Publication V

Vanhatalo S, Tallgren P, Andersson S, Sainio K, Voipio J, Kaila K. DC-EEG discloses prominent, very slow activity patterns during sleep in preterm infants. Clinical Neurophysiology, 2002, 113:1822-1825.

"Oppikirjan julkaiseminen on päivän kunnia ja loppuelämän häpeä.

Väitöskirja on päivän häpeä mutta loppuelämän kunnia."

tuntematon

Expedited communication

DC-EEG discloses prominent, very slow activity patterns during sleep in preterm infants

S. Vanhatalo[a,b,*], P. Tallgren[a], S. Andersson[c], K. Sainio[d], J. Voipio[a], K. Kaila[a]

[a]*Department of Biosciences, University of Helsinki, Helsinki, Finland*
[b]*Department of Child Neurology, Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland*
[c]*Department of Pediatrics, Hospital for Children and Adolescents, University of Helsinki, Helsinki, Finland*
[d]*Department of Clinical Neurophysiology, University of Helsinki, Helsinki, Finland*

Abstract

Objectives: The objective of this study is to test the hypothesis that the immature human brain exhibits slow electrical activity that is not detected by conventional (i.e. high-pass filtered) electroencephalography (EEG).

Methods: Six healthy preterm infants (conceptional age 33–37 weeks) were recorded bedside with direct current (DC) EEG during sleep. Epochs with quiet sleep were selected to study the delta frequency bursts during discontinuous EEG patterns (*trace discontinu or trace alternant*), and we compared the waveforms obtained without filtering (i.e. genuine DC-EEG) to those seen after high pass filtering of the same traces.

Results: In all infants, DC-EEG demonstrated that the typical delta frequency bursts are consistently embedded in very large amplitude (200–700 μV) and long lasting (1–5 s) occipitally negative transients, which are not seen in conventional EEG.

Conclusions and significance: Our study demonstrates that (i) the most prominent spontaneous EEG activity of a sleeping preterm infant consists of very slow, large amplitude transients, and (ii) the most salient features of these transients are not seen in conventional EEG. Proper recording of this type of brain activity by DC-EEG provides a novel way for non-invasive assessment of neonatal brain function. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Direct current-electroencephalograph; Sleep; Preterm infants

1. Introduction

A major feature of electroencephalographic (EEG) activity in the immature brain is the abundance of slow activity, which is gradually replaced by higher frequencies (Scher, 1998; Watanabe et al., 1999; Lamblin et al., 1999; Niedermeyer, 1999). Due to high-pass filtering (usually at 0.5 Hz), conventional clinical EEG distorts slow activity patterns and hence leads to a change in their visual appearance. Slow EEG events can be faithfully monitored with direct current (DC) stable electrodes and a DC-coupled amplifier, which enable recordings with a bandwidth beginning from 0 Hz (Bauer et al., 1989; Speckmann and Elger, 1999). So far, no DC-EEG studies have been published on human infants. This study was set out to test the hypothesis that the immature human brain exhibits slow activity that is not detectable with conventional EEG. We analyzed specifically discontinuous EEG patterns (*trace discontinu or trace alternant*; hereafter commonly referred to as TA) during quiet sleep in preterm infants, since these consist of clearly identifiable episodes with a well-established dominance of slow frequency waves (Lamblin et al., 1999; Niedermeyer, 1999).

2. Methods

Six neurologically healthy, preterm infants at conceptional age from 33 to 37 weeks (35.5 ± 1.8 weeks (SD), and postnatal age 2–4 weeks) were recorded. All recordings were made after feeding, and the children slept during most of the time. The DC-EEG was recorded from the scalp using a custom-designed DC-EEG amplifier (long-term stability better than 1 μV/h, bandwidth 0-160 Hz, amplitude resolution 2.4 μV, high input impedance differential preamplifiers equipped with circuits for automatic electrode offset voltage compensation and testing of electrode-skin contact impedance) with 4–8 electrodes referenced to mastoids, and the ground electrode placed on
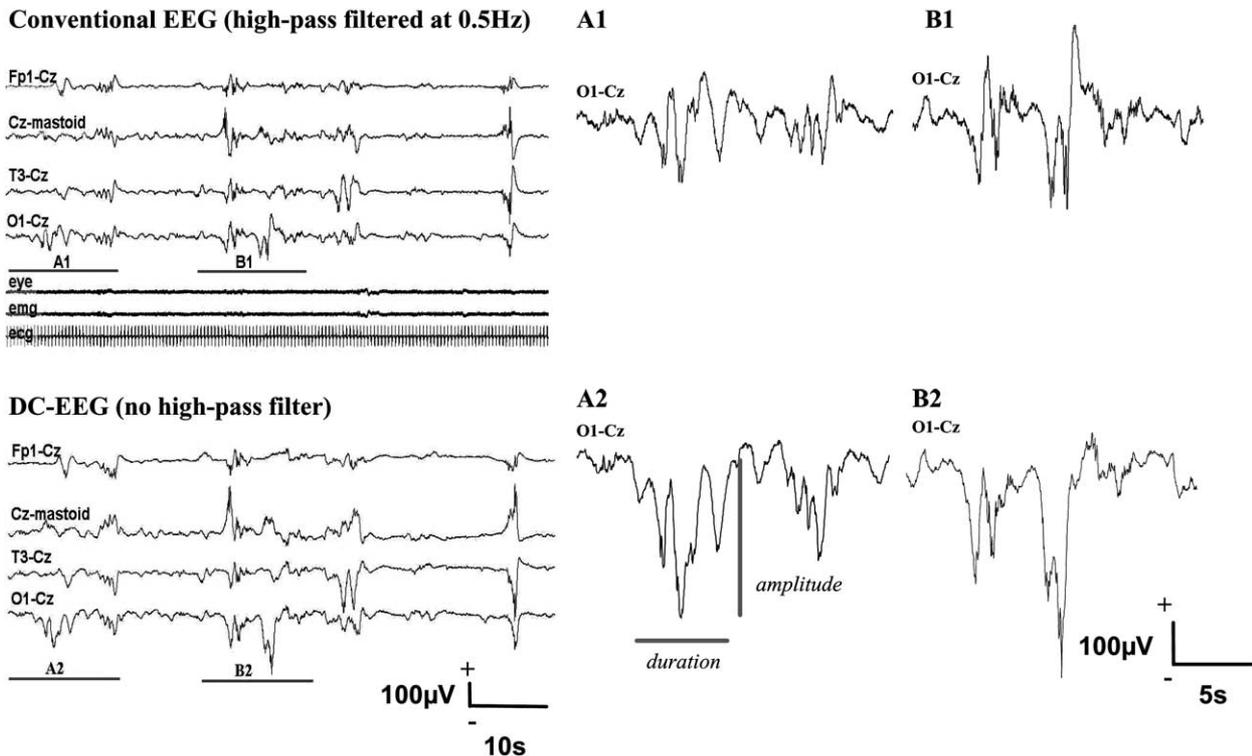
Fig. 1. Discontinuous EEG activity of an infant at 33 weeks of conceptional age. All traces are from the same recording. Traces on the left are 60 s epochs with either conventional EEG settings or DC-EEG. In the right column there are 15 s epochs (O1–Cz) taken from depicted locations (A and B, respectively). Note the prominent large negative (downwards) transients in the DC-EEG. Bars in the inset show an example of how the amplitude and duration were defined from the transients.

the forehead. Due to the height of the electrode holders (8 mm) most recordings were made unilaterally. In addition, 3 polygraphic channels (EKG, eye movement, and submental EMG electrodes) were recorded and the child's behavior was continuously observed in order to identify sleep stages. We used Ag/AgCl electrodes (type LP220, In Vivo Metric, CA, USA) with $12 \, mm^2$ of active area mounted in a plastic cup. A separate electrode holder lifted the electrode surface 6 mm above the skin level forming a closed space that was filled with electrode gel (Berner Ltd, Helsinki, Finland). The large volume of the gel in the electrode cup and holder, and the tight contact of the holder with the skin beneath prevented the electrode gel from drying which is imperative to avoid drifts generated by changes in junction potentials (Geddes and Baker, 1968). The skin beneath the electrodes was scratched to abolish skin-generated potentials (Picton and Hillyard, 1972; Wallin, 1981). Signals were acquired at 500 Hz by a 12 bit data acquisition card and computer. The software for data recording and analysis was programmed under Labview (National Instruments, Austin, Texas, USA).

The recorded EEG segments with TA activity were analyzed both by DC-EEG (i.e. without high-pass filters) and by using conventional EEG filter settings (i.e. with 0.5 Hz high-pass filter). High-pass filtering of DC-EEG signal was performed with a digital infinite impulse response (IIR) type filter (roll off -20 dB/decade or -6 dB/octave). For closer analysis, we chose 120 clearly identifiable (Lamblin et al., 1999) TA transients (20 from each child) and measured their duration and amplitude. Duration of the transient was defined as the time when the trace was clearly deviated from the baseline, and the amplitude was the peak amplitude measured from the visually identified mean baseline (see Fig. 1).

Informed consent was obtained from the parents. This study was approved by the Ethics Committee of the Hospital for Children and Adolescents, Helsinki University Central Hospital.

3. Results

Technically successful DC-EEG traces with very little or negligible drift could be readily recorded at bedside. With a conventional EEG frequency response starting from 0.5 Hz, a typical TA transient consisted of an initial sharp wave, followed by large amplitude delta frequency waves (1–4 Hz) and higher frequencies (Fig. 1). However, removal of high pass filtering resulted in a marked change in the EEG waveform of the TA transients (Fig. 1): the most

prominent deflections were large, slow negative transients at the occipital and temporo-parietal derivations. The amplitude of these large slow waves in occipital derivations (O1 or O2 referred to Cz) ranged between 200 and 700 μV (mean 265 ± 60 μV), and their duration typically ranged from 1 to 5 s (3.2 ± 0.8 s). The overall form of the transients varied somewhat, but they always consisted of a very slow deflection with overriding faster (>1 Hz) waves. Thus, the difference between DC-EEG and conventional EEG was clearly evident in the overall shape and polarity of the transients. In the DC-EEG a typical transient was a pronounced slow negative wave with superimposed faster events at delta and higher frequencies. In contrast, conventional EEG mostly yielded series of waves that were symmetrically arranged over the baseline, and they visually resembled the delta waves seen riding on the large transient in DC-EEG.

4. Discussion

Our study demonstrates that DC-EEG recordings may be readily performed bedside on human infants, and that DC-EEG reveals a significant amount of slow activity patterns not detected by conventional EEG. The present findings raise a number of important issues that should be taken into account in neonatal EEG measurements. DC-EEG recordings reveal slow EEG activity without distorting the signals. Since high-pass filtering of slow waves gives rise to the generation of artefactual rebounds, such responses with a frequency below the high-pass cut-off frequency will be seen as multiple faster waves in conventionally-recorded EEG.

The above considerations, and the data shown in Fig. 1 raise the obvious concern that the visually identified delta activity in conventional recordings of neonatal EEG is a part of a large, monophasic signal. From a purely neurophysiological point of view this is probably more interesting than from a clinical one. This is because clinical practice is mostly based on subjective pattern recognition of EEG recordings and their comparison to the subject's clinical state, a procedure that is perhaps not markedly misled by systematic signal distortion. However, the striking abundance of the very slow EEG patterns raise a need to explore their potential importance in a clinical context as well.

As genuine DC-EEG amplifiers are not yet commonly used in clinical practice, it would be of potential importance to be able to record these slow EEG events using more conventional EEG techniques. Reasonable recording of slow EEG transients of the kind described presently is, of course, theoretically possible if the time constant of the AC amplifier is sufficiently long (with a minimum of tens of seconds for the transients studied here) and if the electrode/skin coupling is DC stable (reversible electrodes plus short circuiting of skin responses). However, without previous empirical information – based on genuine DC-EEG – about the inherent temporal characteristics of a particular type of slow EEG signal, it will be impossible to judge a priori whether a given AC-EEG recording system even with a long time constant will fully cover the relevant frequency band. One should note here also that most clinical EEG amplifiers have time constants that can be set to a maximum of 1–10 s, which precludes accurate recordings of any kinds of transients with a duration of several seconds.

In conclusion, the preterm infant brain exhibits pronounced, very slow activity patterns with main frequencies much lower than what can be recorded using standard clinical EEG (Lamblin et al., 1999). In this context, it is intriguing to note the similarities between the slow activity observed in this study and the synchronous neuronal activity described in animal experiments which is thought to play a major role in the functional and structural shaping of neuronal circuitries in immature brain tissue (Penn and Shatz, 1999; Garaschuk, et al., 2001). Abnormal spontaneous activity is likely to underlie many common neurodevelopmental disorders (Penn and Shatz, 1999), and the clinical EEG diagnosis of several acquired neonatal brain disorders is based on findings of altered spontaneous activity (Scher, 1998; Watanabe et al., 1999). Hence, the DC-EEG technique may open new avenues for the assessment of both physiological and pathophysiological aspects of neonatal brain functions.

References

Bauer H, Korunka C, Leodolter M. Technical requirements for high-quality scalp DC recordings. Electroenceph clin Neurophysiol 1989;72:545–547.

Garaschuk O, Linn J, Eilers J, Konnerth A. Large-scale oscillatory calcium waves in the immature cortex. Nat Neurosci 2001;3:452–459.

Geddes LA, Baker LE. Principles of applied biomedical instrumentation, New York, NY: Wiley, 1968.

Lamblin MD, Andre M, Challamel MJ, et al. Electroencephalography of the premature and term newborn. Developmental features and glossary. Neurophysiol Clin 1999;29:123–219.

Niedermeyer E. Maturation of the EEG: development of waking and sleep patterns. In: Niedermeyer E, Lopes da Silva F, editors. Electroencephalography: basic principles, clinical applications, and related fields, 4th ed. Baltimore, MD: Williams and Wilkins, 1999. pp. 15–27.

Penn AA, Shatz CJ. Brain waves and brain wiring: the role of endogenous and sensory-driven neural activity in development. Pediatr Res 1999;45:447–458.

Picton TW, Hillyard SA. Cephalic skin potentials in electroencephalography. Electroenceph clin Neurophysiol 1972;33:419–424.

Scher MS. Understanding sleep ontogeny to assess brain dysfunction in neonates and infants. J Child Neurol 1998;13:467–474.

Speckmann E-J, Elger CE. Introduction to the neurophysiological basis of the EEG and DC potentials. In: Niedermeyer E, Lopes da Silva F, editors. Electroencephalography: basic principles, clinical applications, and related fields, 4th ed. Baltimore, MD: Williams and Wilkins, 1999. pp. 15–27.

Wallin BG. Sympathetic nerve activity underlying electrodermal and cardiovascular reactions in man. Psychophysiology 1981;18:470–476.

Watanabe K, Hayakawa F, Okumura A. Neonatal EEG: a powerful tool in the assessment of brain damage in preterm infants. Brain Dev 1999;21:361–372.