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Original article

High-frequency EEG activity in epileptic encephalopathy with suppression-burst

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Abstract

Objective: We explored high-frequency activity in the suppression-burst (SB) pattern of interictal electroencephalogram (EEG) in early infantile epileptic encephalopathy including Ohtahara syndrome (OS) and early myoclonic encephalopathy (EME) to investigate the pathophysiological characteristics of SB.

Methods: Subjects included six patients with the SB EEG pattern related to OS or EME (Group SB). The results were evaluated in comparison to tracé alternant (TA) observed during the neonatal period in nine patients to rule out possible nonspecific relationships between high-frequency activity and periodic EEG patterns (Group TA). EEG was digitally recorded with a sampling rate of 500 Hz and the analysis was performed in each of the particular bipolar channel-pairs. We visually selected 20 typical consecutive burst sections and 160 inter-burst sections for comparison from the sleep record of each patient and performed the time–frequency analysis. We investigated the maximum frequencies of power enhancement in each derivation in both groups.

Results: In Group SB, a significant increase in power at a frequency of 80–150 Hz was observed in association with the bursts, particularly in the bilateral parieto-occipital derivations, in all patients. In Group TA, on the contrary, no significant increase in high-frequency power was found. The maximum frequencies of power enhancement were significantly higher in Group SB than in Group TA ($p < 0.001$ by repeated-measures ANOVA).

Conclusion: Interictal high frequencies of up to 150 Hz were detected in the suppression-burst EEG patterns in epileptic encephalopathy in early infancy. Further studies will be necessary to identify the role of the interictal high-frequency activity in the pathophysiology of such early epileptic encephalopathy.

Keywords: High-frequency oscillations; Ohtahara syndrome; Early myoclonic encephalopathy; Tracé alternant; Time–frequency analysis

1. Introduction

Analysis of high-frequency oscillations (HFOs) beyond the gamma band has been enabled by the recent technical development of digital electroencephalography (EEG). Remarkably, HFOs are suggested to have a close relation with epileptogenicity and ictogenicity.

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Gamma activity in scalp EEGs has been reported in ictal EEGs associated with epileptic spasms (ESs) in West syndrome and with the interictal suppression-burst (SB) pattern in epileptic encephalopathy in early infancy [1–3]. Likewise, high-frequency activity >80 Hz has now been observed in scalp and cortical ictal EEGs of ESs [4–7], but it has not yet been clearly identified in association with the SB pattern.

The SB pattern in EEG characterizes epileptic encephalopathy during the neonatal period and early infancy including Ohtahara syndrome (OS) and early myoclonic encephalopathy (EME). The SB pattern and ES in series both consist of recurring bursts of activity, and it has already been indicated that there is a mutual transition between the ictal activity of ES and the bursts in peri-ictal SB, and that gamma activity is augmented in association with the change in EEG pattern from SB to the ictal activity of ES [2]. Hence the SB pattern is suggested to have a close relation with the generative mechanisms of ES.

We have therefore hypothesized that the bursts in SB, which are already known to be accompanied by activity occurring as high as the gamma band, may be associated with the generation of high-frequency activity >80 Hz that is not readily visible through ordinary analysis. To prove this hypothesis, we attempted to use a statistical time-frequency analysis method that we had developed for the analysis of high-frequency changes associated with intracranially recorded epileptic discharges [8,9]. In addition, we similarly analyzed the EEG pattern known as tracé alternant (TA), which occurs during quiet sleep in neonates, for comparison in order to exclude the possibility that the generation of high frequencies may be a non-specific finding associated with any type of cyclic bursting pattern during the neonatal period and early infancy.

2. Subjects and methods

2.1. Patients

Subjects with the SB pattern in EEG (Group SB) were a total of six patients at 44–55 weeks post-conceptional age (the sum of gestational age and chronological age), comprising three with OS and three with EME. The onset of both OS and EME is very early, typically under three months of age, and occurs most commonly in the neonatal period. OS is characterized by (1) epileptic spasms (tonic spasms) with or without clustering, though additional partial seizures and rare myoclonus may occur in some patients, (2) consistent appearance of SB with regular periodicity in both waking and sleep EEGs, and (3) heterogeneous etiologies including brain malformations and gene mutations; EME is characterized by (1) fragmentary myoclonia as the main seizure type, (2) partial seizures, (3) later appearance of massive myoclonia or epileptic spasms, (4) SB which may present only during sleep or be most prominent during sleep, and (5) unknown etiology though genetic or metabolic origins have been suggested [10–12].

Subjects whose TA in EEG was observed for comparison (Group TA) were nine newborns at 36–43 weeks of post-conceptional age who were being examined with EEG for various reasons including low birth weight, fetal hydrops, cerebral ventricular dilatation, neonatal convulsions, intraventricular hemorrhage, and agenesis of the corpus callosum. The patients with the SB pattern are indexed by numbers with the prefix S and those with TA by numbers with the prefix T (Table 1).

We are aware that comparison between SB and TA is not ideal because the ages of the patients are different, but we undertook this comparison to achieve a methodological confirmation which would otherwise have been impossible.

2.2. EEG recording and analysis

EEG was recorded with a sampling rate of 500 Hz using the Nihon-Kohden (Tokyo, Japan) Neurofax digital EEG system. The international 10–20 electrode placement system was used, and the analysis was performed in each of the following bipolar channel-pairs: F3-C3, F4-C4, P3-O1, and P4-O2.

Both the SB pattern and the TA pattern were recorded during quiet/non-REM sleep. We then visually selected 20 typical artifact-free consecutive burst sections and 160 inter-burst sections from the sleep record of each patient for the time–frequency analysis described below. Each burst section was a 3 s segment of EEG data, as it included not only the 1 s onset part of the burst but also 2 s of the inter-burst period immediately before the burst. Every burst section was manually selected using the moment of the burst's onset as a trigger. Each inter-burst section included a non-overlapping low-amplitude EEG epoch lasting 512 ms.

A representative EEG trace showing the SB pattern recorded from Patient S2 with OS is depicted in Fig. 1A: bursts of bilaterally diffuse irregular high amplitude slow waves containing spikes with a duration of 1–2 s periodically repeated with intervals of low amplitude suppression phase lasting for 3–4 s each.

A representative EEG trace of TA recorded from Patient T4 with ventricular dilatation observed in the prenatal period is shown in Fig. 1B: bursts of diffuse slow waves containing some sharp transients occurred periodically and lasted for a few seconds each with relatively low amplitude intervals. In TA, compared with the SB pattern, bursting slow waves were not very high in amplitude and lacked truly epileptic discharges, and activity during the relatively long inter-burst intervals was not flat.