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Semiautomatic quantification of spiking in patients with continuous spikes and waves in sleep: Sensitivity to settings and correspondence to visual assessment

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HIGHLIGHTS

- An objective paradigm for quantification of continuous spikes and waves in sleep (CSWS) is needed for both scientific and clinical use.
- Semiautomatic quantification of spike index (SI) with appropriate parameter settings is a robust and a promising tool.
- SI of the first hour of sleep is representative of the whole night SI.

ABSTRACT

Objective: To define the optimal analysis protocol for semiautomatic quantification of spike index (SI) in continuous spikes and waves in sleep (CSWS).
Methods: Ten overnight EEGs (nine patients) with abundant spiking were used to quantify SI with a previously published semiautomatic quantification based on spike detection with BESA software. We studied (i) dependency of SI on maximal interspike interval (maxISI) defining the continuous discharge, (ii) sensitivity of SI to variations in the spike search protocol, and (iii) stability of SI over time. Finally, the semiautomatic method was compared with the quantification based on visual scoring by two neurophysiologists.
Results: MaxISI of 3 s appeared to yield the best combination of sensitivity and stability in SI quantification. The SI of the first hour of sleep did not differ significantly from the SI of the whole night. Mean error of the semiautomatic method compared to visual scoring was only seven percentage units.
Conclusions: Semiautomatic quantification of SI functions well with maxISI of 3 s, and the first hour of sleep represents the whole night SI with a clinically relevant accuracy.
Significance: This method opens a possibility for objective quantification of near-continuous epileptiform spiking during sleep, and it supports the use of shorter epochs for quantitative assessment of CSWS.

1. Introduction

Continuous spikes and waves in sleep (CSWS), or electrical status epilepticus during sleep (ESES) is an EEG diagnosis, originally defined as having at least 85% of NREM sleep covered by continuous spikes and waves (Patry et al., 1971; Tassinari et al., 2000, 2009). CSWS is usually associated with epileptic encephalopathy manifesting as variable cognitive and behavioral impairments which are permanent in most patients (Roulet Perez et al., 1993; Veggiotti et al., 1999; Tassinari et al., 2000; Scholtes et al., 2005; Liukkonen et al., 2010). The quantified (percentage) amount of spiking is considered important for both assessing the impact of spiking activity on cognition (Billard et al., 1990; Beaumanoir, 1995; Guzzetta et al., 2005; Van Hirtum-Das et al., 2006; Scheltens-de Boer, 2009), and for evaluation of the success of drug treatment (Aeby et al., 2005; Inutsuka et al., 2006). In this context, it is striking that there is no unambiguous definition of how to calculate the percentage of spiking. An objective paradigm for quantification of CSWS would be necessary for both scientific and clinical use.

CSWS analysis is based on visually estimating the amount of spike and wave discharges, and it yields a dichotomic classification of CSWS (present or absent). More advanced and laborious

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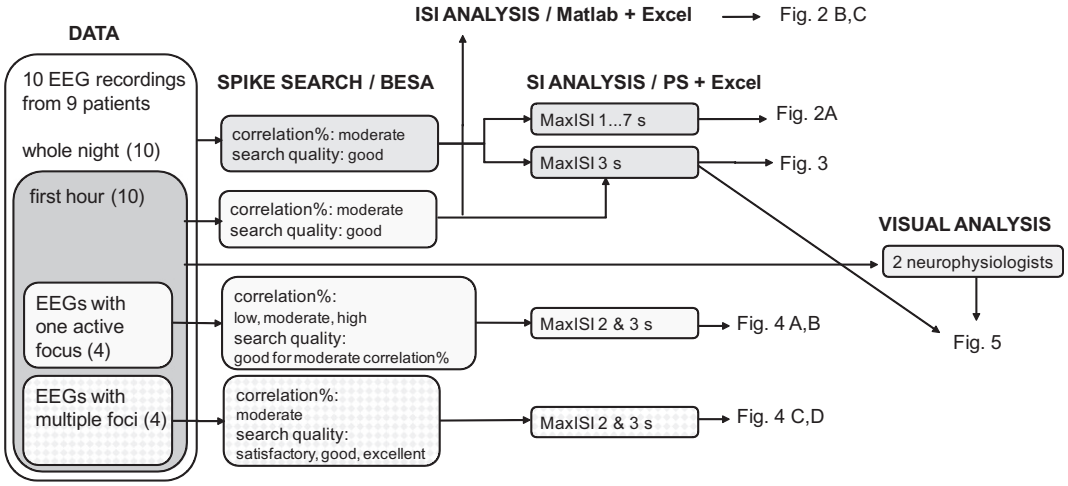

Fig. 1. Study design. SI = spike index, ISI = interspike interval, maxISI = maximum interspike interval, PS = script used to calculate SI, correlation% = correlation threshold for the spatio-temporal spike search, BESA = brain electrical source analysis-software.

approach is to calculate a spike index (SI), which indicates the percentage of NREM sleep covered by spike and waves (Morikawa et al., 1985; Galanopoulou et al., 2000; Aeby et al., 2005). The methods previously used to determine SI are, however, too diverse to enable comparability between studies (Patry et al., 1971; Tassinari et al., 2000; Aeby et al., 2005; Inutsuka et al., 2006; Galanopoulou et al., 2000; Liukkonen et al., 2010). The core problems here are the striking lack of agreement about (i) how to define a 'continuous' discharge, and (ii) what would be the minimum duration of sleep needed for a reliable SI calculation.

Manual quantitation of SI is too time-consuming to be used in the clinical setting, or even in most scientific research. To overcome this, a semiautomated method for calculation of SI was recently published by Larsson et al. (2009, 2010). This method is based on a spike search using spatio-temporal pattern match in the commercial BESA Research® software (Scherg et al., 2002; Bast et al., 2004), followed by a further analysis of the spike detection logs with a purpose-built MATLAB® script (hereafter called PS). Another recent study has used the semiautomated spike detection of ESES in Landau–Kleffner syndrome with a different focus and algorithm (Martín Miguel et al., 2011).

While semiautomatic quantification of SI can apparently overcome several pitfalls of subjective visual reading, it also includes a number of steps the effect of which on the final outcome has not been examined in detail. First, the spike used as a search template is chosen manually, and the accuracy of search is controlled visually by the EEG reader. Second, BESA software performs the spike search by using a predefined correlation threshold, which obviously affects the number of spikes found. Third, the PS algorithm quantifies SI using an operator-defined upper limit for individual spike intervals (maxISI) to count them as a continuous discharge.

The results reported with the semiautomated quantification by the original authors have been respectable in terms of both the size of datasets and the apparent clinical utility of the SIs obtained. However, we felt a need to understand this tool better and optimize it. To attain this, we (i) studied the natural characteristics of spiking in CSWS, (ii) varied the analysis protocol of semiautomated quantification, (iii) assessed further the stability of SI over a whole night sleep, and (iv) studied the comparability of SI with manual marking by human experts using the same definitions of continuous discharge.

Table 1
Electroclinical details of the patients.

EEG	Pat.	Age at epilepsy dg (yrs)	Age at CSWS dg (yrs)	Age at EEG studied here (yrs)	Etiology	MRI	Seizure type at EEG studied here	EEG spike focus
1	1	2.5	6.0	6.0	Unknown	Normal	Psychomotor → right clonic Unclassified[a]	FL, **PR**
2	2	4.2	9.2	9.7	Unknown	Normal	Psychomotor	FCR
3	3	4.2	6.1	7.3	Symptomatic perinatal vascular	MCA infarction	Atypical absence	**FL**,TPL, FR
4	4	2.8	5.7	7.6	Symptomatic perinatal vascular	PVL, HC	Atypical absence Psychomotor	FL, **PL**, **FR**
5	5	5.6	5.6	5.6	Idiopathic (familial)	Normal	Atypical absence Facial clonic	FL, **PL**
6	6	4.0	6.4	6.4	Idiopathic (familial)	Normal	Tonic–clonic Facial clonic	CL, TL, **CR**
7	7	2.5	5.4	5.9	Symptomatic perinatal vascular	PVL, right thalamic lesion	Psychomotor Atypical absence	FL, **FR**, TR, **PR**
8	8	3.8	6.2	8.0	Symptomatic perinatal vascular	PVL HC	Psychomotor → right clonic	FL
9	9	2.3	2.8	3.1	Idiopathic	Normal	Absence Facial clonic Left arm clonic	FCR
10	2	4.2	9.2	12.2	Unknown	Normal	Psychomotor	FR

[a] Eye blinking and short arrest (absence unverified), F = frontal, T = temporal, C = central, P = parietal, TP = temporo-parietal, FC = fronto-central, L = left, R = right, MCA = middle cerebral artery, PVL = periventricular leucomalacia, HC = hydrocephalus. EEG focus with most abundant spiking in CSWS is marked in bold.