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A reappraisal of secondary bilateral synchrony

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Abstract

Objective: A reappraisal was made with respect to a classical observation of the mode of instrumental phase reversals on inter-ictal EEG of seemingly bilateral synchronous spike-and-wave discharges in patients with either idiopathic generalized epilepsies (IGE) or symptomatic localization-related frontal lobe epilepsies (FLE). It was pointed out in the original observation by Tükel and Jasper that one phase reversal at midline or near the midline on the side of the parasagittal epileptogenic lesion designated as secondary bilateral synchrony (SBS) was found in patients with frontal lobe epilepsy (FLE), whereas a double phase reversal was found over the homologous frontal electrodes (F3 and F4) designated as primary bilateral synchrony (PBS) in patients with IGE. *Methods:* Twenty-three patients (IGE: 15, and FLE: 8) revealing bursts of seemingly bisynchronous spike-wave discharges in interictal EEGs were retrospectively studied. Discharge patterns were defined as stable phase reversal pattern if the site of phase-reversal was consistent, and as unstable pattern if the site of phase-reversal was not consistent but shifting in the same patient. *Results:* Stable one phase-reversal pattern was found more frequently in FLE (50%) than in IGE patients (26.7%), and stable double phase-reversal pattern more frequently in the IGE (33.3%) than in the FLE group (12.5%). Notably, unstable pattern was found almost equally in both IGE and FLE patients (40% and 37.5%, respectively).
Conclusions: Recognition of SBS or PBS in accordance with original observation was found not to clearly differentiate FLE from IGE in patients showing seemingly bisynchronous spike-wave complexes. The variability of instrumental phase-reversals can be accounted for by the fact that the localization of maxima of negative spike of the spike-and-wave complexes varies considerably.

INTRODUCTION

Penfield and Jasper remarked: "An epileptogenic lesion of the mesial or inferior aspect of a frontal lobe, although it is one-sided, may produce bifrontal synchronous discharges".[1] A few years later, Tükel and Jasper returned to the problem proposing: "The wave and spike of petit mal is a primary bilateral synchronous discharge . . . ; it appears not to be related to a unilateral cortical focus, but may be of subcortical origin …. On the other hand, a bilateral synchronous discharge which can be shown to arise from a unilateral cortical focus we shall call secondary bilateral synchrony".[2] Spikes of the complexes show a single phase reversal at or near the midline referring to secondary bilateral synchrony (SBS), in contrast with a double phase reversal over right (F4) and left (F3) frontal areas referring to primary bilateral synchrony (PBS).[2]

The advent of digital EEG apparatus has enabled us to reformat an EEG segment into various montages. In this study, an attempt was made to reexamine this classical observation based on the site of phase reversal shown by patients with idiopathic generalized epilepsies and frontal lobe epilepsy.

METHODS

Twenty-three patients were studied whose diagnosis was idiopathic generalized epilepsy (IGE, 15 patients) or symptomatic localization-related frontal lobe epilepsy (FLE, 8 patients) according to the International Classification of Epileptic Seizures (1981)[3] and Epileptic Syndrome and Epilepsies (1989)[4], and their interictal EEGs showed on gross inspection bursts of bilateral synchronous and almost symmetrical spike-and-wave discharges. The clinical course of individual patients was followed up in the National Epilepsy Center, Shizuoka for at least 1 year.

Twenty-one scalp electrodes were placed according to the international 10-20 system. Nihon Koden EEG apparatus of CNN-1000/2000 System with the bandpass filter set at 0.5-120Hz and

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sampling rate of 500 Hz were used. At least two (2 to 7, mean: 4.9 tracings) scalp EEG recordings were obtained for each patient. Waking and sleep scalp recordings of at least one hour of duration were routinely performed, and only the bursts of spike-and-wave discharges taking place during awaking tracing were selected for analysis. Most of recordings were obtained when patients were taking anti-epileptic agent(s). Phase reversals are visually recognized by opposing alignment of the same potential of spikes of spike-and-wave complexes in transverse sequential bipolar linkage to identify the site of maximum negativity across Fz, or F3 and F4. The phase reversals were divided into two patterns in this study: 1) one phase-reversal pattern consistently took place either on the midline (Fz) or on one side of frontal leads (F3 or F4), 2) a double phase-reversal pattern, in which phase reversals occurred at the homotopic frontal leads. Moreover, if it was observed that the site of phase reversal for >20% of spikes for all of the bursts in the same and subsequent recordings was inconstant in a given patient, such phase-reversal was named unstable pattern. In contrast, when the site of phase-reversals for ≥ 80% of spikes for all paroxysms was constant in all of the recordings in a given patient, such a pattern was named stable pattern. The polarity reversals in transverse bipolar montage were reconfirmed by longitudinal montage when necessary. Presence of triggering focal spikes (5) was not included in the selection criteria of SBS in this study.

Clinical information inclusive of seizure types, onset age, family history, neurological and neuro- psychological examinations, findings of neuroimaging, and response to anti-epileptic drugs (AEDs) were summarized based on the protocol of the individual patients.

RESULTS

The clinical features and EEG findings including phase-reversal pattern of the 23 patients are summarized in Table 1 and 2. Comparison of gender, onset age of seizures and age at investigation showed no significant differences between the IGE and FLE groups. A relatively higher incidence of abnormal neurological and neuroimaging findings was found in the FLE (62.5% and 50%, respectively) group compared to the IGE group (0% and 6.67%), and favorable response to AEDs significantly differed between the IGE and FLE groups (100% vs. 11%).

Comparing interictal EEG expressions between the IGE and FLE groups, both focal epileptiform paroxysm and focal slow activity were found significantly more frequently in the FLE group in comparison with the IGE group (87.5% vs. 6.7%, and 62.5% vs. 0%, respectively). Stable one phase-reversal pattern was found more frequently in the FLE group (50%) than in the IGE patients (26.7%), and stable double phase-reversal pattern was more frequent in the IGE (33.3%) than in the FLE group (12.5%). Unstable pattern was found in both IGE and FLE patients at a comparable rate (40% and 37.5%, respectively).

Representative phase-reversal patterns are shown in Figures 1 and 2.

Table 1. Demographic/clinical features of the 23 patients

	IGE (15 cases)	FLE (8 cases)
Gender (F/M)	9/6	5/3
Age at examination (yr)	27.8	27.8
Onset age (yr)	11.2	8.9
Abnormal neurologic findings	0	5 (62.5%)
Clinical seizure type		
Focal		
CPS / absence-like seizure	0	7 (87.5%)
Others (aura / version /postural/ sGTC)	0	7 (87.5%)
Generalized		
Absence	11 (73.3%)	0
Myoclonus	5 (33.3%)	1 (12.5%)
GTC	10 (66.7%)	0
Abnormal neuroimaging findings	1 (6.7%)	4 (50.0%)
Favorable response to AEDs	15 (100%)	2 (11%)

IGE: idiopathic generalized epilepsy, FLE: frontal lobe epilepsy, sGTC: secondary generalized tonic-clonic seizure, AED: antiepileptic drugs.

Table 2. EEG findings in patients with IGE or FLE

	IGE (15 cases)	FLE (8 cases)
Focal epileptiform discharges	1 (6.7%)	7 (87.5%)
Focal slow waves	0	5 (62.5%)
Phase-reversal pattern		
Stable		
One phase-reversal	4 (26.7%)	4 (50%)
Double phase-reversal	5 (33.3%)	1 (12.5%)
Unstable	6 (40%)	3 (37.5%)

Focal epileptiform findings include localized and/or lateralized spikes, spike-wave complexes, or polyspikes. Focal slow waves include regional or lateralized slow activity.

DISCUSSION

While frequently commented upon, secondary bilateral synchrony (SBS) has rarely received critical analysis. Historically, the concept emerged with a parallel concept of "highest level" seizures arising in a now abandoned, hypothetical "centrencephalon".[1] Tükel and Jasper had proposed that "the wave and spike of petit mal epilepsy is a primary bilateral synchronous discharge, it appears not to be related to a unilateral cortical focus, but may be of subcortical origin. This type of discharge we shall call primary bilateral synchrony (PBS). A bilaterally synchronous discharge which can be shown to arise from a unilateral cortical focus, we shall call secondary bilateral synchrony (SBS)."[2] The authors also tried to differentiate PBS from SBS by visual inspection of EEG tracings, and noted that PBS and SBS were characterized by findings that two phase reversals take place over homotopic frontal leads in PBS, while one phase reversal occurs either on midline or near the midline on the side of the epileptogenic lesion in SBS.[2]

Tükel and Jaspers' classical observation made several points that have not been taken into consideration in most subsequent discussion. In a number of studies to distinguish between PBS and SBS, sophisticated neurophysiological techniques have been developed[6-9], however, they are not practical for the purpose of daily practice.

The present study revealed that one phase-reversal occurred more commonly in FLE patients than in IGE patients (50% vs. 26.7%) while the double phase-reversal pattern is more commonly seen in IGE patients than in FLE patients (33.3% vs. 12.5%). Although a difference between IGE/PBS and FLE/SBS is plausible, the distinction between the two is not always clear. Furthermore, an unstable pattern in which the site of phase-reversal was not consistent in one EEG recording or among different tracings for the same patient, was seen in both IGE and FLE groups at a comparable rate (40% and 37.5% respectively). This variability of instrumental phase-reversals can be accounted for by the fact that the localization of maxima of negative spike of the spike-and-wave complexes varies.

After visually analyzing EEGs of patients with absences, Weir has concluded that maximal voltage of negative spike occurs over frontal regions. Voltage of this spike fluctuates widely among patients and within bursts, usually being highest early in the burst.[10] Lately, Rodin and Ancheta have reported results of computerized mapping of fields of 3-Hz spike-wave bursts. Maximal negativity of the individual complexes was mainly in the frontal areas, and the way in which these maxima were reached varied markedly. Even in the most regular patterns, successive spikes-wave complexes within one seizure could have different origins and different spread of the field.[11] Finally, Daly pointed out that morphology of spike-waves varies significantly among different patients and different times in the same patient. Although usually bilaterally symmetrical, complexes may show shifting or even persistent asymmetries.[12] These facts signify that the fields of epileptiform discharges can vary enormously, and also suggest there are multiple discrete sites of cortical onset during 3-Hz spike-wave. The latter assumption was also supported by studies of 3-Hz spike-wave bursts in which MEG and functional magnetic resonance imaging were used.[13,14]

The variability of instrumental phase-reversals can be accounted for by the fact that the localization of maxima of negative spike of the spike-and-wave complexes varies considerably in time and location.

Fig.1 (a, b) ***SBS with stable one phase-reversal pattern at F4. See text.*** (Calibration: 40μV; 1 s).

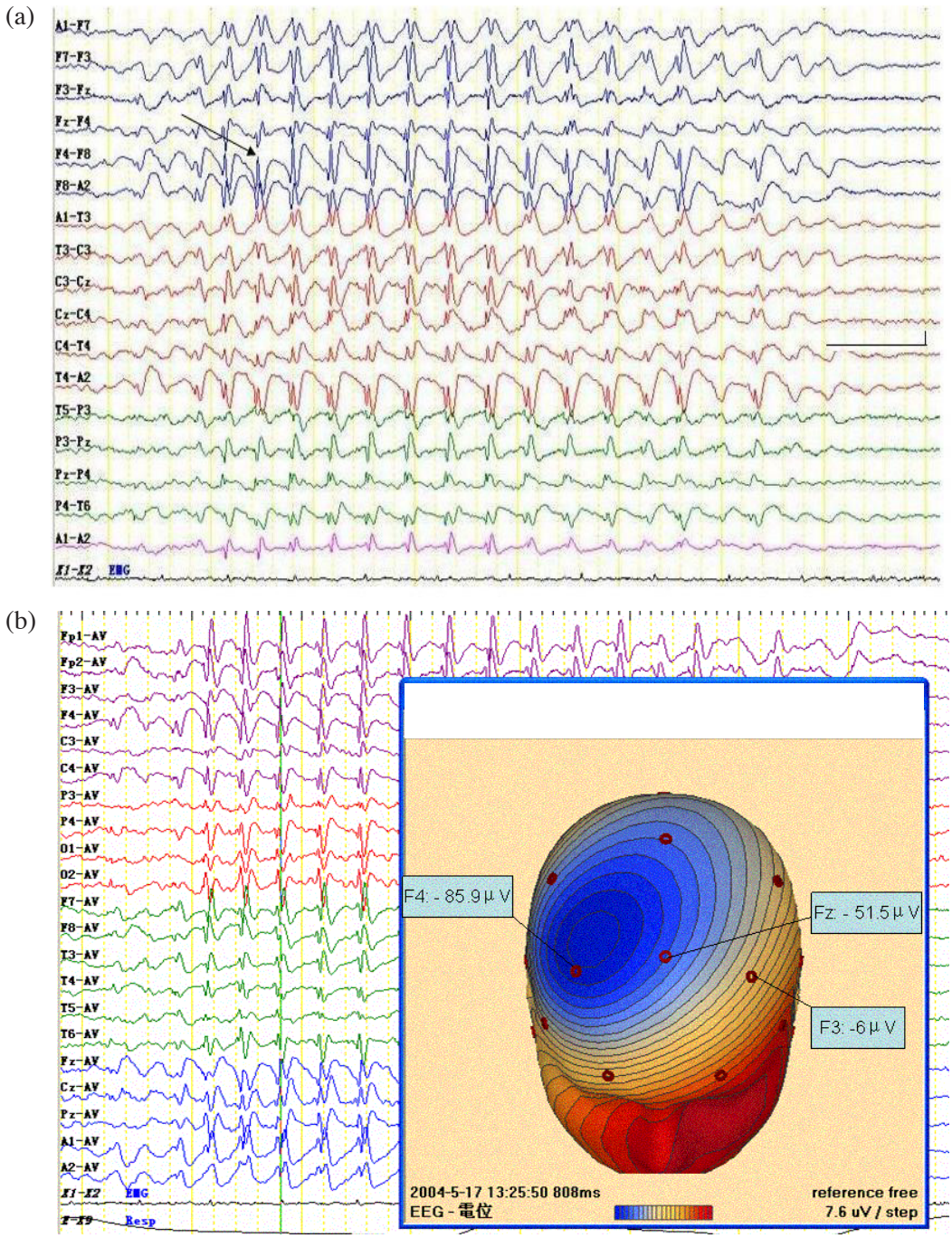
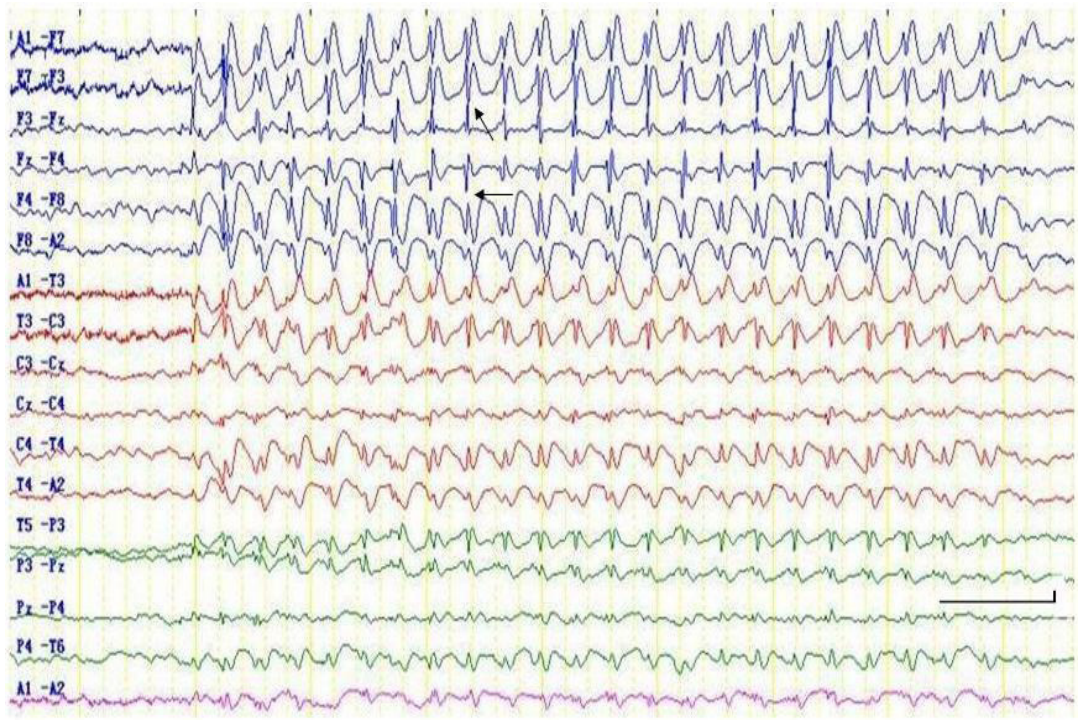


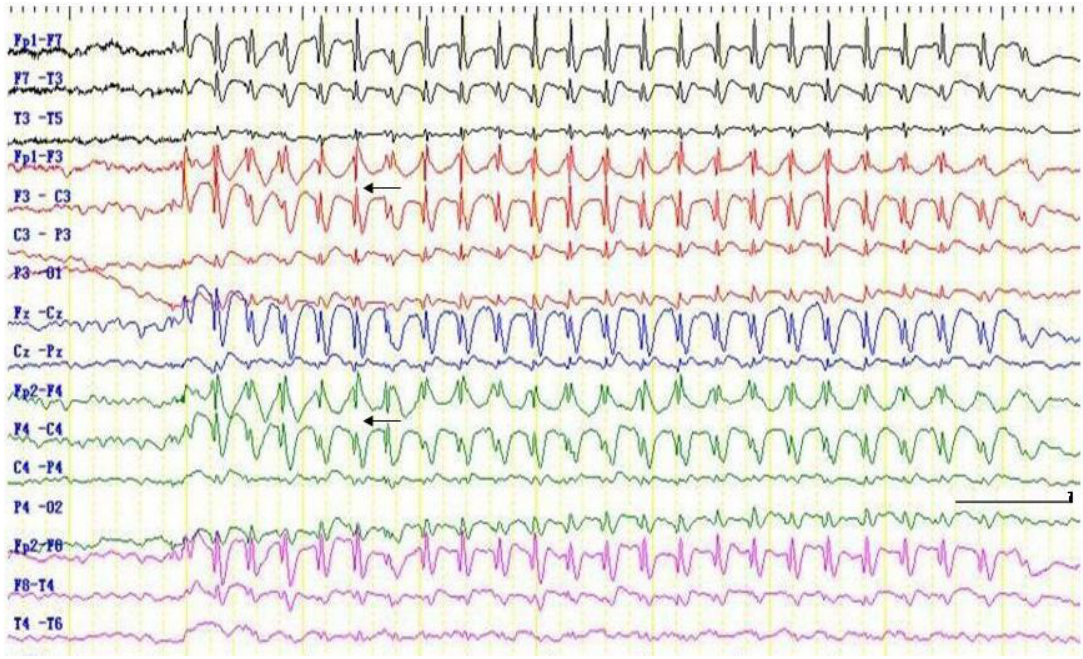
Fig.1: ***Stable SBS pattern with one phase-reversal.*** A 30-year-old woman with mild mental subnormality developed episodes of impairment of consciousness lasting 1-2 minutes at the age of 6. At the age of 24, she showed asymmetric tonic seizures of arms with head and eye aversion to the left side followed by generalized tonic-clonic seizures, which were documented by video-EEG monitoring. CT and MRI were normal, and ictal SPECT showed hyperperfusion in the right temporoparietal region. (a): In transverse bipolar montage, bilateral and symmetrical 2.5-3Hz spike-and-waves with one phase reversal at F4 (actually, phase reversals at F4, Cz, Pz, but with the maximum negativity at F4) was observed (indicated by arrow). This finding was stable and did not change in position from one recording to another. (b): The voltage topography of the same spike in average potential reference derivation showing a maximum of negative field potential near F4.

Fig.2 (a,b,c) ***SBS with stable double phase-reversal pattern at F3 (a) and F4 (b).*** **See text.** (Calibration: 60μV; 1 s).

(a)



(b)



(c)

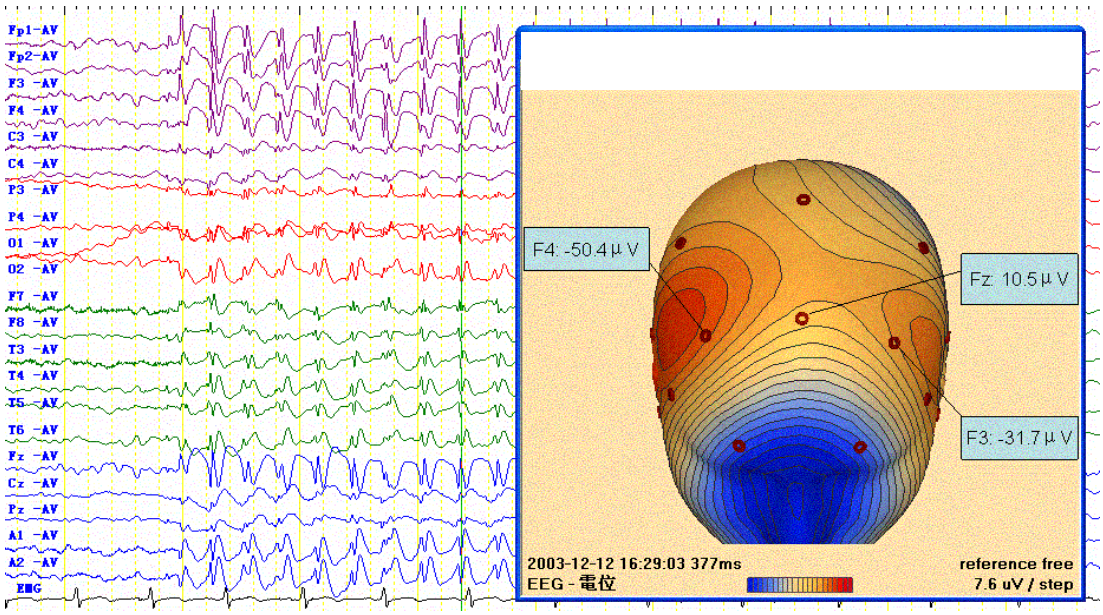


Fig 2: ***Stable SBS pattern with a double phase-reversal.*** At the age of 10, this 20-year-old male patient had absence-like seizures lasting 30 seconds 3-5 times a day and generalized tonic-clonic seizures preceded by head aversion to the right. Hyperperfusion was seen in the left frontal region on ictal SPECT and no abnormality on brain MRI. In transverse montage (a) there exist two phase reversals over left (F3) and right (F4) (arrows), which are reconfirmed by the longitudinal montage of the same burst (b) (arrows). (c) F3 and F4 were in the vicinity of two negative maxima in voltage topography of the same spike in average potential reference derivation.

Our paper suggests that when repeated EEG recordings in the same patient shows a stable pattern with one phase reversal, FLE should be considered ahead of IGE and when a stable pattern with double phase reversals is encountered, IGE is more common. Other investigative modalities may help to strengthen these observations on EEG (eg MRI or PET abnormalities) seeing that for both FLE and IGE, an unstable pattern is a common occurrence.

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