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An improved method for measuring mismatch negativity using ensemble empirical mode decomposition

Chun-Hsien Hsu[a,*], Chia-Ying Lee[a], Wei-Kuang Liang[b]

[a] Institute of Linguistics, Academia Sinica, No. 128, Section 2, Academia Road, 115 Taipei, Taiwan, ROC
[b] Institute of Cognitive Neuroscience, National Central University, Jhongli, Taiwan, ROC

HIGHLIGHTS

- We adopt EEMD method and evaluate the statistical significance of ERM measurements.
- ERMs can reflect effects of lexical tone changes even with a less number of trials.
- EEMD method is helpful to promote clinical and developmental assessments based on EEG.

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ABSTRACT

Background: Mismatch negativity (MMN) is a component of event-related potentials (ERPs). Conventional approaches to measuring MMN include recording a large number of trials (e.g., 1000 trials per participant) and extracting signals within a low frequency band, e.g., between 2 Hz and 8 Hz.
New Method: Ensemble empirical mode decomposition (EEMD) is a method to decompose time series data into intrinsic mode functions (IMFs). Each IMF has a dominant frequency. Similar to ERP measurement, averaging IMFs across trials allows measurement of event-related modes (ERMs). This paper demonstrates a protocol that adopts EEMD and Hilbert spectral analyses and uses ERMs to extract MMN-related activity based on electroencephalography data recorded from 18 participants in an MMN paradigm. The effect of deviants was demonstrated by manipulating changes in lexical tones.
Results: The mean amplitudes of ERMs revealed a significant effect of lexical tone on MMN. Based on effect size statistics, a significant effect of lexical tone on MMN could be observed using ERM measurements over fewer trials (about 300 trials per participant) in a small sample size (five to six participants).
Comparison with Existing Method(s): The EEMD method provided ERMs with remarkably high signal-to-noise ratios and yielded a strong effect size. Furthermore, the experimental requirements for recording MMN (i.e., the number of trials and the sample size) could be reduced while using the suggested analytic method.
Conclusions: ERMs may be useful for applying the MMN paradigm in clinical populations and children.

1. Introduction

In event-related potential (ERP) studies of human auditory perception, the mismatch negativity (MMN) response has received substantial attention (Näätänen, 2003; Näätänen et al., 1978). MMN can be elicited by deviant stimuli, which occur among repetitive standard stimuli in oddball paradigms. The contrast between standard and deviant sounds is manipulated by modifying a variety of acoustic features, such as pitch (Moreau et al., 2013), duration (Chobert et al., 2012), and intensity (Schröger, 1996). MMN typically manifests as a negative ERP that peaks about 150–200 ms after deviant stimulus onset. Across these studies, a robust effect of the size of deviance has been shown in MMN. That is, as the discriminability between the standard and the deviant stimuli increases, MMN amplitudes increase, and the MMN response sometimes occurs earlier.

As MMN can be elicited in the absence of attention and with no task requirements, it is particularly suitable for studying clinical populations and children. Researchers have used MMN to explore neurological mechanisms in normal participants and have demonstrated some clinical applicability. For example, MMN has been used as a valid predictor of recovery from coma (Daltrozzo

* Corresponding author. Tel.: +886 2 2652 5000x6132; fax: +886 2 2785 6622.
E-mail address: kevinhsu@gate.sinica.edu.tw (C.-H. Hsu).

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et al., 2007). MMN has also been used as an index for investigating schizophrenia (Michie, 2001), degenerative brain disorders (Jung et al., 2006), and dyslexia (Kujala et al., 2001).

The conventional method of estimating MMN involves first estimating ERPs of standards and deviants by averaging several epochs of electroencephalography (EEG) data that correspond to onset of stimuli. Then, differences between waveforms are calculated by subtracting the ERPs of standards from those of deviants. Therefore, participants need to hear standards and deviants hundreds of times. To improve the statistical significance of ERP studies, a simple approach is increasing the number of trials. However, this approach prolongs experimental times for recording EEG data and might not be suitable for studying clinical populations and children.

Some analytic methods have been used to improve measurements of MMN. These methods were based on the idea that that MMN activity might have a specific topological distribution and a dominant frequency band. To extract MMN-related activity based on its topological features, one can use independent component analysis (ICA) (Cong et al., 2010). To extract MMN activity by extracting EEG oscillation within a frequency band, there are methods such as optimal digital filtering (Kalyakin et al., 2007), wavelet decomposition (Cong et al., 2011), and empirical mode decomposition (EMD) (Cong et al., 2009). This paper will not exhaustively compare the pros and cons of these different methods. Instead, we aim to provide a practical demonstration to show that an advanced version of EMD, i.e., ensemble empirical mode decomposition (EEMD) (Wu and Huang, 2009), can be used to extract latent ERP activity from single-trial EEG data, and to evaluate the statistical significance of EEG data based on the EEMD method.

EEMD and its origin method, EMD, are components of the Hilbert-Huang transformation (HHT), which has been proposed by Huang and colleagues for analyzing nonlinear and non-stationary data (Huang et al., 1998). The procedure of HHT consists of two parts: EMD and Hilbert spectral analysis. EMD is an adaptive method to decompose waveforms into several intrinsic mode functions (IMFs). Although EMD has the ability to extract ERPs, it has a drawback—the mode mixing problem (Huang et al., 2003). That is, a feature of time-frequency activities is not fixed in one IMF, which makes it difficult to determine ERPs and the corresponding IMFs. To overcome the problem of mode mixing, Wu and Huang (2009) have recommended EEMD, a noise-assisted data analysis method. The output of EEMD is a set of IMFs generated from ensemble means of trials by repeating EMD on the same signal with different sets of Gaussian noise. The technical details of EEMD have been described by Al-Subari et al. (2015a, 2015b).

Since ERPs are known as low-frequency waveforms (Nitschke et al., 1998), Hilbert spectral analysis, the second step of HHT, can be used to evaluate the frequency of each IMF. Hilbert spectral analysis provides the instantaneous frequency of each IMF. According to Huang et al. (2011), the instantaneous frequency could represent the nonlinear and non-stationary signals without resorting to the mathematical artifact of harmonics. Like measuring ERPs, averaging IMFs across trials provides event-related modes (ERMs). Based on the instantaneous frequency of ERMs, ERP components can be extracted by summing ERMs (Cong et al., 2009; Williams et al., 2011; Wu et al., 2012) or using an ERM within a frequency range (Al-Subari et al., 2015b). For example, Cong et al. (2009) have demonstrated an application of EMD for analyzing MMN. In their study, time-frequency spectra of ERMs with frequencies between 2 and 8.5 Hz were used to estimate MMN waveforms, because Kalyakin et al. (2007) suggested that activities within this frequency range could reflect MMN. For ERPs of sentence comprehension, Williams et al. (2011) used EMD to extract ERMs between 1 and 10 Hz. For olfactory ERPs, Wu et al. (2012) used ERMs between 0.5 and 11.5 Hz. For visual perception, Al-Subari et al. (2015b) demonstrated that ERMs could reflect P100 and N200 elicited in a contour integration task.

To date, however, few studies have demonstrated EEMD analyses of EEG data. It is important to explore the extent to which the EEMD could improve the sensitivity of measuring ERP components. In particular, with regard to measuring MMN responses, answering this question would be helpful to promote clinical and developmental assessments based on MMN. In the present study, the dataset of adult EEG in Cheng et al. (2013) was utilized. The effect of lexical tone changes on MMN amplitude in early and late time windows has been addressed in detail in previous studies (Cheng et al., 2013). Specifically, Cheng et al. use Mandarin lexical tones in a multiple-deviant oddball paradigm. The results showed that MMN activity for acoustically dissimilar contrasts (described below) was significant between 100 ms and 200 ms. Therefore, the present study focused on mean amplitudes between 100 ms and 200 ms and evaluated the statistical significance of MMN activity in ERMs. We adopted the method of single-trial based EEMD analysis suggested in Al-Subari et al. (2015b) to extract ERMs as a measurement of MMN. Furthermore, subsets of trials were randomly sampled to explore whether MMN could be measured using ERMs with few trials.

2. Materials and methods

2.1. Experimental design and EEG dataset

Since this experiment has been discussed in detail elsewhere (Cheng et al., 2013), only a brief introduction is provided in this article. The participants in the MMN experiment were 18 native speakers of mandarin Chinese (two women, age range = 18–29) with normal hearing. Participants passively listened to streams of auditory stimuli. This study was approved by the Human Subject Research Ethics Committee/Institutional Review Board of Academia Sinica, Taiwan. Written consent forms were obtained from all participants. The stimuli consisted of three Mandarin syllables with different lexical tones: yi1 “clothing” (T1), yi2 “aunt” (T2), and yi3 “chair” (T3), which share the same vowel,/i/, but carry different tonal contours. The T3 was assigned as the standard, with T1 and T2 as deviants. The T1/T3 pair represents the larger deviant contrast, and the T2/T3 pair represents the smaller deviant contrast. Each stimulus lasted 250 ms, and the inter-stimulus interval was 500 ms. The experimental session started with 20 trials of the standard, followed by 1000 trials with 80% standards and 20% deviants (10% for each deviant). During the experiment, participants were instructed to play a puzzle computer game called “super-box” silently.

EEG signals were amplified by SYNAMPS2® (Neuroscan, Inc.) in DC mode, low-pass 100 Hz, and digitized at a sampling rate of 500 Hz. EEG data were recorded from 64 Ag/AgCl electrodes (Quick-Cap, Neuromedical Supplies, Sterling, USA), arranged according to the international 10-20 system, including a reference electrode located between CZ and CPZ and a ground electrode located between FPZ and FZ. Six additional electrodes were attached over the left and right mastoids, supra- and infra-orbital ridges of the left eye (VEOG), and outer canthi of both eyes (HEOG).

Before estimating ERPs and ERMs, the EEG data were re-referenced to the average of the left and right mastoids. Continuous EEG was segmented into epochs from 100 ms prior to the onset of the stimulus to 700 ms after the onset. The first 20 trials and epochs with artifacts exceeding $\pm$100 μV were rejected. To ensure that the number of trials between the standard and deviant were comparable; only the standard trials that were preceded by at least three successive standards were included in analyses. For each participant, at least 45 accepted deviants were required to