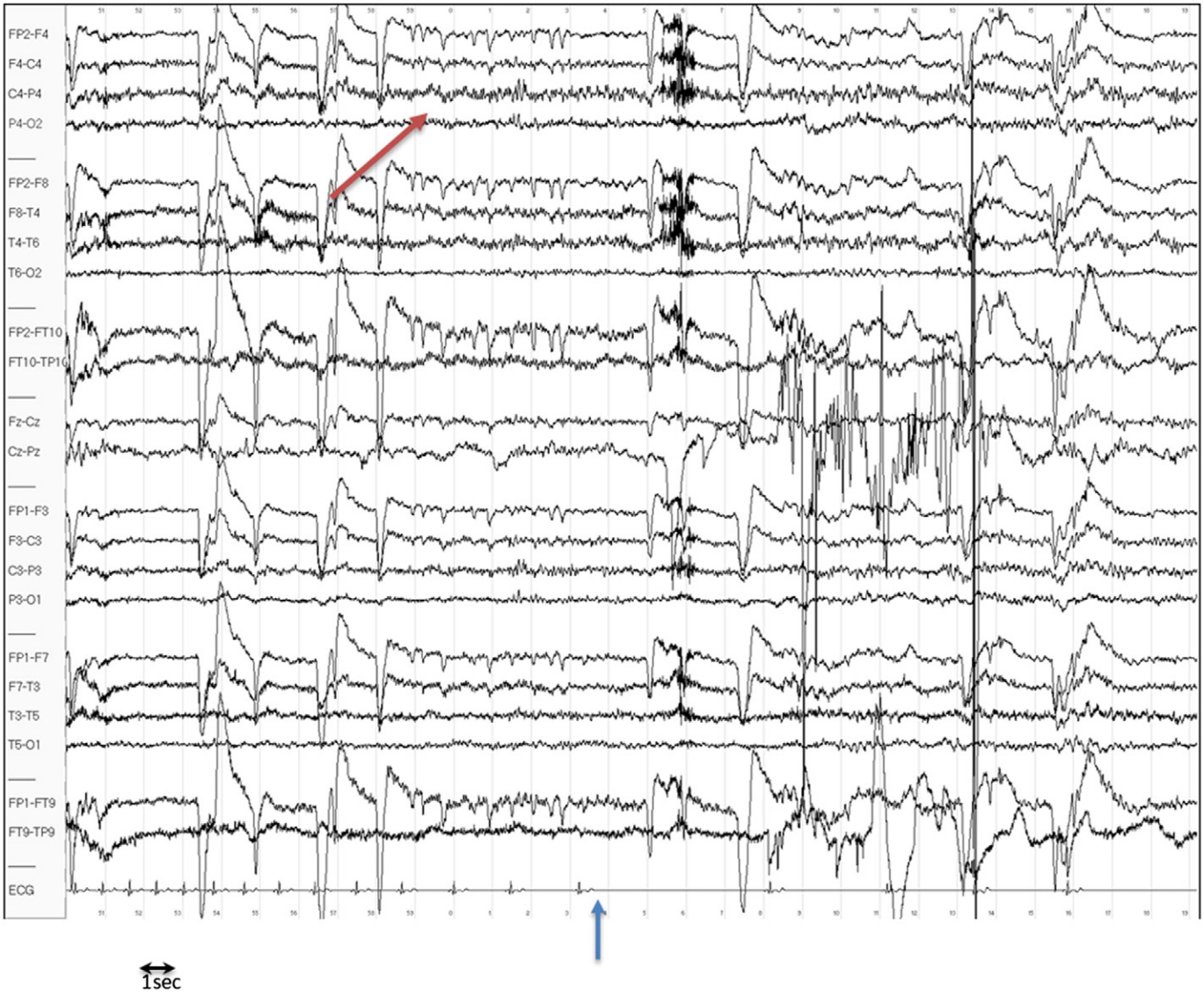

Fig. 3. Ictal recording during video/EEG monitoring (patient 4). Changes in EEG activity were prominent in the right TPO junction (red arrow) in the form of rhythmic activity. The ECG revealed transient asystolia (blue arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Please cite this article as: Hewett R, et al, Benign temporo-parieto-occipital junction epilepsy with vestibular disturbance: An underrecognized form of epilepsy? Epilepsy Behav (2011), doi:10.1016/j.yebeh.2011.05.017

had other features of seizure activity (visual and autonomic symptoms, as well as secondary generalization), 9 were initially seen by otorhinolaryngologist or cardiologist before review by a neurologist. The symptoms were eventually considered to be seizures based on a combination of clinical presentation, EEG abnormalities, and response to treatment.

Nevertheless, this does not exclude concurrent cardiovascular disease. Indeed, two patients were noted to have had one short episode of atrial fibrillation. Patients 8 and 11 were immediately started on flecainide and sotolol, respectively, but the episodes of vestibular disturbance improved with AED administration. One patient had a positive tilt-table test, accounting for episodes of loss of consciousness. However, the patient was also considered to have seizures, accounting for her more vertiginous events demonstrating the overlap and the difficulty in establishing the etiology of vestibular disturbances. In addition, the only patient with an ictal EEG, with a normal echocardiogram and Holter recording, demonstrated ictal asystole for several seconds with associated loss of consciousness and no generalization (Fig. 3). Her seizure semiology consisted of colorful images, body tingling, anxiety, and heat in the chest, which were symptoms shared by some of the other patients with loss of consciousness (see Table 1).

This case series also demonstrates that interictal EEG abnormalities are observed predominantly over the parietal or TPO electrodes. The exact anatomical localization of the epileptogenic zone is not possible in these cases, but both semiology and electrophysiological data point toward localization in the temporo-parietal junction, suggesting involvement of the posterior representation of the vestibular cortices. A large body of experience indicates that the human vestibular cortex is localized in different areas of the perisylvian region (posterior insula, retroinsular cortex, parietal operculum, temporal bank of the Sylvian fissure) and in the parietal cortex (inferior parietal lobule, intraparietal sulcus) [7,15–17]. This is in agreement with the vestibular manifestations reported in 11% of patients in a large surgical series of parietal lobe epilepsy [18] and, more recently, in 23% of patients with drug-resistant parietal epilepsy examined with depth electrodes [19]. In addition we observed that a majority of patients (11/14) had right-sided epileptic abnormalities. A predominance of the right hemisphere in vestibular processing has been demonstrated in both healthy subjects and patients [20].

Other manifestations in this series of patients included visual changes, paresthesias, and changes in body perception (autoscopy). This is in keeping with theories suggesting an overlap of mechanisms underlying body representation and vestibular function [21,22]. In the present series, no clear etiological factor was found; in particular, there is no obvious genetic link. Four patients had some form of family history, though none with a first-degree relative. The normal imaging excludes any macroscopic structural lesion. Whether the possible association with cardiac involvement and vagal hyperactivity is due to a common genetic predisposition for both conditions (for instance, via ion channel alterations) is still speculative.

Finally, an important characteristic feature of these patients has been their pharmacoresponsiveness. The apparent good outcome of this epilepsy could prompt its characterization as a “benign” form of epilepsy. Benign partial epilepsies of adolescence have been described [23], though are not recognized in current ILAE syndrome classifications [14].

In conclusion, we have described a pharmacoresponsive nonlesional epilepsy presenting with vestibular disturbances that could be more than just one of a heterogeneous group of cryptogenic partial epilepsies. A prospective study of all patients who present to epilepsy clinics complaining of vestibular disturbances will help to better delineate this epilepsy and define its incidence.

References

[1] Brandt T. Vestibular epilepsy. Vertigo: its multisensory syndromes. London: Spinger-Verlag; 1999. p. 233–9.
[2] Brandt T, Daroff RB. The multisensory physiological and pathological vertigo syndromes. Ann Neurol 1980;7:195–203.
[3] Penfield W, Kristiansen K. Epileptic seizure patterns. Springfield, IL: Charles C Thomas; 1951.
[4] Smith BH. Vestibular disturbances in epilepsy. Neurology 1960;10:465–9.
[5] Kluge M, Beyenburg S, Fernandez G, Elger CE. Epileptic vertigo: evidence for vestibular representation in human frontal cortex. Neurology 2000;55:1906–8.
[6] Lopez C, Heydrich L, Seeck M, Blanke O. Abnormal self-location and vestibular vertigo in a patient with right frontal lobe epilepsy. Epilepsy Behav 2010;17:289–92.
[7] Lopez C, Blanke O. The thalamocortical vestibular system in animals and humans. Brain Res Rev 2011;67:119–46.
[8] Bladin PF. History of "epileptic vertigo": its medical, social, and forensic problems. Epilepsia 1998;39:442–7.
[9] Crompton DE, Berkovic SF. The borderland of epilepsy: clinical and molecular features of phenomena that mimic epileptic seizures. Lancet Neurol 2009;8:370–81.
[10] Hughes JR, Drachman DA. Dizziness, epilepsy and the EEG. Dis Nerv Syst 1977;38:431–5.
[11] Kogeorgos J, Scott DF, Swash M. Epileptic dizziness. Br Med J (Clin Res Ed) 1981;282:687–9.
[12] Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. Epilepsia 1989;30:389–99.
[13] Bartolomei F, Khalil M, Wendling F, et al. Entorhinal cortex involvement in human mesial temporal lobe epilepsy: an electrophysiologic and volumetric study. Epilepsia 2005;46:677–87.
[14] Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia 2010;51:676–85.
[15] Brandt T, Botzel K, Yousry T, Dieterich M, Schulze S. Rotational vertigo in embolic stroke of the vestibular and auditory cortices. Neurology 1995;45:42–4.
[16] Dieterich M. Functional brain imaging: a window into the visuo-vestibular systems. Curr Opin Neurol 2007;20:12–8.
[17] Kahane P, Hoffmann D, Minotti L, Berthoz A. Reappraisal of the human vestibular cortex by cortical electrical stimulation study. Ann Neurol 2003;54:615–24.
[18] Salanova V, Andermann F, Rasmussen T, Olivier A, Quesney LF. Parietal lobe epilepsy: clinical manifestations and outcome in 82 patients treated surgically between 1929 and 1988. Brain 1995;118(Pt 3):607–27.
[19] Bartolomei F, Gavaret M, Hewett R, et al. Neural networks underlying parietal lobe seizures: a quantified study from intracerebral recordings. Epilepsy Res 2011;93:164–76.
[20] Dieterich M, Bense S, Lutz S, et al. Dominance for vestibular cortical function in the non-dominant hemisphere. Cereb Cortex 2003;13:994–1007.
[21] Devinsky O, Feldmann E, Burrowes K, Bromfield E. Autoscopic phenomena with seizures. Arch Neurol 1989;46:1080–8.
[22] Lopez C, Halje P, Blanke O. Body ownership and embodiment: vestibular and multisensory mechanisms. Neurophysiol Clin 2008;38:149–61.
[23] Caraballo RH, Cersosimo RO, Fejerman N. Benign focal seizures of adolescence: a prospective study. Epilepsia 2004;45:1600–3.

Please cite this article as: Hewett R, et al, Benign temporo-parieto-occipital junction epilepsy with vestibular disturbance: An underrecognized form of epilepsy? Epilepsy Behav (2011), doi:10.1016/j.yebeh.2011.05.017