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Corticokinematic coherence as a new marker for somatosensory afference in newborns

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HIGHLIGHTS

- We analyzed coherence between EEG and passive finger and wrist movements in newborns.
- In all newborns, EEG of the contralateral central scalp was coherent with the movements.
- Passive movements could be used to assess somatosensory function in neonatal intensive care.

ABSTRACT

Objective: Somatosensory evoked potentials have high prognostic value in neonatal intensive care, but their recording from infants is challenging. Here, we studied the possibility to elicit cortical responses in newborns by simple passive hand movements.
Methods: We examined 13 newborns (postnatal age 1–46 days) during clinically indicated 19-channel electroencephalography (EEG) recordings in the neonatal intensive care unit; EEG indications included birth asphyxia and suspected epileptic seizures. The experimenter moved the infant's wrist or fingers at 1 or 2 Hz for 5–10 min, separately on both sides. We measured movement kinematics with an accelerometer attached to the infant's hand and computed coherence between the EEG and acceleration signals (corticokinematic coherence, CKC).
Results: Statistically significant CKC (amplitude 0.020–0.511) with characteristic scalp topography was observed in all infants at twice the movement frequency. CKC was contralaterally dominant on the central scalp (median laterality index 0.48 for right-hand and −0.63 for left-hand movements).
Conclusions: Passive movements elicit cortical responses that can be readily observed in clinical EEG recordings from newborns in the intensive-care environment.
Significance: CKC is a novel, noninvasive marker for the somatosensory system. Its robustness and practical ease make it attractive for bedside assessment of neurologically compromised newborns.

1. Introduction

Improving early neurological care and later neurodevelopmental outcomes of infants with perinatal adversities is a key challenge (Marlow et al., 2005; Robertson and Finer, 1993) that would greatly benefit from practical and objective bedside methods for an early assessment of various aspects of the newborn's brain function. Somatosensory evoked potentials (SEPs) offer a reliable and robust method to address the functionality of afferent somatosensory pathways, and several recent studies suggest that SEPs can provide very early prediction of the outcome, for example, in hypoxic–ischemic encephalopathy (for reviews, see Kontio et al., 2013; Majnemer and Rosenblatt, 1996). However, the conventional method based on electric stimulation of the infant's median nerve

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requires considerable technical expertise, thus limiting the practical availability of SEPs to only few neonatal intensive care units (NICUs) (Vanhatalo and Lauronen, 2006).

Recent magnetoencephalographic (MEG) studies on healthy adults have demonstrated that somatosensory afference can be studied reliably also using a much simpler stimulation method: continuous passive movements. Cortical signals from the primary sensorimotor (SMI) cortex entrain to the movement pace, leading to measurable corticokinematic coherence (CKC) (Bourguignon et al., 2011, 2012; Piitulainen et al., 2013b, 2015). Whereas cortical somatosensory responses to electric nerve stimulation reflect mixed somatosensory input with both tactile and proprioceptive contributions, adult studies suggest that CKC represents mainly proprioceptive afference with only a minor tactile contribution (Bourguignon et al., 2015; Piitulainen et al., 2013b).

In the present study, our aim was to find out whether CKC can be detected reliably already in newborn infants. We carried out the recordings in the most demanding conditions, that is, in the noisy NICU environment as a part of clinically-indicated electroencephalography (EEG) recordings. Notably, this context would also have the highest clinical demand for CKC-based somatosensory assessment. To provide suggestions for future clinical work, we examined technical and practical requirements that would validate the utility of CKC as a part of clinical care.

2. Methods

The recordings were performed during clinically indicated EEG measurements in the NICU of the Children's Hospital of Helsinki University Hospital. This study was part of a project that develops novel diagnostics at the Department of Children's Clinical Neurophysiology, approved by the relevant Ethics Committee of the Children's Hospital.

2.1. Patients

We here present data from 13 patients (8 boys, 5 girls; gestational ages at birth from 31 + 1 to 41 + 6 weeks + days; postnatal age 1–46 days). A 14th infant had to be excluded due to deterioration of the EEG signals by excessive restlessness caused by her jitteriness after a hypoxic-ischemic insult. The most common indications for the EEG recordings in the group were birth asphyxia and suspected epileptic seizures. One infant (P11) suffered from Erb's paresis on the left side and another (P12) from clonus on the right side. The other infants did not show lateralized symptoms. Table 1 presents relevant details of the included infants.

2.2. Movement stimulation

A clinical neurophysiologist (co-author SV) moved the infant's hands during routine EEG recordings while the infant was asleep. The stimuli were unilateral, continuous, regular extension–flexion movements of all fingers or the palm, flexing at the metacarpophalangeal level or at the wrist, respectively. Fig. 1 shows the stimulation setup (see also Supplementary Video 1). The on-line accelerometer signals on the EEG display (Supplementary Fig. S1) gave the necessary visual feedback to help the experimenter maintain a sufficiently steady stimulation rhythm. In total, we were able to perform 36 stimulation runs (2–4 per infant), each with 5–10 min of movement at either 1 or 2 Hz. For one infant (P10), only the right hand could be stimulated due to extensive bandage covering the left hand. In the other infants, both hands were stimulated in separate runs. Table 1 summarizes the measurements for each infant.

2.3. Recordings

2.3.1. EEG

EEG signals were recorded with a NicoletOne™ EEG system (Natus Medical Inc., Pleasanton, CA, USA) and 19 sintered Ag/AgCl electrodes attached to an EEG cap (Waveguard™, ANT Neuro, Enschede, Netherlands). The recording passband was 0.053–500 Hz and the sampling rate 2000 Hz. EEG signals were acquired with reference to the Cz electrode.

2.3.2. Somatosensory evoked potentials (SEPs)

As part of the clinical EEG recordings, SEPs were gathered from 9/13 infants. The median nerve was stimulated with 0.2-ms constant-current pulses delivered once every 2 s for $\sim$10 min per side using a battery-powered portable electrical peripheral-nerve stimulator (ENERGY Light integrated stimulator, Micromed, Mogliano Veneto, Italy). The stimuli were delivered at the wrist with a pair of small disk electrodes separated by 2–3 cm (Supplementary Fig. S2). Stimulus intensity (range 9–25 mA) was individually adjusted to be just above the motor threshold. SEPs were recorded for clinical purposes and analyzed with BESA® Research (BESA GmbH, Gräfelfing, Germany). They were used in the current study only as additional neurophysiological data, and we will not elaborate on the details of their analysis (interested readers are referred to Nevalainen et al., 2015).

2.3.3. Acceleration

A 3-axis accelerometer (ADXL335 iMEMS Accelerometer, Analog Devices Inc., Norwood, MA, USA) with dedicated, in-house-made (Aalto NeuroImaging, Aalto University, Espoo, Finland), battery-powered electronics was used to record the kinematics of the passive movements. The accelerometer was attached to the infant's fingers that were firmly bound together with the sensor using elastic bandage. Acceleration signals were recorded on additional polygraph channels in the EEG data set, using the same passband and sampling rate as for the EEG signals.

2.4. Data preprocessing

2.4.1. EEG

Co-author SV, experienced in pediatric EEG, visually examined the EEG data and annotated major movement artifacts. Artifacts contaminated 0–127 s (mean 30 s) of the individual stimulation runs, thus leaving 4–10 min of clean data for the analysis. To improve spatial specificity of the EEG signals and to avoid the global influence of a single reference channel, we transformed the EEG from the Cz-referential recording to current-source-density representation with the spherical-spline surface-Laplacian algorithm (Perrin et al., 1989, 1990) as implemented by Kayser and Tenke (2006a,b). This procedure was considered appropriate as we did not attempt to model the sources of the EEG signals. All subsequent computations were performed on these transformed EEG signals.

2.4.2. Acceleration

First, acceleration signals were high-pass filtered at 0.5 Hz. Then, the Euclidean norm of the three orthogonal acceleration signals—representing the magnitude of acceleration—was computed to obtain one orientation-independent acceleration signal for the CKC analysis (Bourguignon et al., 2011). We chose to use the Euclidean norm as the orientation of the accelerometer varied slightly during the stimulation due to, for example, spontaneous position changes of the infants.