

Prevalence of benign epileptiform variants

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ABSTRACT

Objective: There are numerous distinctive benign electroencephalographic (EEG) patterns which are morphologically epileptiform but are non-epileptic. The aim of this study was to determine the prevalence of different benign epileptiform variants (BEVs) among subjects who underwent routine EEG recordings in a large EEG laboratory over 35 years.

Methods: We retrospectively studied the prevalence of BEVs among 35,249 individuals who underwent outpatient EEG recordings at London Health Sciences Centre in London, Ontario, Canada between January 1, 1972 and December 31, 2007. The definitions of the Committee on Terminology of the International Federation of Societies for EEG and Clinical Neurophysiology (IFSECN) were used to delineate epileptiform patterns (Chatrian et al. A glossary of terms most commonly used by clinical electroencephalographers. *Electroenceph Clin Neurophysiol* 1974;37:538–48) and the descriptions of Klass and Westmoreland [Klass DW, Westmoreland BF. Nonepileptogenic epileptiform electroencephalographic activity. *Ann Neurol* 1985;18:627–35] were used to categorize the BEVs.

Results: BEVs were identified in 1183 out of 35,249 subjects (3.4%). The distribution of individual BEVs were as follows: benign sporadic sleep spikes 1.85%, wicket waves 0.03%, 14 and 6 Hz positive spikes 0.52%, 6 Hz spike-and-waves 1.02%, rhythmic temporal theta bursts of drowsiness 0.12%, and subclinical rhythmic electrographic discharge of adults in 0.07%.

Conclusion: The prevalence of six types of BEVs was relatively low among the Canadian subjects when compared to the reports from other countries.

Significance: BEVs are relatively uncommon incidental EEG findings. Unlike focal epileptic spikes and generalized spike-and-waves, BEVs do not predict the occurrence of epilepsy. Accurate identification of the BEVs can avoid misdiagnosis and unnecessary investigations.

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1. Introduction

Electroencephalogram (EEG) remains the primary tool in the investigation of patients with epilepsy. However, not all sharply contoured EEG potentials are associated with epileptic seizures and their presence may lead to misinterpretation of EEG (Benbadis and Tatum, 2003; Krauss et al., 2005). Various terminologies are used to denote these non-epileptiform sharp transients such as epileptiform activity in the EEGs of non-epileptic subjects (Zivin

and Marsan, 1968), non-epileptogenic epileptiform electroencephalographic activity (Klass and Westmoreland, 1985), or benign epileptiform variants (Drury and Beydoun, 1993; Westmoreland, 1996). They fall into six main types: benign sporadic sleep spikes (BSSS), wicket waves, 14 and 6 Hz positive spikes, 6 Hz spike-and-waves, rhythmic temporal theta burst of drowsiness (RTTD), and subclinical rhythmic electrographic discharge of adults (SREDA) (Fig. 1).

BEVs are not an expected finding in a normal record, and yet are not routinely considered abnormal or at least poorly correlated with pathophysiology. They commonly occur during drowsiness and light sleep. They seldom occur in wakefulness or deep sleep (Klass and Westmoreland, 1985; Westmoreland, 1996). A number of factors such as technique of EEG recording, patient demographics, and

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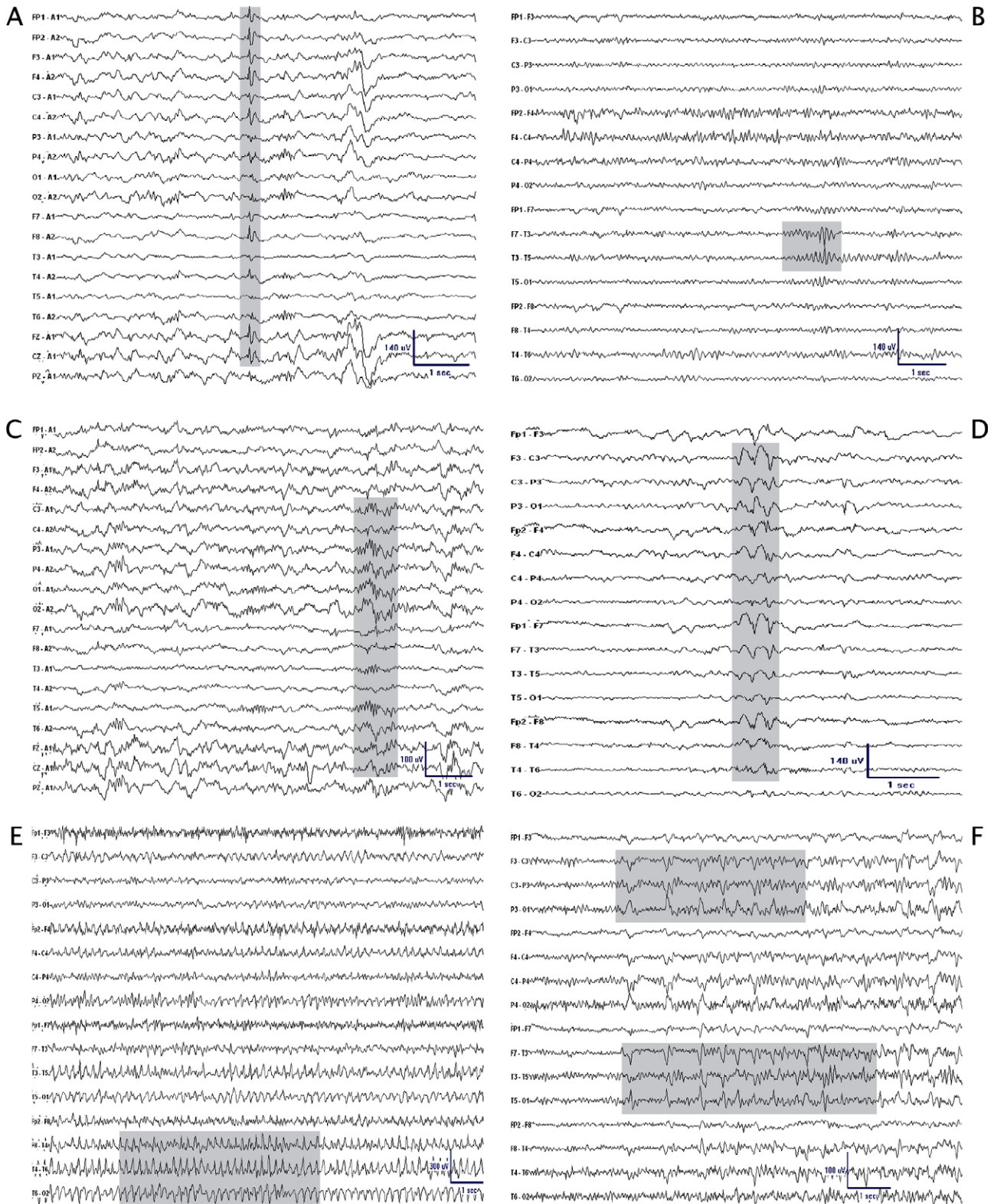


Fig. 1. Representative samples of benign epileptiform variants from our patients. (A) Benign sporadic sleep spikes in a 46-year-old female. (B) Wicket waves in the left temporal region in a 45-year-old male. (C) 14 and 6 Hz positive spikes in an 18-year-old male. (D) Six Hz spike-waves in a 22-year-old female. (E) Rhythmic temporal theta burst of drowsiness in a 11-year-old male. (F) Subclinical rhythmic electrographic discharge of adults recorded from a 45-year-old female.

physician expertise in their recognition could influence the prevalence of BEVs.

This study describes the frequency of BEVs among subjects who underwent routine EEG recording in the EEG laboratory at London Health Sciences Centre (LHSC) in London, Ontario, Canada. This

laboratory serves a large population consisting of all ages at the Middlesex County and the surrounding areas in the Southwestern Ontario. This study aims to ascertain the prevalence of BEVs in a large EEG laboratory serving all ages from a large geographical area in Canada for over 35 years and to compare and contrast our re-

sults with similar studies from other countries. Several studies have confirmed their lack of association with epileptic seizures (Reiher and Klass, 1968; Reiher and Lebel, 1977; White et al., 1977; Klass and Westmoreland, 1985; Westmoreland, 1996; McLachlan and Luba, 2002).

2. Materials and methods

2.1. EEG laboratory

Our electroencephalography (EEG) laboratory has served most of Southwestern Ontario since 1972. EEGs were done on 16 channel analog Grass equipment until 1998. Since then, EEGs have been captured digitally using a 21 electrode array placed according to the international 10–20 system of EEG electrodes (Jasper, 1958) connected to a 32 channel headbox from XLTEK (Oakville, Ont.). EEG recordings were performed using: Ten 20 conductive EEG paste, Nuprep EEG gel for skin preparation (Weaver and company, Aurora, USA) to keep skin impedance below 5 K Ω , 10 mm Grass gold plated disc electrodes (Grass technologies, Astro-Med Inc. Product-Group, USA). The setup had a channel sampling rate of 250 Hz, an anti-aliasing filter of 70 Hz, low frequency filter of 0.16 Hz, and an optional 60 Hz notch filter. The video screen display had a horizontal scaling equivalent of 25–35 mm/s and a screen resolution of 1280 \times 1024 pixels. Long-term archival was accomplished using writable CDs and DVDs (CD-R/DVD-R) to store digital EEG recordings. The guidelines of the American Society of Clinical Neurophysiology (1994, 2006) and the Task Force of The Canadian Society of Clinical Neurophysiologists (2002) were utilized for performing EEG recordings. Spontaneous sleep or drowsiness was obtained in the majority of patients. Sphenoidal, nasopharyngeal electrodes or depth recordings were not used.

Since 1980, we implemented a comprehensive database system (Microsoft Access 1997/SQL Server 1997) known as Epilepsy Search Database (ESD) for identification and coding of EEG findings and subsequent retrieval of patient and EEG information. The program was partially written in assembler language to enhance speed and efficiency of operation. The data are coded according to a controlled terminology of 400 terms (e.g. Term #197: wicket, Term #174: SREDA, etc.). Standardized encoding of data and dynamic file expansion minimized disk storage requirements (Lemi-

eux et al., 1984). It was this database system that was queried for retrieval of EEG classification data, using single or multiple search indices corresponding to each BEV.

2.2. Patient population and data collection

Outpatients who underwent EEG recordings in our EEG Laboratory between January 1, 1972 and December 31, 2007 were included in this study. Patients were referred for reasons encompassing conditions such as: seizure disorders, stroke, encephalitis, psychological or behavioral symptoms, metabolic encephalopathy, dementia, blackouts, headaches, and dizziness.

While the majority of BEVs occur during sleep and drowsiness, our study showed a small sub-population of EEG records that were BEV positive during wakefulness. Therefore, the occurrence of BEVs during wakefulness, drowsiness or sleep were included.

We used the modified Mayo System to classify the EEG findings (Mayo Clinic and Mayo Foundation, 1991; Lemieux et al., 1984), the definitions of the Committee On Terminology of the International Federation of Societies for EEG and Clinical Neurophysiology (IFSECN) (Chatrion et al., 1974) to delineate the epileptiform patterns, and the descriptions of Klass and Westmoreland (1985) to categorize the BEVs. All archived EEG reports were reported by experienced electroencephalographers.

3. Results

3.1. EEG cohort

During this study period, 35,249 outpatients underwent 54,945 EEG recordings which contained awake, drowsy and sleep tracings. The population was comprised of 17,492 males and 17,757 females. Their ages ranged from newborn to 100 years, with a mean age of 36.16 years. Their distribution by age was as follows: 15 years or younger, 19%; 16–55 years, 58%, and 56 years or older, 23%.

3.2. BEV cohort

We identified 1399 EEG records as having BEV(s) amongst 1183 (3.356%) patients. 276 (19.7%) EEG records demonstrated BEVs exclusively during wakefulness. There were 566 males and 617 females, with a mean age of 34.6 years. Overall, there were 1,279 BEV

Table 1
Prevalence and demographic characteristics of benign epileptiform variants (BEVs) among 35,249 general outpatient subjects.

BEVs	Frequency		Percentage of (%)			Age (years) Range, mean \pm SD	Gender (male:female)	P-value (Chi-square)
	# of records	# of patients	BEV+ records (N = 1399)	BEV+ patients (N = 1183)	Outpatients (N = 35,249)			
Outpatient	54,945	35,249	–	–	–	0–100 36.16 \pm 22.35	17,492: 17,757	–
BEV+	1399	1183	–	–	3.356	4–94 34.60 \pm 17.23	566:617	0.221
BSSS	814	652	58.184	55.114	1.850	4–94 39.75 \pm 17.80	345:307	0.093
Wicket waves	13	13	0.929	1.099	0.037	32–76 55.36 \pm 13.31	5:8	0.421
14 and 6 Hz positive spikes	193	185	13.796	15.638	0.525	4–67 23.23 \pm 10.49	82:103	0.149
6 Hz spike-waves	565	360	40.386	30.431	1.021	5–77 28.75 \pm 12.99	159:201	0.038*
RTTD	48	43	3.431	3.635	0.122	8–71 27.49 \pm 15.83	19:24	0.476
SREDA	31	26	2.216	2.198	0.074	9–80 52.10 \pm 16.51	9:17	0.126

BSSS, benign sporadic sleep spikes; RTTD, rhythmic temporal theta burst of drowsiness; SREDA, subclinical rhythmic electrographic discharge of adults; SD, standard deviation.
* $P < 0.05$.

Table 2

Age- and sex-specific prevalence rates of benign epileptiform variants (BEVs) among our 35,249 outpatients.

Age groups	BEVs prevalence rate (%)																	
	14 and 6 Hz positive spikes			6 Hz spike waves			RTTD			Wicket waves			BSSS			SREDA		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
0–5	–	0.003	0.003	–	0.003	0.003	–	–	–	–	–	–	0.003	0.003	0.006	–	–	–
6–15	0.057	0.051	0.108	0.054	0.040	0.094	0.017	0.011	0.028	–	–	–	0.037	0.028	0.065	0.003	–	0.003
16–25	0.102	0.142	0.244	0.170	0.216	0.386	0.014	0.028	0.043	–	–	–	0.176	0.224	0.400	0.003	–	0.003
26–35	0.045	0.060	0.105	0.128	0.167	0.295	0.003	0.011	0.014	–	0.006	0.006	0.238	0.199	0.437	0.003	0.003	0.006
36–45	0.017	0.026	0.043	0.054	0.079	0.133	0.009	0.006	0.014	–	–	–	0.145	0.133	0.278	–	–	0.009
46–55	0.009	0.011	0.020	0.020	0.037	0.057	0.009	0.006	0.014	0.003	0.011	0.014	0.125	0.150	0.275	0.009	0.011	0.020
56–65	–	–	–	0.017	0.020	0.037	–	0.006	0.006	0.006	–	0.006	0.122	0.068	0.190	0.009	0.014	0.023
>65	0.003	–	0.003	0.009	0.009	0.017	0.003	–	0.003	0.006	0.006	0.011	0.133	0.065	0.199	–	–	0.011
All ages	0.233	0.292	0.525	0.451	0.570	1.021	0.054	0.068	0.122	0.014	0.023	0.037	0.979	0.871	1.850	0.026	0.048	0.074

BSSS, benign sporadic sleep spikes; RTTD, rhythmic temporal theta burst of drowsiness; SREDA, subclinical rhythmic electrographic discharge of adults; M, male; F, female; T, total (both sexes).

instances (i.e. unique pairings of a BEV type with an individual patient) (Table 1).

3.3. Prevalence rates of BEVs

The distribution of BEVs in BEV+ patients was as follows: BSSS 55.11%, wicket waves 1.01%, 14 and 6 Hz positive spikes 15.64%, 6 Hz spike-waves 30.43%, RTTD 3.63%, and SREDA 2.20%. Table 2 shows the distribution of BEVs by type, age groups, and gender. In patients with BEVs, the prevalence of epileptic discharges was 475/1,183 (40.2%).

Table 2 shows the age and sex-specific prevalence for all the BEVs. The 14 and 6 Hz positive spikes, 6 Hz spike-and-waves, and RTTD occurred most frequently among the subjects between ages 16 and 25 years with a prevalence of 0.2%, 0.4%, and 0.03%, respectively. The prevalence of wicket waves (0.01%) and SREDA (0.02%) peaked among the subjects between ages 46 and 55 years while BSSS (0.4%) peaked in the age group of 26–35 years. Representative examples of BEVs from this lab are shown in Fig. 1.

4. Discussion

There are not many single centre reports on the prevalence of the various types of BEVs (Radhakrishnan et al., 1999). However, individual BEVs have been reported from developed countries such as BSSS (White et al., 1977), wicket waves (Reiher and Lebel, 1977), 6 Hz spike-and-waves (Hughes, 1980), and SREDA (Miller et al., 1985; Westmoreland and Klass, 1997). Our all inclusive population

study from a large EEG laboratory was a suitable setting to address this question despite its inherent limitations.

4.1. Review of literature and comparison of data

The most frequently encountered BEV was BSSS (51%) and was detected in 1.9% of all the subjects. White et al. (1977) reported BSSS in 24% of normal subjects using nasopharyngeal electrodes. Reported prevalence rates of BSSS range from 1.4% to 24% (Reiher and Klass, 1968; White et al., 1977). Wicket waves were identified in 0.84% by Reiher and Lebel (1977). Wicket waves were encountered in only 0.04% of the total eligible subjects in this study. The 14 and 6 positive-spikes were detected in 0.5% and RTTD in 0.1% of our subjects. Gibbs et al. (1963) reported a prevalence of 0.5% for RTTD, whereas Maulsby (1979) reported RTTD in 2% of adult EEG records. SREDA occurred in 0.07% of our EEG records, and in 1/2500 (0.04%) EEG recordings from the Mayo Clinic (Westmoreland and Klass, 1997). The prevalence of 1.02% for 6 Hz spike-and-wave was observed in this study is similar to the reported rate of 0.2–4.5%. The 6 Hz spike-and-wave pattern was noted in 1.5% of 195 healthy young men by Tharp (1966). Hughes (1980) reported 6 Hz spike-and-waves in 2.5% of the subjects over 30 years. A comparison of the prevalence rate of BEVs from selected reports with that of ours is provided in Table 3.

The technique of EEG recording and its interpretation, patient demographics, or as yet unidentified factors (genetic or environmental) could be responsible for the variations in the published prevalence rates. A contra-lateral ear reference montage, and greater inter-electrode distance best demonstrates variants such

Table 3

Selected reports of prevalence of individual Benign epileptiform variants.

Author(s) (year of publication)	Study population (patients)	Duration of study (years)	State(s) of patient during EEG recording	BSSS (%)	WW (%)	14 and 6 Hz PS (%)	6 Hz SW(%)	RTTD (%)	SREDA (%)
Gibbs et al. (1963)	50,000	Not known	Awake, drowsy and sleep	–	–	–	–	0.5	–
Lombroso et al. (1966)	155 controls (13–15 yrs of age)	Not known	Awake and sleep	–	–	58	–	–	–
White et al. (1977)	599	2	24 hr sleep deprivation and nasopharyngeal electrodes	20	–	–	–	–	–
Reiher and Lebel (1977)	4458	6	Awake and sleep	–	0.8	–	–	–	–
Hughes (1980)	61,467	30	Awake, drowsy and sleep	–	–	–	2.5	–	–
Westmoreland and Klass (1997)	108	16	Awake and sleep	–	–	–	–	–	0.04
Radhakrishnan et al. (1999)	1778	2	Awake, drowsy and sleep	8.16	0.96	5.68	2.76	0.79	–
Current study (2008)	35,249	35	Awake, drowsy and sleep	1.9	0.04	0.52	1.02	0.12	0.07

BSSS, benign sporadic sleep spikes; WW, wicket waves; 14 and 6 PS, 14 and 6 Hz positive spikes; 6 Hz SW, 6 Hz spike-and-waves; RTTD, rhythmic temporal theta burst of drowsiness; SREDA, subclinical rhythmic electrographic discharge of adults.

as BSSS and 14 and 6 Hz positive spikes (White et al., 1977; Klass and Westmoreland, 1985; Blume et al., 2002). Care should be taken to note the wake-sleep transition periods, where BEVs usually could be detected (Klass and Westmoreland, 1985).

4.2. Age and BEV prevalence

Age-specific variation in the prevalence of BEVs have been reported: 14 and 6 Hz positive spike pattern occurred in teenagers (Lombroso et al., 1966), 6 Hz spike-and-waves and RTTD in adolescents and young adults (Gibbs et al., 1963; Hughes, 1980), BSSS and wicket waves occurred in the adults (Reiher and Lebel, 1977; White et al., 1977), and SREDA in middle-aged and elderly subjects (Miller et al., 1985; Westmoreland and Klass, 1997). A significant gender related variation for 6Hz spike-and-waves reported by Hughes (1980) could also be confirmed in our study (Table 1).

The age specific prevalence in our study peaked in the 16–25 year age group for 14 and 6 Hz positive spikes, 6 Hz spike-and-waves and RTTD. Wicket waves occurred most frequently between ages 46 and 55 years while BSSS peaked in the age group of 26–35 years. Lombroso et al. (1966) reported a prevalence of 14 and 6 Hz positive spikes of 58% in teenage boys. The low prevalence (0.5%) of 14 and 6 Hz positive spikes in our study could be due to the poor representation of the teenage group. The highest prevalence for SREDA in the 46–55 year age group in our study was remarkably similar to other studies (Westmoreland and Klass, 1981; Miller et al., 1985; Westmoreland and Klass, 1997).

It remains unclear whether these benign EEG variants are more likely to occur in cortex rendered hyper-excitable by epilepsy or in association with other conditions (McLachlan and Luba, 2002). Further, there is no evidence that the presence of BEVs influences the outcome of epilepsy surgery; however, no studies have specifically addressed this issue including the current report. Thomas and Klass (1968) found that the occurrence of 6 Hz spike-and-wave in an otherwise normal recording was associated with seizures in 36% of the subjects compared to 24% in those without 6 Hz spike waves. Similarly, Hughes and Gruener (1984) found that BSSS predicted seizures in 48% compared to 15% without such a finding. Further, the incidence of BSSS in the EEGs of Japanese patients with epilepsy was 8.6% compared to 2.5% of those without epilepsy (Saito et al., 1987). There continues to be reports, particularly in the psychiatry literature, of the predictive value of BEVs for mood disorders or the so-called neuro-vegetative symptoms such as dizziness, nausea and palpitation. (Hughes, 1996; Boutros et al., 1998; Inui et al., 1998). The EEG findings should be interpreted in the context of the overall clinical picture (Westmoreland, 1996). In a study conducted by Molaie et al. (1991) to determine the effect of epilepsy and sleep deprivation on the prevalence of benign epileptiform transients of sleep (BETS), it was concluded that BETS were likely normal variants, but they noted a high occurrence of them among the epileptic patients. Oletsky et al. (1998) reported a patient with absence seizures with generalized 3 Hz spike-and-wave complexes in whom 14 and 6 Hz positive spikes were frequently seen in isolation and they concluded that this association of positive spikes with generalized spike-and-wave complexes may not always be coincidental. Therefore, BEVs must be interpreted with great caution particularly in a clinical setting where epilepsy is strongly suspected. Other modern diagnostic tools such as Independent Component Analysis (ICA) may provide additional help in differentiating BEVs from epileptic discharges (Makeig et al., 1996; Jung et al., 2005; Urrestarazu et al., 2006; Ventouras et al., 2007; Patel et al., 2008).

4.3. Possible explanations for the low BEV prevalence in this study

An important factor to consider is the inclusion and exclusion criteria when reporting BEV prevalence. As our institution utilizes

spontaneous sleep EEG recordings, without the usage of sedatives, we were interested in the overall prevalence of BEVs and approached the reporting of BEVs directly from the raw outpatient population. This differs from the study by Radhakrishnan et al. (1999), who examined a smaller population composed of only individuals with adequate sleep studies. It is our opinion that due to variability in the level of drowsiness or sleep achieved with a spontaneous sleep protocol, as well as the inexact nature of determining drowsiness or sleepiness through EEG, reporting prevalence numbers from our adequate sleep study sub-population would pose significant limitations.

Hughes (1980) found 6 Hz spike-waves to be more prevalent among Caucasians, while wicket waves were noted to be more prevalent among non-Caucasians (Hughes and Olson, 1981). A low prevalence of photoparoxysmal response was reported in the black population of Africa when compared with whites (De Graaf et al., 1995). Thus racial, geographic, or ethnic influences have been noted to influence certain EEG findings including the BEVs. Whether the low BEV prevalence in this study can be ascribed to such influences as genetic variations in North American population is conjectural.

The poor representation of younger age groups in our study population could also account for the low prevalence of certain types of BEVs such as 14 and 6 Hz positive spikes. The lack of association of BEVs with epileptic seizures is well established (Reiher and Klass, 1968; Reiher and Lebel, 1977; White et al., 1977; Klass and Westmoreland, 1985; Westmoreland, 1996; McLachlan and Luba, 2002). Finally, retrospective nature of this study plus the interobserver variability in reporting the BEVs are additional factors that might have contributed to the low prevalence of BEVs in this study.

4.4. Limitations of this study

This study has certain limitations applicable to any retrospective laboratory-based study. The true prevalence of a phenomenon is best determined by ascertaining its occurrence in a normal population (Jabbari et al., 2000). Unfortunately, clinical EEG studies are obtained on laboratory patients who form a selected and non-randomized group. Well designed prospective population EEG studies plus other clinical and laboratory data will be essential in confirming the benign nature of non-epileptic epileptiform transients.

4.5. Implications of this study

This study shows a relatively low prevalence for BEVs among subjects from a single large laboratory in Canada compared to those reported from other countries. BEVs appear in a minority of subjects but are not rare. Accurate identification of the BEVs by visual analysis of EEG requires considerable training and experience. A challenge for particularly the novice electroencephalographer is to distinguish BEVs from their pathological counterparts which they resemble, namely focal spikes and generalized spike-and-waves. In some countries, there may be a shortage of board-certified EEG technologists and electroencephalographers. Physicians who are requesting EEG tests should not be bewildered by the many terms for EEG patterns that may be encountered in the EEG reports. They should be aware, however, of the vast differences in value of these benign patterns for clinical diagnosis. Most electroencephalographers consider that in general these are incidental findings which, unlike other types of focal epileptic spikes and generalized spike-and-waves, do not predict the occurrence of epilepsy (Reiher and Klass, 1968; White et al., 1977; Reiher and Carmant, 1991; Beun et al., 1998; Jabbari et al., 2000; McLachlan and Luba, 2002; Tatum et al., 2006). The low prevalence and distinctive features of BEVs support this latter contention.

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