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Spatial patterning of the neonatal EEG suggests a need for a high number of electrodes

Maryam Odabaee [a], Walter J. Freeman [b], Paul B. Colditz [a], Ceon Ramon [c,d], Sampsa Vanhatalo [a,e,f,*,1]

[a] The University of Queensland Perinatal Research Centre and UQ Centre for Clinical Research (UQCCR), Royal Brisbane and Women's Hospital, Brisbane, Australia
[b] Department of Molecular and Cell Biology, University of California at Berkeley, CA 94720, USA
[c] Department of Electrical Engineering, University of Washington, Seattle, WA 98195, USA
[d] Department of Bioengineering, Reykjavik University, Reykjavik University, Iceland
[e] Department of Children's Clinical Neurophysiology, Helsinki University Central Hospital, Helsinki, Finland
[f] Department of Neurological Sciences, University of Helsinki, Finland

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ABSTRACT

There is an increasing demand for source analysis of neonatal EEG, but currently there is inadequate knowledge about i) the spatial patterning of neonatal scalp EEG and hence ii) the number of electrodes needed to capture neonatal EEG in full spatial detail. This study addresses these issues by using a very high density (2.5 mm interelectrode spacing) linear electrode array to assess the spatial power spectrum, by using a high density (64 electrodes) EEG cap to assess the spatial extent of the common oscillatory bouts in the neonatal EEG and by using a neonatal size spherical head model to assess the effects of source depth and skull conductivities on the spatial frequency spectrum.

The linear array recordings show that the spatial power spectrum decays rapidly until about 0.5–0.8 cycles per centimeter. The dense array EEG recordings show that the amplitude of oscillatory events decays within 4–6 cm to the level of global background activity, and that the higher frequencies (12–20 Hz) show the most rapid spatial decline in amplitude. Simulation with spherical head model showed that realistic variation in skull conductivity and source depths can both introduce orders of magnitude difference in the spatial frequency of the scalp EEG.

Calculation of spatial Nyquist frequencies from the spatial power spectra suggests that an interelectrode distance of about 6–10 mm would suffice to capture the full spatial texture of the raw EEG signal at the neonatal scalp without spatial aliasing or under-sampling. The spatial decay of oscillatory events suggests that a full representation of their spatial characteristics requires an interelectrode distance of 10–20 mm.

The findings show that the conventional way of recording neonatal EEG with about 10 electrodes ignores most spatial EEG content, that increasing the electrode density is necessary to improve neonatal EEG source localization and information extraction, and that prospective source models will need to carefully consider the neonatally relevant ranges of tissue conductivities and source depths when source localizing cortical activity in neonates.

Introduction

Recent work in neuroimaging (Dudink et al., 2012; Fransson et al., 2011; Lodygensky et al., 2010) and in developmental neurobiology (Colonnese and Khazipov, 2012; Hanganu-Opatz, 2010; Vanhatalo and Kaila, 2010) has made it clear that brain functions are already highly specialized early in development. Functional assessment of neonatal brain activity is currently severely hampered by the poor spatial resolution provided by conventional neonatal EEG recording (Andre et al., 2010), which hardly suffices to distinguish brain lobes from each other. In order to meet the need for better spatial parcellation, several methods have been recently devised to enable recording of high density EEG (hdEEG) from the neonatal head in the laboratory environment (Fifer et al., 2006; Roche-Labarbe et al., 2008; Vanhatalo et al., 2008), and even in the neonatal intensive care unit (Stjerna et al., 2012; Vanhatalo et al., 2008).

The theoretical benefits of increasing the number of recording electrodes are clear (see e.g. Grieve et al., 2003, 2004). Improved spatial

Abbreviations: EDF, European Data Format; hdEEG, high density EEG; PSDx, spatial power spectral density; PSDt, temporal power spectral density; SAT, spontaneous activity transient.

* Corresponding author at: Department of Clinical Neurophysiology, Children's Hospital, Helsinki University Hospital, PO Box 280, FIN-00029 HUS, Finland.
E-mail address: sampsa.vanhatalo@helsinki.fi (S. Vanhatalo).
[1] Current address: Perinatal Research Centre, University of Queensland Center for Clinical Research (UQCCR), Royal Brisbane and Women's Hospital (RBWH), Herston 4029, Australia.

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resolution obtained from a higher number of electrodes has made it possible to record cerebral activities that were previously not known, or were difficult to localize (e.g. Scherg et al., 2002; Tucker et al., 2007). Most importantly, an increase in spatial sampling has opened the pathway to a genuine source localization of neonatal EEG (Beauchemin et al., 2011; Despotovic et al., 2012; Roche-Labarbe et al., 2008), akin to what is routinely done with adult EEG already.

It is intriguing in this context, that we do not know how much EEG information can be obtained from the baby scalp. This richness in amplitude texture can be perceived as "spatial patterning" of the neonatal scalp EEG (hereafter referred to as "spatial patterning"), and it has been measured in adults by estimating the spatial frequency content of the scalp EEG (Freeman et al., 2003; Srinivasan et al., 1998). This would be a necessary piece of information to define the number of EEG electrodes that are needed to record the brain activity in full detail, to estimate the errors related to the conventional under-sampling of EEG (see also Grieve et al., 2004), as well as to aid in constructing realistic forward and inverse solutions for neonatal EEG source localization. The spatial resolution of scalp EEG signals is impaired by smearing due to the scalp and skull. Because these barriers are of lower impedance in infants, the degradation is much less severe (see also Despotovic et al., 2012), so information about brain function is more accessible, and detailed spatial information should be readily measureable from the scalp (Grieve et al., 2003, 2004).

In this study, we explored the spatial patterning of neonatal EEG by using recordings with an ultrahigh density linear array (2.5 mm interelectrode distance) and high density (64 channel) EEG caps in healthy newborn babies. Our aim was to address two fundamental, complementary questions: i) How complex is the EEG amplitude on the neonatal scalp? and ii) How large are the oscillatory bouts measured on the neonatal scalp?

Methods and materials

The study consists of three complementary parts. The first part uses a custom-fabricated linear array of electrodes (see also Freeman and Quian Quiroga, in press; Freeman et al., 2003) to obtain a theoretical estimate of the spatial EEG patterning in selected scalp locations. The second part uses a commercial high density (hdEEG, 64 channels) EEG cap in order to estimate the spatial extent of focal fluctuations of amplitudes, and to estimate the "practical" spatial EEG extent ("patterning") from oscillatory events in the neonatal EEG (Andre et al., 2010; Vanhatalo and Kaila, 2006 and 2010; Khazipov and Luhmann, 2006). These events appear as short bursts of higher frequency activity, often nested (Vanhatalo et al., 2005) within slow waveforms and have multiple names related to their visual appearance (e.g. delta brush, however see Table 1 in Vanhatalo and Kaila, 2010 for further considerations). In the third part, we employd a spherical head model with neonatal dimensions to see i) whether our empirically measured spatial power spectral density (PSDx) can be reproduced by using a simple parametric model, and ii) how skull layer conductivity or source depth affect the PSDx. These aimed to pilot the pathway to translate our results into future realistic head models.

Subjects and recordings

Subjects

EEG recordings were obtained from term newborns ($n=2$ for the linear array study; $n=5$ for the hdEEG recordings). EEG data were recorded in the Department of Children's Clinical Neurophysiology (Helsinki University Central Hospital) using a Cognitrace amplifier with sampling rate of 256 Hz or 512 Hz and an inbuilt average reference (ANT B.V., Enschede, The Netherlands, www.ant-neuro.com). 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.

Linear array recording

A linear electrode array was custom made by embedding 50 electrode pins (material Ag/AgCl; diameter 1 mm; obtained from Biomed Product, USA) into a silicone strip with a 2.5 mm interelectrode distance (Fig. 1). The linear array was interfaced with the amplifier using a flat cable attached to a standard DB37 connector. Additional ground and reference electrodes were added as conventional cup electrodes (material Au), placed on the opposite side of the head. The scalp was cleaned and dried, and the array was lightly bound over either the parietal or occipitoparietal scalp or over the fontanel (extending from about POz position along the midline to fontanel).

hdEEG recording

Sixty-four channel hdEEG caps were used (Waveguard, ANT B.V., Enschede, The Netherlands, www.ant-neuro.com; see also Stjerna et al., 2012). A video clip showing an EEG recording of this kind is shown in the link www.nemo-europe.com/en/educational-tools.php.

Data analysis

Linear array experiment

Lack of gel (as in conventional EEG recordings) and the poor mechanical stability of the electrode–skin interface created a challenge for obtaining signal segments that were clean enough from artefacts. We selected epochs where there were more than twenty adjacent electrodes with sufficiently clean signal. Altogether 54 s of such EEG from seven different time windows were identified ((range 1.1–19 s; mean length 7.7 s. An *n* epoch is shown in Fig. 1. Epochs were exported in EDF format for further analysis after bandpass filtering at 3–30 Hz to remove mains-related artefacts and trace instability due to mechanical movements.

Single missing traces (for an example, see Fig. 1C; traces #19 and #48) were interpolated using nearest two neighbouring channels, which introduces a spatial lowpass filter, and hence a small but unavoidable underestimation of the higher spatial frequencies. Then, PSDx was calculated from the vectors created from the signal values across the channels at each sampling (see Fig. 1D; see also Freeman et al. (2003). Due to the EEG sampling frequency, this results in 256 PSDx traces per second. We then calculated the median value of each spatial frequency bin from each EEG epoch.

The use of spatial frequency spectrum to estimate the optimal electrode density (i.e. spatial frequency) can be considered analogous to the common use of temporal frequency spectrum (PSDt) to estimate the required (temporal) sampling frequency of the EEG signal. The canonical form of the spatial spectrum is three segments: a flat low-frequency segment, a middle segment with rapid fall in power with increasing frequency, and a flat high-frequency segment resembling that of white noise (see Freeman et al., 2000). Most of the desired information is contained in the middle segment between two inflections. The first step is to define the point in the spectrum where it reaches the noise floor (termed the "upper inflection point" in Results) and gives the upper end of the frequency range that should ideally be captured. The second step is to calculate the number of electrodes with the specified interelectrode spacing that are needed to sample the entire range of spatial frequency (Freeman et al., 2003; Srinivasan et al., 1998). The lower inflection point gives an estimate of the desired width of the array. According to the Nyquist theorem, more than two samples are required to capture each cycle at the highest frequency and preferably three samples are required for the "practical" Nyquist frequency). The width of the array must be great enough to encompass at least one cycle of the lowest spatial frequency. In the temporal domain, these would be cycles per second (or Hz) and recording duration in seconds, whilst in the spatial domain they are cycles per centimeter and dimensions of an array in cm. For instance, in the case of 1 cycle/cm, one should have at least two electrodes in each centimeter (i.e. 5 mm interelectrode spacing) to sample adequately the given spatial pattern in EEG oscillation. The product of the sampling frequency in number