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Volumetric imaging of brain activity with spatial-frequency decoding of neuromagnetic signals

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HIGHLIGHTS

- Analyses of multi-frequency brain activity at the source level.
- A novel grid-frequency kernel for volumetric imaging of brain activity.
- Detection of high-frequency brain activity with a non-invasive MEG approach.
- Localization of bilateral auditory cortical sources with frequency signatures.
- Delineation of epileptogenic zones with high-frequency neuromagnetic signals.

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ABSTRACT

Background: The brain generates signals in a wide frequency range (~2840 Hz). Existing magnetoencephalography (MEG) methods typically detect brain activity in a median-frequency range (1–70 Hz). The objective of the present study was to develop a new method to utilize the frequency signatures for source imaging.
New method: Morlet wavelet transform and two-step beamforming were integrated into a systematic approach to estimate magnetic sources in time–frequency domains. A grid-frequency kernel (GFK) was developed to decode the correlation between each time–frequency representation and grid voxel. Brain activity was reconstructed by accumulating spatial- and frequency-locked signals in the full spectral data for all grid voxels. To test the new method, MEG data were recorded from 20 healthy subjects and 3 patients with verified epileptic foci.
Results: The experimental results showed that the new method could accurately localize brain activation in auditory cortices. The epileptic foci localized with the new method were spatially concordant with invasive recordings.
Comparison with existing methods: Compared with well-known existing methods, the new method is objective because it scans the entire brain without making any assumption about the number of sources. The novel feature of the new method is its ability to localize high-frequency sources.
Conclusions: The new method could accurately localize both low- and high-frequency brain activities. The detection of high-frequency MEG signals can open a new avenue in the study of the human brain function as well as a variety of brain disorders.

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1. Introduction

The brain generates both low and high-frequency electromagnetic signals (Bowyer et al., 2012; Haegelen et al., 2013; Zijlmans et al., 2012). Low frequency brain signals (LFBS < 1 Hz) are typically referred as direct current (DC) and infraslow activity (Bowyer et al., 2012). High frequency brain signals (HFBS > 70 Hz) are also called high frequency oscillations (HFOs), ripples or fast ripples (Engel et al., 2009; Gotman, 2010; Haegelen et al., 2013; Worrell et al., 2008). The highest frequency component identified in the brain is approximately 2500–2800 Hz (Usui et al., 2010; Xiang et al., 2013). Median frequency brain signals (MFBS) in a frequency range of 1–70 Hz are typically used in clinical practice (Barkley and Baumgartner, 2003; Gross et al., 2013). Though the brain generates signals in a wide frequency range, the relationship between frequency ranges and spatial location of brain signals remains largely unknown.

Newly developed high-sampling-rate magnetoencephalography (MEG) technology has made it possible to record brain signals in both low and high frequency ranges (~12,000 Hz) (Heinrich and Bach, 2004; Xiang et al., 2010; Xiang and Xiao, 2009). In addition, modern MEG systems also have a whole-cortex sensor array that can capture the spatial information of brain activity in a variety of angles (Vrba et al., 2004). Previous studies have developed several algorithms for localizing brain activity with MEG signals in a low frequency range (Brookes et al., 2011; Cheyne et al., 2007; Huang et al., 2004; Mosher et al., 2009; Nagarajan et al., 2006; Robinson et al., 2012; Sekihara et al., 2004; Tadel et al., 2011; Vrba et al., 2010). Recent reports have demonstrated that high-frequency MEG signals can also be utilized to localize brain activity (Dalal et al., 2008; Xiang et al., 2009a, 2010).

Increasing evidence indicates that HFBS are not only new biomarkers for epilepsy but also provide a window for developing novel source localization methods (Gotman, 2010; Worrell et al., 2012; Xiang et al., 2009a, 2010). The combination of spatial filter (beamformer) and time–frequency analysis has the potential to analyze both low and high-frequency signals at source levels (Krause et al., 2010; Laaksonen et al., 2008). Since MEG signals are the spatiotemporal summation of synchronous activity from at least 10,000–50,000 neurons (Murakami and Okada, 2006), the frequency and spectral signatures of MEG data encode the spatiotemporal patterns of a group of neurons, which represent the functional organization of brain activity. The frequency and spectral signatures of MEG data in both low and high frequency ranges provide important information for computational reconstruction of functional brain activity (Lina et al., 2014).

It is well known that the conventional beamformer cannot detect coherent or correlated MFBS (Dalal et al., 2006; Popescu et al., 2008), let alone weak HFBS. It is necessary to develop specialized methods to deal with coherent sources. Since HFBS typically appear on a small group of sensors in a whole-cortex MEG system (Gummadavelli et al., 2013; Xiang and Xiao, 2009) using fewer sensors, beamformer can aid in the detection of MEG high-frequency components. In addition, previous reports (Popescu et al., 2008) have shown that partial sensor coverage (PSC) can minimize the coherent source effect at low-frequency signals. Therefore, from a methodological point of view, using fewer MEG sensors which are sensitive to a targeted source beamformer can aid in the detection of high-frequency components and at the same time reduce the coherent source effect at low-frequencies (Popescu et al., 2008). Of note, incorporating the two principles into a MEG source localization method is very interesting and important.

The objective of the present study was to develop a novel method to utilize both low and high-frequency neuromagnetic signals to better localize brain activity. The detailed mathematic algorithms for localizing each voxel with MEG data in multi-frequency bands for the entire brain were explored. Both experimental and simulated data were used to verify the new approach. Auditory MEG data were used as experimental data because auditory sources are well-known "correlated sources" that typically used for testing new methods (Popescu et al., 2008). Epilepsy data were used because the source locations were verified invasively. Building on recent reports (Blakely et al., 2014; Ding and Yuan, 2013; Gramfort et al., 2013), we hypothesize that the new method which utilizes the frequency and spectral signatures of multi-frequency MEG is superior to the conventional beamforming as well as widely used dipole modeling. In comparison to previous reports on similar approaches (Dalal et al., 2011; Diwakar et al., 2011; Prendergast et al., 2013; Zhang et al., 2013), the major innovation of the present study was the unitization of the frequency signatures for source localization and the optimization of wavelet-based beamformers for detecting weak high-frequency signals. Building on previous reports (Popescu et al., 2008), we have improved beamformers by combining PSC and coherent source region suppression (CSRC) into a new approach. A successful reconstruction of brain activity with multi-frequency MEG signals may open a new avenue in the study of the human brain function as well as a variety of brain disorders.

2. Material and methods

2.1. Theoretical background

The discovery of high-frequency brain signals has prompted the development of methods specifically optimized for the detection of neuromagnetic high-frequency signals using MEG (Miao et al., 2014). Building on previous reports (Dalal et al., 2008; Popescu et al., 2008; Xiang et al., 2009a), the present study aimed to utilize the frequency signature of neuromagnetic signals for localizing brain activity. To that end, we optimized wavelet algorithms by providing a dynamic sigma value for better detection of high-frequency brain signals. In addition, we integrated a vector beamformer and a scalar beamformer into a systematic approach for better source localization. Furthermore, we incorporated PSC and CSRS to minimize the weakness of beamformers. We have developed a two-source-image technique to detect the coherent sources in the first place for targeted filtering. Specifically, our method computes one source image with all sensors (SIA) and another source image with selected sensors (SIS) or a group of source-specific sensors. Since fewer sensors can reduce the coherent source effect (Pang et al., 2003; Popescu et al., 2008), the image generated by subtracting SIA from SIS can detect the potential coherent sources in the first place. Once the potential coherent source is detected in the first place, the targeted filtering can then set corresponding weights according to CSRS. Alternatively, the coherent sources could also be predetermined by investigators according to conventional or classical knowledge, such as auditory cortical activation described in previous reports (Pang et al., 2003; Popescu et al., 2008). To facilitate the storing of the information produced by wavelet and beamformer, this study moved one step further by developing multi-parameters per location for magnetic source images. Fig. 1 shows the flowchart of our new approach. Unless otherwise mentioned throughout the mathematical formalism, scalars are denoted by plain italics letters or symbols, vectors are denoted by lower case bold letters, and matrices are denoted by upper case bold letters.

2.2. Time frequency decomposition with a dynamic sigma value

To detect high-frequency brain signals, we used wavelet transforms to decompose time-domain waveforms to time–frequency-domain spectral data. In the present study, we used Morlet wavelet