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BRAIN RESEARCH

Research Report

Neuromagnetic correlates of developmental changes in endogenous high-frequency brain oscillations in children: A wavelet-based beamformer study

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ABSTRACT

Recent studies have found that the brain generates very fast oscillations. The objective of the present study was to investigate the spectral, spatial and coherent features of high-frequency brain oscillations in the developing brain. Sixty healthy children and 20 healthy adults were studied using a 275-channel magnetoencephalography (MEG) system. MEG data were digitized at 12,000 Hz. The frequency characteristics of neuromagnetic signals in 0.5–2000 Hz were quantitatively determined with Morlet wavelet transform. The magnetic sources were volumetrically estimated with wavelet-based beamformer at 2.5 mm resolution. The neural networks of endogenous brain oscillations were analyzed with coherent imaging. Neuromagnetic activities in 8–12 Hz and 800–900 Hz were found to be the most reliable frequency bands in healthy children. The neuromagnetic signals were localized in the occipital, temporal and frontal cortices. The activities in the occipital and temporal cortices were strongly correlated in 8–12 Hz but not in 800–900 Hz. In comparison to adults, children had brain oscillations in intermingled frequency bands. Developmental changes in children were identified for both low- and high-frequency brain activities. The results of the present study suggest that the development of the brain is associated with spatial and coherent changes of endogenous brain activities in both low- and high-frequency ranges. Analysis of high-frequency neuromagnetic oscillation may provide novel insights into cerebral mechanisms of brain function. The noninvasive measurement of neuromagnetic brain oscillations in the developing brain may open a new window for analysis of brain function.

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1. Introduction

In the resting state, the brain generates a wide range of activities (Bragin et al., 1999). Some of these are probably behaviorally relevant, whereas others occur during pathological conditions such as seizures (Bragin et al., 1999). Low-frequency brain signals (<100 Hz) including delta (0.5–3 Hz), theta (4–7 Hz), alpha (8–12 Hz) and beta (12–30 Hz) activities have been found with electroencephalography (EEG) in the brain (Speckmann and Elger, 2005). Alpha activity is the most robust brain activity in the occipital region (Ramantani et al., 2006). In clinical practice, low-frequency brain signals have been used for the diagnosis of brain disorders, particularly, epilepsy for many decades (Epstein and Andriola, 1983). High-frequency brain signals (HFBS) (>100 Hz), also known as high-frequency oscillation, ripple or fast ripple are a recent discovery (Bragin et al., 2002). HFBS have been recorded from the normal brain in animals, for example, the brainstem, cuneothalamic relay neurons, thalamus, thalamocortical radiation, thalamocortical terminals and medial lemniscus (Mochizuki and Ugawa, 2005). HFBS have also been recorded in pathological conditions in human brains. For example, invasive recordings have confirmed that the epileptic brain generates HFBS (Alegre et al., 2006). It seems that HFBS warrant further investigation as new biomarkers for brain function.

The developmental pattern of HFBS in the child's brain has rarely been studied. It remains largely unclear how HFBS mature and become operative during brain development (Le Van et al., 2006). Conventional invasive recordings such as electrocorticogram (ECoG) may capture HFBS in surgical patients' brain. However, ECoG has very limited applications in the study of HFBS in healthy children. The available techniques for non-invasively measuring HFBS are EEG and magnetoencephalography (MEG). Although MEG and EEG have their own strengths and weaknesses, it is well recognized that MEG has the advantages of superior spatial localization (Papanicolaou et al., 2005) and analysis of coherences of brain activity (Srinivasan et al., 2007). The recent developments of magnetic signal processing technologies have made it possible to volumetrically localize high-frequency neuromagnetic signals (Xiao et al., 2006). Noticeably, to characterize the spatial and coherent patterns of brain activities, MEG is a potentially capable technology.

Recently, HFBS up to 1500 Hz have been found in the brain (Okada et al., 2005) and previously performed studies in our lab have determined that modern MEG systems have the capability to capture them (Kotecha et al., 2008). However, it remains unclear if the endogenous HFBS can be detected in the normal developing brain and how they change with age. In fact, we have not found any report on neuromagnetic signals up to 2000 Hz in the child's brain. From our point of view, the investigation of endogenous HFBS is essential and interesting. First, evoked HFBS have been identified in the brain and used for evaluating brain function (Crone et al., 2006; Gobbele et al., 1998; Murakami et al., 2008; Xiang and Xiao, 2008). Therefore, it is necessary to determine if there are endogenous HFBS. If there are endogenous HFBS, we need to determine how those spontaneous HFBS are related to the evoked HFBS. Second, HFBS have been identified in the brain with epilepsy and other disorders (Jacobs et al., 2009; Zijlmans et al., 2009). One logical question is: are those HFBS are physiological or pathological? This question is in urgent need of answers for the clinical management of epilepsy (Engel et al., 2008). Third, the maturational change of endogenous brain activity in high-frequency ranges remains unclear though it is critical for understanding the functional development of the brain (Le Van et al., 2006). To identify developmental delays or abnormalities with HFBS in various pathological conditions, the normal developmental pattern of HFBS is the corner stone. Consequently, it is of paramount importance to investigate the developmental changes of HFBS in the child's brain.

The objective of this study was to characterize the developmental patterns of the endogenous high-frequency neuromagnetic activities in the child's brain using MEG. To quantify the developmental patterns of the frequency, spatial and coherent features of high-frequency neuromagnetic signals, time-frequency analysis and spatial filtering (or beamformer) technologies were used in the present study. We hypothesized that the endogenous high-frequency brain activities in the developing brain had a measureable baseline that changed with age. It is anticipated that the normative patterns of HFBS will lay a foundation for identification of developmental delay and/or abnormalities in children with various brain disorders, such as epilepsy.

2. Results

2.1. *Spectrograms*

The outstanding neuromagnetic activity in the low-frequency range (0.5–100 Hz) was alpha activity (8–12 Hz). Neuromagnetic signals in this frequency range were identified for all participants (80/80, 100%). Delta (0.5–3 Hz) activity was identified for 54 participants (54/80, 68%). The neuromagnetic signals identified in other frequency bands including theta (4–7 Hz), beta (12–30 Hz), and gamma (30–100) activities were relatively weak (see Fig. 1).

High-frequency neuromagnetic signals were relatively weak as compared to low-frequency neuromagnetic signals. There were two clear components in 1040–1050 Hz and 1400–1600 Hz (see Fig. 2). However, since the magnetic signals in 1040–1050 Hz were also identified in our MEG tests without participants, the component in 1040–1050 Hz was considered as noise. The neuromagnetic signals in 1400–1600 Hz were very strong in 26 participants. Unfortunately, this component had a great inter-individual variation. In addition, it was localized to non-brain regions for eight participants. We considered that this component needed further investigation and confirmation. We found that neuromagnetic signals in 800–900 Hz were localized in the brain for 52 participants (52/80, 65%). Consequently, the component in 800–900 Hz was considered as the most robust brain activity in 100–2000 Hz. To statistically determine if the localization of the signals in 800–900 Hz in the brain was caused by true brain signals, we performed probability analyses. Assuming the localization error could be as much as 0.5 cm, the probability of random noise that was mistakenly localized to the brain was very

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