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Neonatal EEG at scalp is focal and implies high skull conductivity in realistic neonatal head models

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ABSTRACT

The potential improvements in spatial resolution of neonatal EEG used in source localization have been challenged by the insufficiencies in realistic neonatal head models. Our present study aimed at using empirical methods to indirectly estimate skull conductivity; the model parameter that is known to significantly affect the behavior of newborn scalp EEG and cause it to be markedly different from that of an adult. To this end, we used 64 channel EEG recordings to study the spatial specificity of scalp EEG by assessing the spatial decays in focal transients using both amplitudes and between-c'hannels linear correlations. The findings showed that these amplitudes and correlations decay within few centimeters from the reference channel/electrode, and that the nature of the decay is independent of the scalp area. This decay in newborn infants was found to be approximately three times faster than the corresponding decay in adult EEG analyzed from a set of 256 channel recordings. We then generated realistic head models using both finite and boundary element methods along with a manually segmented magnetic resonance images to study the spatial decays of scalp potentials produced by single dipole in the cortex. By comparing the spatial decays due to real and simulated EEG for different skull conductivities (from 0.003 to 0.3 S/m), we showed that a close match between the empirical and simulated decays was obtained when the selected skull conductivity for newborn was around 0.06–0.2 S/m. This is over an order of magnitude higher than the currently used values in adult head modeling.

The results also showed that the neonatal scalp EEG is less smeared than that of an adult and this characteristic is the same across the entire scalp, including the fontanel region. These results indicate that a focal cortical activity is generally only registered by electrodes within few centimeters from the source. Hence, the conventional 10 to 20 channel neonatal EEG acquisition systems give a significantly spatially under sampled scalp EEG and may, consequently, give distorted pictures of focal brain activities. Such spatial specificity can only be reconciled by appreciating the anatomy of the neonatal head, especially the still unossified skull structure that needs to be modeled with higher conductivities than conventionally used in the adults.

Introduction

Recent advances in developmental neuroscience as well as in medical care of preterm and ill infants have significantly increased the interest in functional brain assessment. Brain activity in babies is most reliably recorded with neonatal EEG. It is now known, however, that the conventional recording configuration with only 6–10 electrodes (André et al., 2010) does hardly suffice to distinguish brain lobes from each other, making its spatial information content severely compromised (Grieve et al., 2004; Odabaee et al., 2013 see also Zwiener et al., 1991). A better spatial parcellation has been recently attempted by devising various means to record high density EEG (hdEEG) from the neonatal head in the laboratory environment (Fifer et al., 2006; Grieve et al., 2008; Odabaee et al., 2012; Roche-Labarbe et al., 2008), and even in the neonatal intensive care units (Stjerna et al., 2012; Vanhatalo et al., 2008; Welch et al., 2013).

Increasing the number of recording electrodes leads to clear theoretical benefits, including recognition of cerebral activities that may, otherwise, go unnoticed or unlocalized. Most importantly, higher electrode number (ie. increased spatial sampling) opens a possibility for genuine

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source localization of neonatal EEG (Beauchemin et al., 2011; Despotovic et al., 2012; Roche-Labarbe et al., 2008).

Recent studies have showed that neonatal/infant scalp EEG has a very high spatial content, or spatial patterning (Grieve et al., 2004; Odabaee et al., 2013). Those works confirm the idea that adding more electrodes would add non-redundant information, however they also show implicitly that spatial smearing of scalp EEG is substantially lower in the neonates (Odabaee et al., 2013) than in the adults (Freeman Walter et al., 2003; Srinivasan et al., 1998a,b). This notion has far reaching implications: The salient low spatial smearing in the neonatal EEG means that the conductive pathways from the cortex (the generator) to the scalp electrodes need to be significantly different in babies compared to adults. An obvious difference is the head geometry where tissue layers are thinner in newborns. The shorter cortex–electrode distance is, by itself, unlikely to explain the observed differences in spatial smearing which in the adults is commonly considered to arise from the poorly conductive skull layer.

Histological comparison of cranial tissues in infants and adults showed that the skull layer undergoes a significant development from the soft and relatively wet, unossified skull matrix (Silau et al., 1995) to a hard and relatively dry (ossified) adult skull bone. It is very conceivable that this histological difference would imply higher skull conductivity and hence less spatial smearing in the neonates. It is not known, however, what skull conductivity values would be plausible in the neonatal EEG source localization. While electric impedance tomography has been developed to provide potential alternative paradigm for empirical estimation of in vivo tissue conductivities in humans (Esler et al., 2010; Turovets et al., 2008), we are not aware of any experimental configurations how conductivity of live human neonatal skull could be measured directly. Skull conductivities have been studied in animal neonates (Pant et al., 2011), but those results cannot be used for human because of the marked differences in the cranial histology in the early development. Studies with EEG source localization of human neonatal EEG (Despotovic et al., 2012; Roche-Labarbe et al., 2008) have avoided the issue by simply adopting conductivity values from prior adult literature, however the lack of empirical reference makes interpretation of those results difficult.

This study was set out to define suitable range of values for neonatal skull conductivity by combining empiric measures of spatial spreading in the neonatal EEG with forward simulations using realistic neonatal head models. We aimed to answer two questions: First, what is the extent of spatial correlations in the neonatal EEG signal? Second, by comparing this information to forward simulations with a realistic neonatal head model, what levels of skull conductivity could explain such spatial correlation in the neonatal scalp EEG?

Methods and materials

The study consists of two complementary parts, one empirical and the other based on simulations. The empirical part uses high density EEG (hdEEG) recordings to analyse spatial decays in signal amplitudes and correlations in the neonatal and adult EEG. The simulation part uses a realistic newborn head model to compute scalp potentials (forward solution) generated by discrete cortical dipoles mimicking cortical sources of focal transients in the real EEG. The simulations were computed for different skull conductivities to find the range of skull conductivity values capable of explaining the empiric observations.

Subjects and hdEEG recording

Four hdEEG recordings were acquired from four different newborns at term age in the Department of Children's Clinical Neurophysiology (Helsinki University Central Hospital) using a Full-band EEG (Vanhatalo et al., 2005) acquisition system with sampling rate of 256 Hz or 512 Hz (Cognitrace; ANT B.V., Enschede, The Netherlands, www.ant-neuro.com). We used a 64 channel hdEEG caps tailored for neonates (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 can be seen by following the link www.nemo-europe.com/en/educational-tools.php. Informed consent was obtained from the parents prior to recordings. This study was approved by the Ethics Committee of the Hospital for Children and Adolescents, Helsinki University Central Hospital.

The four adult EEG recordings used in this study were kindly provided by Dr. German Gomeq-Herrero. They were recorded with a 256-channel EEG system (Geodesic Inc, www.egi.com) for unrelated studies in VU University of Amsterdam, The Netherlands.

Preprocessing and electrode grouping

Preprocessing

The data was first inspected visually using the ASA review software (ANT B.V. Enschede, The Netherlands). Artifact free epochs were selected irrespective of the sleep state. Data was then filtered with a 30 Hz lowpass FIR filter prior to exporting it into European Data Format (EDF). All data was processed using common average reference. Further analysis was performed in MATLAB (MathWorks, Natick, Massachusetts, U.S.A) environment using customized scripts described below.

Electrode grouping

In our initial analysis, we wanted to assess whether decays in EEG spatial correlation and/or EEG amplitudes depend on the scalp area. This is particularly important in neonates where fontanel, a wider skull opening in the midline, is often claimed without evidence to distort the scalp EEG potentials. To investigate this, we compared spatial decays among three groups of electrodes (see Fig. 1C): Group 1 electrodes included those located above the confluent layers of the skull over central–parietal–temporal–occipital regions. Group 2 constituted the midline electrodes that always stand above or at the edges of the fontanel. Group 3 electrodes were those in the frontal region where the skull layer is mostly closed, but the frontal EEG phenomena are separated from other brain areas in the neonates (André et al., 2010). When performing a within group analysis, we only computed amplitude/correlations among electrodes that belonged to the same group (eg. group 2 decay did only reflect decay of amplitude/correlation along the midline). Finally, we also grouped all electrodes together and computed spatial decays in all directions irrespective of its initial grouping.

Analysis of spatial amplitude decay

Focal transients are a common and salient occurrence in both normal and abnormal neonatal EEG (André et al., 2010; Castro Conde et al., 2004; Okumura et al., 2003). They are characterized by a short and relatively sharp appearance and spatial distribution that is consistent with an underlying cortical origin. In this study, focal transients were marked by a board certified EEGer (S.V.) using the ASA review software, and further analysis was performed using MATLAB. The electrode with the highest amplitude peak at the marked location was chosen as the reference electrode, and all potential values from other electrodes were plotted as a function of distance from this reference electrode. Notably, reference electrode in this context means the electrode that was plotted at location zero in the spatial decay graphs (see Figs. 1 and 2), and it is not to be confused with the recording reference which in our study was grand average. This procedure was repeated for all focal transients, which yielded a total of 110 transients (group 1 $n = 38$; group 2 $n = 21$; group 3 $n = 51$). Finally, a linear regression was computed over the nearest 5 cm (for newborns) or 10 cm (for adult) from the index electrode. Electrodes whose amplitudes were found to be >90% of the reference value were excluded from further analysis in order to mitigate the effects of noise and other artifacts (see also Discussion).