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Fengyu Cong

Evaluation and Extraction of Mismatch Negativity through Exploiting Temporal, Spectral, Time-frequency, and Spatial Features

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ABSTRACT

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Finnish Summary
Diss.

This study is dedicated to the evaluation and extraction of mismatch negativity (MMN) from EEG recordings through exploitation of its temporal, spectral, time-frequency and spatial features.

Compared to the conventional wavelet transformation, Hilbert-Huang transformation can more effectively represent the temporal and spectral features of MMN. To qualify the correlation of recordings among single trials (CoRaST), the proposed frequency domain MMN model with Fourier transformation only requires less than one percent of the computational time which the conventional inter-trial coherence costs, promising to implement CoRaST in real-time systems.

In the time domain, a robust and reliable method to extract the MMN component is proposed through exploitation of its temporal, frequency and spatial information. The core of this novel method includes the wavelet decomposition (WLD) and independent component analysis (ICA). Thus, it is denoted as wICA. The proposed wICA can outperform the conventional difference wave using the temporal information, optimal digital filter using the frequency band information of MMN and ICA using the spatial information.

In the time-frequency domain, nonnegative matrix factorization (NMF) and nonnegative tensor factorization (NTF) can decompose the time-frequency represented EEG to obtain the desired time-frequency represented MMN and P3a components simultaneously, releasing the independence assumption among sources which ICA requires, and discovering more knowledge between normal children and clinical children in our study.

Moreover, the proposed methods in this study may also be usable in the research into other MMNs and other event-related potentials since they may also have similar temporal, spectral, time-frequency and spatial features as the MMN attended to in this study.

Keywords: electroencephalography (EEG), event-related potential (ERP), mismatch negativity (MMN), temporal, spectral, time-frequency representation, wavelet decomposition, independent component analysis, back-projection, nonnegative matrix/tensor factorization

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To all, KIITOS PALJON!

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ABBREVIATIONS

ADHD	Attention deficit hyperactivity disorders
BSS	Blind source separation
DW	Difference wave
EEG	Electroencephalography
EMD	Empirical mode decomposition
ERP	Event-related potential
ERSP	Event-related spectral perturbation
FFT	Fast Fourier transform
HHT	Hilbert-Huang transformation
ICA	Independent component analysis
IMF	Intrinsic mode function
ISI	Inter-stimulus interval
ITC	Inter-trail coherence
MMN	Mismatch negativity
NMF	Nonnegative Matrix Factorization
NTF	Nonnegative Tensor Factorization
ODF	Optimal digital filtering
PCA	Principal component analysis
RD	Reading disability
ROI	Region of interest
SAR	Support to absence ratio
sICA	single-trial based ICA
SOA	Stimulus onset asynchrony
SNR	Signal to noise ratio
wICA	Wavelet decomposition-ICA
WLD	Wavelet decomposition

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1 INTRODUCTION

This chapter presents the research motivation, overview and goal of this study.

1.1 Research motivation

The electrical activity in the human brain produced by the firing of neurons can be safely recorded through electrodes distributed over the scalp, and such recordings are named electroencephalography (EEG) (Niedermeyer and Lopes da Silva, 2004). The first paper to introduce EEG for the description of the on-going electrical activities/sources of the brain was written by a German psychiatrist—Professor Hans Berger in 1929 and was published in German (Berger, 1929). Fig. 1 depicts the first recorded human EEG waveform by Professor Berger in 1925. The horizontal coordinate represents the time in seconds and the vertical denotes the amplitude of the EEG waveform in micro voltage. The lower curve is 10 cycles sine wave to mark the time scale and the upper is the EEG recordings from Berger's young son. This EEG waveform demonstrates the brain's electrical activity around 10Hz. It has typically been known as the Berger rhythm and now, it is referred to as the alpha oscillation.

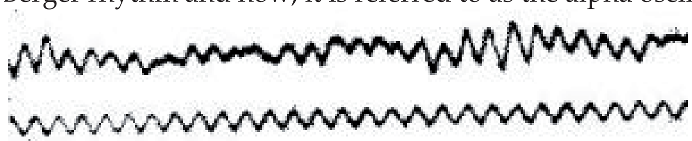

FIGURE 1 EEG waveform recorded by Prof. Berger

Since EEG was recorded by Professor Berger, it has been used to discriminate brain activities between typical and clinical populations. For example, Berger also studied the diagnosis of epilepsy with EEG. Currently, the clinical use of EEG includes the diagnosis of coma, encephalopathy, brain death, tumors, strokes and other focal brain disorders (Niedermeyer and Lopes da Silva, 2004).

EEG can reflect the on-going brain activities. However, in our everyday life, people often respond to many afferent things, for example, a sudden call, a flash light, a changing image and so on. In these situations, brain activity is related to those events. Moreover, the on-going EEG may include thousands of on-going brain processes, but the event-related response in the brain to the outside stimuli might reflect one human thought or perception. The event-related response was first studied by the Davis couple between 1935 and 1936 who published their studies in 1939 (Davis et al., 1939; Davis, 1939). Today, the recordings of the event-related response have been named as the event-related potentials (ERPs) (Luck, 2005). ERP studies did not progress a great deal until the 1960s. At that time, researchers started using computers for calculation, greatly improving work efficiency. There are tens of ERPs now for different studies. An ERP is usually named according to its latency and polarity and even according to the special features. For example, 'N1' represents that this ERP has a negative peak under the reference to nose, and that its latency is around 100ms after the onset of the stimulus (Näätänen, 1992); 'ERN' denotes 'error related negativity', and is usually observed after erroneous responses (Gehring et al., 1993; Yeung et al., 2004).

The response to a stimulus in a single trial is usually not well-structured and therefore the ERP is often extracted from the on-going EEG through averaging and filtering over the EEG recordings of dozens, hundreds, even thousands of trials in the time-domain (Duncan et al., 2009; Picton et al., 2000b). As a result, only the evoked (phase locked) brain activities still remain in the averaged trace and, although some induced (non-phase locked) brain activities may also be elicited by the outside stimulus, they usually disappear after averaging (David et al., 2006).

ERP can reveal the sensory information from the views of reception, processing, selective attention, memory updating, semantic comprehension, and other types of cognitive activity and has been studied extensively in clinical research (Duncan et al., 2009). In particular, a negative ERP, named Mismatch Negativity (MMN), was identified by Professor Risto Näätänen and colleagues in 1978 (Näätänen et al., 1978). These authors described MMN as a ''physiological mismatch process caused by a sensory input deviating from the memory trace ('template') formed by a frequent 'background' stimulus'' (p. 324). Mmoreover, MMN can be attention free, i.e., to generate MMN a participant does not necessarily pay attention to the stimulus paradigm; its amplitude is very small, and usually is up to several micro volts with a peak latency of 100-200ms (Näätänen, 1992).

Since MMN was isolated in 1978, dozens of research groups all over the world have been studying MMN. The society of interest in MMN has grown extensively over the past three decades and five congresses focused on MMN have already been held. These include: 1st in Finland (1998), 2nd in Spain (2000), 3rd in France (2003), 4th in the United Kingdom (2006), and 5th in Hungary (2009). The sixth will take place in New York, USA in 2012. Nowadays, hundreds of researchers from all over the world participate in the MMN conference. Without doubt, MMN has become an important stream in research of cognition, clinical neuroscience, and neuro-pharmacology (Duncan et al., 2009; Garrido et al., 2009). Among these investigations, data processing plays a fundamental and critical role. Unfortunately, although over 1000 papers have been published in various scientific journals as reporting the study of MMN, few are entirely devoted to the analysis of the data processing for MMN with the advanced signal processing methods, in contrast to the conventional difference wave and digital filters (Alain et al., 1999; Atienza et al., 2005; Burger et al., 2007; Kalyakin et al., 2007, 2008 & 2009; Marco-Pallarés et al., 2005; Picton et al., 2000a; Sabri and Campbell, 2002; Sinkkonen and Tervaniemi, 2000). One reason may be that MMN is one of the small ERPs and its peak amplitude is only up to several micro volts and, especially concerning children's MMN, EEG recordings of MMN are much noisier. This makes the data processing methods, especially the data-driven methods, very hard to achieve. Therefore, this also results in the importance of the problem. The other reason may be that the advanced signal processing methods are novel and complicated and may not be well understood by researchers in the MMN field.

Without question, the advanced signal processing techniques can be important and helpful to the research of MMN. MMN has its own features in the time, frequency and time-frequency domain. However, these features are not sufficiently exploited by the existing data processing methods for MMN. Thus, this study is targeted towards the design of methods to evaluate and extract MMN from EEG recordings through exploitation of its own temporal, spectral, time-frequency and spatial features in the time, frequency and time-frequency domains with the single channel and multichannel methods, respectively.

1.2 Overview of introductory

This thesis studies methods to evaluate MMN and extract MMN from the EEG recordings.

The evaluation includes the representation and qualification of MMN. With reference to the former topic, Hilbert-Huang transformation (HHT) is used to achieve the time-frequency representation of MMN to better reveal its temporal and spectral features in contrast to the conventional wavelet transformation; concerning the latter, a frequency domain MMN model is developed to formulate a fast algorithm for the measurement of the correlation of recordings among single trials. This method has the potential to be used in the real-time data collection system during ERP experiments.

The MMN component can be extracted in the time domain and time-frequency domain, respectively. In the former domain, the study discusses the application of wavelet decomposition (WLD) and independent component analysis (ICA) with the features of MMN and designs a robust and reliable procedure to extract MMN. In the latter domain, to compensate the shortcoming of ICA concerning the strong assumption of independence among sources, nonnegative matrix/tensor factorization (NMF/NTF) is used to extract the time-frequency represented MMN and P3a components simultaneously in the time-frequency domain for the analysis of brain activity between typically developing children and clinical children.

The thesis is divided into two parts: The first is the summary of the original publications, and the second is the list of the included articles. The remainder of the first part is organized as below: Chapter 2 introduces the paradigm to elicit MMN and the properties of MMN; Chapter 3 reviews the state-of-the-art with regard to data processing for MMN; Chapter 4 summarizes the contribution of this study; Chapter 5 draws the conclusion and discusses this thesis.

1.3 Research questions

The research questions of this study are as follows:

1) How to represent MMN more accurately?
2) How to measure the correlation of recordings among single trials for MMN quickly?
3) How to design a robust and reliable method to extract MMN from EEG recordings?
4) Can we learn more knowledge from MMN recordings through better signal processing methods?
5) What can we finally obtain from EEG recordings if they are modeled as the linear transformation of the latent variables?

Next, the study will answer these questions.

2 PARADIGM TO ELICIT MISMATCH NEGATIVITY AND ITS FEATURES

This chapter introduces the paradigm to elicit MMN, the corresponding knowledge of MMN and its temporal, spectral, time-frequency and spatial features.

2.1 Paradigm to elicit MMN

Today, it is well known that MMN can be elicited through an oddball paradigm. Under this elicitation procedure, MMN has been interpreted through the memory-based model (Näätänen, 1992), regularity-violation model (Winkler, 2007) and the adaptation model (May and Tiitinen, 2009). This study obeys the first model and can be illustrated as shown in Fig.2.

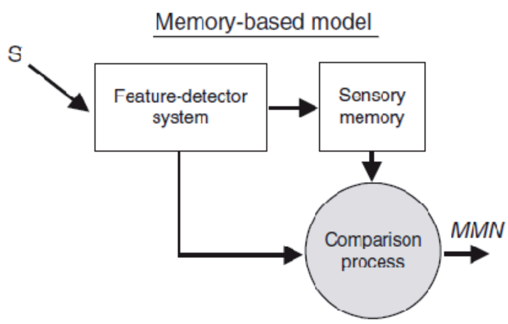

FIGURE 2 Memory-based MMN model (Adapted from May & Tiitinen, 2009)

For example, several consecutive standard stimuli make the brain formulate the sensory memory and then the incoming deviant stimulus is slightly different to the information in the formed memory and the brain will implement a comparison process. In such a scenario, MMN can be generated. For the auditory stimulus, the deviant type can be the duration, the intensity, the frequency, the location, and so on (Duncan et al., 2009). For the visual stimulus, it can be emotions and orientations (Astikainen and Hietanen, 2009; Astikainen et al., 2008).

Typically, an oddball paradigm to elicit MMN includes two concepts about the duration. One is an inter-stimulus-interval (ISI) and the other is a stimulus-onset-asynchrony (SOA). ISI is the duration of a silent gap between two adjacent stimuli. SOA is the time period from the onset of the one stimulus to the onset of the next stimulus.

The conventional oddball paradigm is frequently used in the study of MMN. It is illustrated in Fig.3 (a). However, one main disadvantage of this type of paradigm is time-consuming. It often takes hours to achieve well-structured MMN of one subject, which is not suitable for young children and clinical populations (Näätänen et al., 2004; Pakarinen et al., 2007 and 2009). Thus, Professor Näätänen and colleagues invented the optimum-1 and optimum-2 paradigms, consisting of five different deviants (Näätänen et al., 2004). Fig.3 demonstrates these deviants. SOA and ISI for (a) and (b) were 500ms and 425ms, and for (c) were 300ms and 225ms. Näätänen and colleagues (2004) declared that both the optimum-1 and optimum-2 could effectively elicit MMN and the new procedures significantly saved much time. In short, to achieve five MMNs under five deviants, the time taken by the conventional oddball paradigm is five times that (15 mins in Näätänen et al., 2004) taken by the optimum-1 procedure.

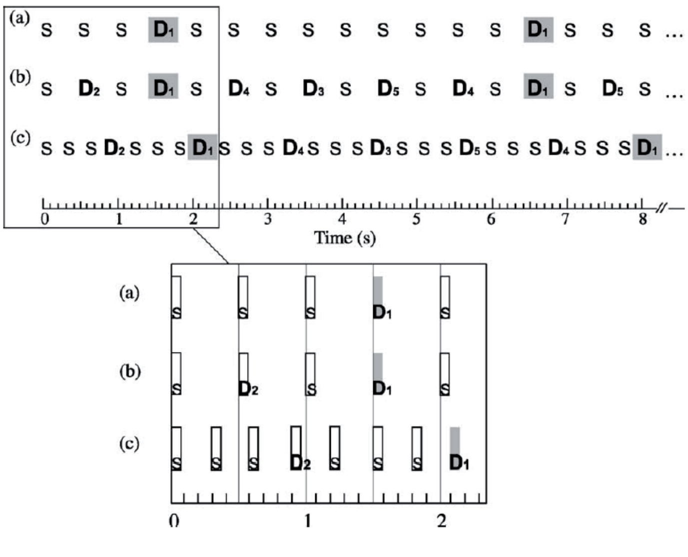

FIGURE 3 Oddball, optimum-1 and optimum-2 paradigms (Adapted from Näätänen et al., 2004)

Meanwhile, it was reported that the optimum-2 paradigm produced smaller MMN peak amplitude (Näätänen et al., 2004). Indeed, under optimum-2, ISI is shorter and standard stimuli are more repeated in contrast to the conventional oddball and optimum-1 paradigms. Thus, such a result reported by Näätänen and colleagues (2004) may conflict with common knowledge in eliciting MMN, i.e., the shorter ISI and more standard stimuli may correspond to a larger MMN peak amplitude (Näätänen, 1992). Nevertheless, Professor Erich Schröger stated that longer ISI could contribute MMN with larger peak amplitudes under the frequency deviant (Schröger, 1996). By now, no solid illustrations for such conflicts have been made.

Another way to obtain fast recordings is through uninterrupted sound, i.e., the ISI is zero. In 1995, Dr. Elina Pihko and colleagues used such a continuous sound to elicit MMN for the investigation of people's ability to detect temporal changes (Pihko et al., 1995). Recently, the same paradigm has also been used in the MMN study of typically developing children, children with reading disabilities (RD) and children with attention deficit hyperactivity disorders (ADHD) (Huttunen et al., 2007; Huttunen-Scott et al., 2008; Kalyakin et al., 2007 and 2008). This took approximately only 15 minutes to collect 700 trials and thus is very promising in the application to young children and clinical groups. As a result, this study also adopts such a continuous sound procedure.

Fig.4 illustrates this paradigm. The uninterrupted sound has alternating 100ms sine tones of 600Hz and 800Hz (repeated stimuli, see Fig.4). There is no pause between the alternating tones and their amplitudes do not change. During the experiment, 15% of the 600Hz tones are randomly replaced by shorter tones of 50ms and 30ms duration (called as dev50 and dev30). The deviants consist of 7.5% of 50ms deviants and 7.5% 30ms deviants. There are at least six repetitions of the alternating 100ms tones between deviants.

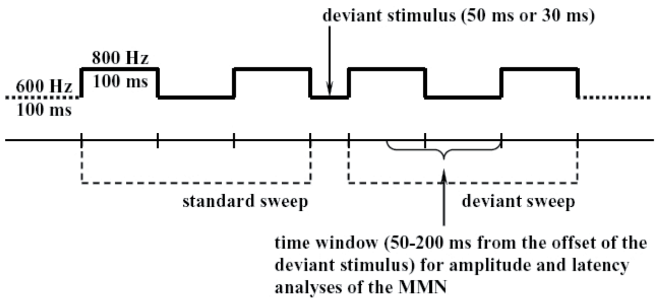

FIGURE 4 A schematic illustration of the stimulus sequence to elicit MMN through the continuous sound (Adapted from Kalyakin et al., 2007)

2.2 Basic psychological knowledge of MMN

As mentioned earlier, MMN can be elicited through the oddball paradigm (Näätänen, 1992). For example, one oddball sequence could be 'S S S S D1 S S S D2 S S S S S D3 S S S…', where 'S' denotes the standard stimulus, i.e., the repeated stimulus, and 'D1', 'D2', or 'D3' represents the deviant stimulus of the same type. The three deviants have different magnitudes of the deviance to the standard stimulus. MMN has such a property: the larger is the magnitude of the deviance, the larger is the peak amplitude and the shorter is the peak latency of the MMN (Näätänen, 1992; Pakarinen et al., 2007). This is the basic psychological knowledge of MMN.

Indeed, although it is impossible to localize the true MMN sources, the MMN functions have been somewhat unveiled (May and Tiitinen, 2009; Näätänen, 1992; Winkler, 2007). Meanwhile, as suggested by Dr. Vigario and Professor Oja (2008), the evaluation of the processing of ERPs should be based on the knowledge of ERPs by the expert. Thus, the criteria used to estimate the success to extract MMN should be based on the analysis of psychological knowledge of MMN. In this study, we use the above mentioned characteristic of MMN in this subsection for the criteria to judge whether the property of MMN is well defined under any data processing method.

2.3 Features of MMN

In the single channel EEG recordings, MMN has its own temporal, spectral and time-frequency features, and from the multichannel, the spatial features between the MMN source and EEG recordings can be exploited. They are introduced as follows.

2.3.1 Temporal feature

ERPs are time-locked according to its elicitation paradigm (Luck, 2005), which contributes its temporal feature. For example, as shown in Fig.4, an MMN peak may appear in the time frame between 50ms and 200ms after the offset of the deviant stimulus (Pihko et al., 1995). Out of that frame, no MMN can be observed. So, the temporal feature is derived from the paradigm to elicit MMN and a time frame within which the MMN peak may appear should be defined to describe its temporal feature.

2.3.2 Spectral feature

The spectral feature of MMN includes two parts. One is the frequency range of MMN and the other is the spectral structure within that frequency range.

Since the digital filter was applied to filter out the interference, the frequency range of MMN has been attractive to researchers. Different frequency bands have been used to remove the interference from the averaged MMN trace. For example, Kalyakin et al. (2007) made a deep analysis on the cut-off frequencies for the MMN frequency band of children and concluded that the optimal MMN frequency band of children was 2-8.5Hz under an uninterrupted sound paradigm; Stefanics G. et al. (2007, 2009) adopted the 2.5-16Hz and 1.5-16Hz to achieve MMN of neonates respectively; for visual inspection of MMN, Sinkkonen and Tervaniemi (2000) recommended a 1-20Hz band; Tervaniemi et al. (1999) had always used 2-10Hz band pass digital filter for subsequently analyzing MMN peak amplitude and latency; Sabri and Campbell (2002) set the band of MMN as 3-12Hz. In summary, the frequency of MMN is very low. Most of the studies simply reported that a certain frequency band was used for MMN. This is not convincing for the further application by other researchers. In order to determine the frequency band of MMN, Kalyakin et al. (2007) designed a special paradigm. It is repeated in this study. This method consists of two groups of digital filters. One is the group of low pass filters to seek the high cut-off frequency and the other is the group of high pass filters to isolate the low cut-off frequency. For example, when the high cut-off frequency of the low pass filter gradually reduces, the peak amplitude of MMN can be measured at every high cut-off frequency. Then, the change of the peak amplitudes may be discovered along the change of the high cut-off frequencies. The frequency with the largest MMN peak amplitude can be considered as the high bound of the MMN frequency range. The low bound of the MMN frequency range can also be found this way. For details, see Kalyakin et al. (2007). Since the data set used in this study is identical to that used by Kalyakin et al. (2007), 2-8.5 Hz is used as the optimal frequency band of MMN hereinafter. For other studies, the frequency band may be determined by the procedure mentioned above.

Another point is to determine the spectral structure within a frequency band. For example, the frequency corresponding to the most powerful energy is a critical parameter within the frequency range of MMN. This has not been well discussed in previous publications. Picton et al. (2000a) considered that most of the MMN's energy lay in the 2-5Hz frequency range. Consequently, in this study, the power of the frequency is regarded to peak below 5 Hz.

2.3.3 Time-frequency feature

Frequency analysis of ERPs is very important. However, the same spectral features in the frequency domain might correspond to different waveforms in the time domain. Thus, it is necessary to perform the time-frequency analysis. Fig.5 demonstrates the advantage in using the time-frequency feature to discriminate different signals. Fig.5-1 depicts the waveforms of two signals. Fig.5-2 describes the spectrums of the two signals. Fig.5-3 and Fig.5-4 show their time-frequency representation. As shown in Fig.5, the difference between the two signals is most evident under the time-frequency representation despite the similar waveforms and almost identical spectral structures that the two signals share. This is the advantage of the time-frequency analysis in discriminating different signals.

Specifically, the rectangle area in Fig.5-3 or 4 determines the ROI. The power in ROI of Fig.5-3 is much larger than that of Fig.5-4. This parameter can be used to select the desired signal. In this case, the ROI is defined through the temporal and spectral features of MMN mentioned above. For example, the time frame of ROI is from 50ms to 200ms and the frequency range of ROI is from 2Hz to 8.5Hz. These four numbers determine a rectangle.

When different signals have determinant variances, respectively, the values of ROIs among them are comparable. Subsequently, the time-frequency feature of MMN can be derived from the averaged power within ROI of the time-frequency representation. It is defined through the averaged power of all time-frequency points within the ROI. Therefore, such a parameter can spontaneously reflect the temporal and spectral information of MMN. However, if the variance of the component is indeterminate, the value of the ROI is not appropriate to discriminate different components. In this case, the support to absence ratio (SAR) (Cong et al., 2010, 2009a, and 2009b) is more appropriate to be regarded as the feature of the time-frequency representation. Specifically, the support is defined as the averaged power of the ROI where MMN appears and the absence is derived through the mean of the left region of the time-frequency representation where MMN is impossible to present. Thus, the scale of a component has no relation to SAR. Although SAR is the value of a ratio, it can still reveal the time-frequency feature of MMN and can also be used to discriminate different signals. Taking into account the example in Fig.5, the averaged power of the ROI in Fig.5-3 is larger than that in Fig.5-4, and certainly, so does the SAR.

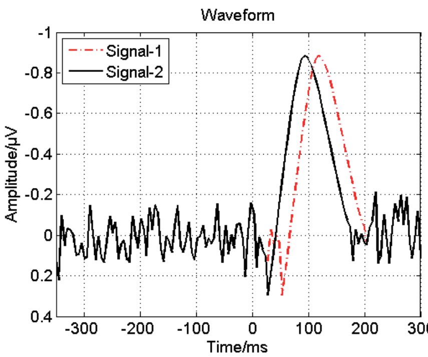

FIGURE 5-1 Waveforms of two signals

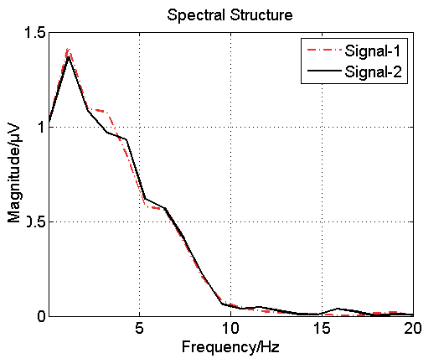

FIGURE 5-2 Spectrums of two signals

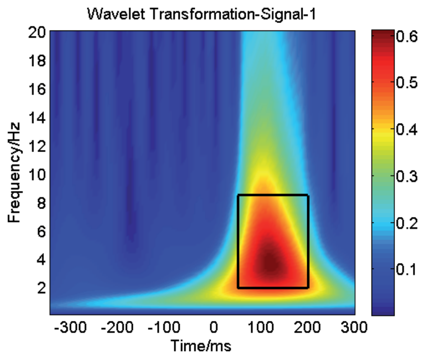

FIGURE 5-3 Time-frequency analysis of signal-1

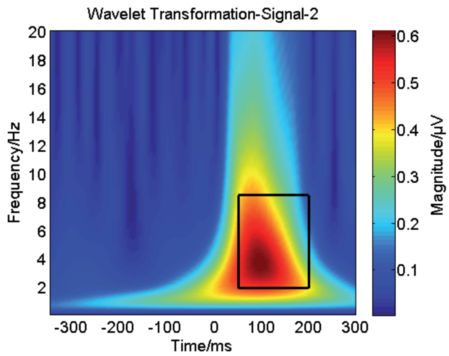

FIGURE 5-4 Time-frequency analysis of signal-2

Both ROI and SAR can represent the time-frequency feature of MMN and can reflect the energy of a signal at a certain time and frequency range. Meanwhile, they have their own characteristics, respectively. The former is more appropriate to reveal the values of the raw recordings, and the latter is more proper to evaluate the degree in separating overlapping components. For example, the averaged power of ROI of MMN may be larger at the frontal area than that at the mastoids. This is because MMN usually has a larger peak at the frontal area; the SAR of MMN calculated from the ordinary averaged trace may be smaller than that computed from the optimally filtered averaged trace. This is because the MMN component remains in the filtered trace and other spontaneous activities have been removed from the averaged trace (i.e., the absence in the definition of SAR has been reduced).

2.3.4 Spatial feature

The spatial information includes two parts: One is the topography of a certain ERP, and the other is the relationship between the brain sources and EEG recordings at the scalp.

2.3.4.1 Topography

Every ERP has a certain distribution over the scalp. The distribution tends to include two aspects. For example, one is related to the energy of the MMN peak amplitude and the other to the polarity of the MMN peak amplitude. These are the topographic features of an ERP. Particularly, MMN elicited by the auditory modality usually has relatively larger peak amplitude at the frontal area, and its polarity is negative at the frontal, central, and parietal area, and is positive at the mastoid under the reference to the tip of the nose (Näätänen, 1992). Such information is very critical to the definition of the proper MMN component.

2.3.4.2 Linear transformation model of latent variables

EEG collected from any point of the human scalp may include activities generated within a large brain area (Makeig et al., 1997 and 1999) and therefore, it may represent the mixture of many spontaneous electrical activities of the brain. In this study, every such electrical activity can be regarded as an electrical source of the brain. Furthermore, the conduction of the electrical signals in nerves is very fast with a velocity approaching 90 feet per second (Kandel, 2006) and the spatial smearing of the EEG data below 1kHz by volume conduction does not result in significant time delay (Hämäläinen et al., 1993; Niedermeyer & Lopes da Silva, 2004). Then, we assume every source can linearly transfer from its location in the brain to any point of the scalp and the transfer function is regarded to be constant during a certain brain process, for example, perception. As a result, the linear transform model of latent variables fits EEG (Makeig et al, 1996, 1997 and 1999). Fig.6 briefly illustrates such a model.

Fig.6 assumes that only three spontaneous sources represented by the waveform exist in the brain and three electrodes record the brain activities at three points on the scalp. The scenario can be explained in that three sources simultaneously transfer from their corresponding locations in the brain to every point on the scalp and recordings at every point are the mixture of three linearly transformed sources. Moreover, each linearly transformed source is the scaled version of the corresponding source, i.e., the multiplication of the source and a rational constant number. This number is the coefficient representing the transfer function from the location of the source in the brain to the point on the scalp. In such a model, the sources are the unknown latent variables and the transfer functions are also unknown and only the EEG recordings are available.

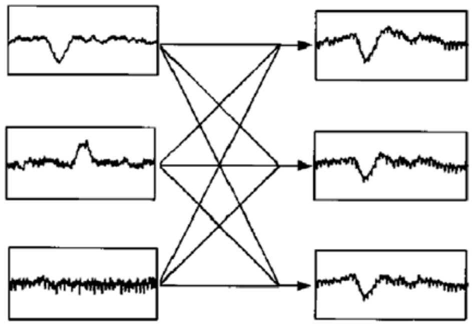

FIGURE 6 Linear transform model of latent variables (Adapted from Makeig et al., 1997)

In Fig.6, the brain sources and recordings are represented through the time series. They can also be expressed in the ways of the spectral structure or the time-frequency representation. This is to say, with the exception of the linear transformation model for the one-dimensional time series, other linear modes for the two or more dimensional data can also be used to estimate the sources of the brain.

Compared to other features of MMN, the feasibility for the application of multichannel signal processing techniques is the advantage of the spatial feature. Moreover, when EEG recordings are modeled through the linear transformation of latent variables, they are regarded as the mixtures of the individually scaled sources of the brain. Thus, the goal of data processing is to extract one pure source from the mixtures. For example, Makeig and colleagues (1996) applied ICA (Comon, 1994) to extract the pure brain source from EEG recordings in 1996. Another extensively used technique is the principal component analysis (PCA) (Skrandies, 1993). Both PCA and ICA can be used to extract the time course of the desired component. The recently developed techniques—nonnegative matrix factorization (NMF) and nonnegative tensor factorization (NTF) (Lee and Seung, 1999; Cichocki et al., 2009 and 2008) can also extract the time-frequency represented components of biomedical sources (Lee et al., 2007 and 2009; Li and Zhang, 2010; Lohmann et al., 2007; Miwakeichi et al., 2004; Morup et al., 2007 and 2006; Sajda et al., 2004).

Next, the state-of—the-art with regard to data processing for MMN will be reviewed, after which, the features in this chapter will be exploited to design data processing methods for the study of MMN.

3 REVIEW OF EXISTING METHODS FOR EVALUATING AND EXTRACTING MISMATCH NEGATIVITY

This chapter first analyzes the drawbacks of the existing methods with regard to evaluation and extraction of MMN from EEG recordings and submits suggestions for novel methods.

3.1 Evaluation of MMN

The evaluation of MMN can be divided into two parts: One is to represent the characteristics of MMN; the other is to inspect the correlation of recordings among single trials to analyze MMN activity.

3.1.1 Representation of MMN

The psychological knowledge of MMN tends to be derived from the parameters representing MMN, such as its peak amplitude and latency (Näätänen, 1992). The peak amplitude depicts the energy of an ERP, and the peak latency demonstrates its temporal information. These two parameters are most extensively used to describe the ERPs (Luck, 2005). Nevertheless, both of these are measured in the time-domain and they cannot reflect the information of an ERP in the frequency or time-frequency domain. In contrast to the representation of the waveform or the spectrum of the biomedical signal, the time-frequency analysis contributes to simultaneously exploit the dynamics of the signal from the view of both temporal and frequency information (Cavanagh et al., 2009; Criado and Ehlers, 2009; Debener et al., 2006 and 2005).

There are two ways to achieve the time-frequency representation of an ERP: One is the event-related spectral perturbation (ERSP) (Delorme and Makeig, 2004) and the second is the time-frequency analysis on the averaged recordings over single trials. To calculate ERSP, two steps are often adopted:

The first step is usually to achieve the time-frequency representation (absolute-value) of the single-trial recordings through wavelet transformation with the second step being to average the time-frequency representations over a number of single-trials. Along this line, both the information of the evoked brain activities and the induced brain activities elicited by the stimulus are included in the ERSP (David et al., 2006). However, the current understanding of ERPs, certainly including MMN, is mostly based on the analysis of the averaged trace over a number of trials (Duncan et al., 2009; Picton et al., 2000b). After averaging, the induced brain activities may disappear and the evoked brain activities still remain. This means that most of the extensively accepted psychological knowledge of ERPs originates from the evoked brain activities. Consequently, to investigate the property of MMN, this study will not implement ERSP for the time-frequency analysis, but perform the time-frequency transformation on the averaged recordings over single trials.

Wavelet transformation has been widely used in the time-frequency analysis for ERPs (Delorme and Makeig, 2004). In contrast to the fast Fourier transformation (FFT) (Mitra, 2005), its advantage is the representation of the non-stationary property of one signal. Indeed, the conventional wavelet transformation is also Fourier-based. Hence, such a characteristic provokes constraints that wavelet transformation should only be well applied to non-stationary signals with a gradual frequency variation, i.e., the inter-wave frequency modulation. However, the intra-wave frequency modulation with sudden frequency changes is more common in practice and the wavelet transformation cannot resolve this because the representation of such a wave could no longer be a simple sine or cosine function when the frequency changes from time to time (Huang et al., 1998). As Dr. Huang and colleagues wrote in 1998 : 'In the past such phenomena were treated as harmonic distortions. Such deformations are better viewed as intra-wave frequency modulation, for the intra-wave frequency modulation is more physical' (Huang et al., 1998, p917).

Moreover, the human brain is a complex-nonlinear system and it generates severely nonlinear and non-stationary signals (Klonowski, 2009). It is worth considering the nonlinear signal processing techniques for the study of a biomedical signal. Hilbert-Huang Transformation (HHT) (Huang et al., 1998) is such a nonlinear time-frequency analysis method. In the past ten years, HHT has been applied to many disciplines, such as analyzing and correcting satellite data, fusing data from multi-sensors, speech analysis and speaker identification, machine health monitoring, and biomedical engineering. Indeed, HHT has been used in the study of the on-going brain signals (Fine et al., 2009; Li et al., 2008), but it is rare to find its application in the research regarding ERPs. Thus, it is worth investigating the applications of wavelet transformation and HHT for the study of the time-frequency represented MMN.

Usually, HHT includes three steps: 1) decompose a signal into different oscillators denoted by intrinsic mode functions (IMFs) through the empirical mode decomposition (EMD); 2) perform Hilbert transformation on each oscillator to achieve its instantaneous amplitude and phase; 3) calculate the derivative of the phase to obtain the instantaneous frequency (Huang et al., 1998). Thus, how to obtain the oscillators of MMN activity from EEG recordings by the first step is critical in the application of HHT to MMN. This study will answer this question in the next chapter.

3.1.2 Inspection of correlation of recordings among single trials

With regard to EEG recordings of an ERP, if the responses to the stimuli to elicit this ERP are consistent among many trials, a well-structured ERP may be produced through averaging such trials. Then, one significant feature of such recordings is that the correlation of recordings among single trials must be high. To investigate this property, the inter-trial coherence (ITC) is often used (Delorme and Makeig, 2004). There are three steps to the calculation of ITC: The first is to implement wavelet transformation to achieve the time-frequency analysis (complex-valued) on recordings of each trial; the second is to obtain the average (complex-valued) over the normalized time-frequency analysis of all trials; the third is to achieve the magnitude of this average to gain the ITC. If the coherence among single trials was high, ITC would approach to '1', otherwise, it would become near '0'.

This procedure has been extensively used, but it often takes expensive computing since the time-frequency analysis has to be implemented on a great deal of trials in the ERP study. This is a shortcoming of ITC. To study ERPs, it is always desireable to inspect the correlation of recordings among single trials as quickly as possible. Hence, this study will formulate another Fourier Transformation based parameter to evaluate the correlation of recordings among single trials through the frequency-domain ERP model (Cong and Ristaniemi, 2008a).

3.2 Extraction of MMN

During the elicitation of MMN, thousands of spontaneous sources are also possibly active in the brain. Due to the small peak that MMN possesses, it is often embedded into the on-going EEG. How to effectively extract it has played a critical role in the study of MMN since it was first reported in 1978.

3.2.1 Extraction of MMN trace

Näätänen and colleagues subtracted the response to the standards from the response to the deviant and subsequently achieved a difference wave (DW) containing MMN (Näätänen et al., 1978). This has become the most used method to extract MMN. Certainly, before DW, the responses to the standard and deviant stimuli have been averaged over a number of trials. This is because the single-trial recordings may not present a well-structured MMN. Under the assumption that the recordings in each single trial are the sum of the responses to the special event buried in Gaussian-distributed noises, such averaging may improve the signal to noise ratio (SNR) with the proportion to the square root of the number of trials (Harmony, 1984).

Ideally, after data processing, only MMN activity should remain in the values used in further analyses and other spontaneous brain activities are removed. Such estimation simulates the process that only an MMN source is active in the brain during the experiment. However, DW only removes the common variance present in standard and deviant data, and other types of activity overlapping MMN is not separated in the time and/or frequency domain. Thus, signal processing techniques, such as digital filtering (eg. Kalyakin et al., 2007; Picton et al., 2000a; Sabri and Campbell, 2002; Sinkkonen and Tervaniemi, 2000; Stefanics G. et al, 2007, 2009; Tervaniemi et al., 1999), wavelet decomposition (WLD) (Atienza et al., 2005; Burger et al., 2007), and independent component analysis (ICA) (Kalyakin et al., 2008 and 2009; Marco-Pallarés et al., 2005), are used to extract MMN. All of these methods are targeted towards revealing the purer MMN related brain activities.

In order to extract the desired ERP, a digital filter makes use of the frequency information of this ERP through extracting the frequency components from a certain frequency band and reconstructing the desired signal from the extracted frequency components. This method is extensively used in the study of MMN because of its robustness, the facilitated application and low cost in computation. However, two main disadvantages of a digital filter limit its performance in extracting ERPs: 1) the digital filter assumes that the signal is stationary, but the real ERP data may not be stationary, conflicting with the assumption; 2) the overlapping frequency components of different signals within the pass band of a digital filter cannot be separated, which causes the output of a digital filter to remain a mixture of different signals.

A wavelet filter is especially designed for the non-stationary signals and it exploits both temporal and frequency information of the signal (Burrus, 1998; Daubechies, 1992). This is the advantage of the WLD procedure. Usually, WLD consists of three steps: 1) decompose the raw signal into some levels with a wavelet; 2) choose certain levels for the reconstruction of the desired signal; 3) reconstruct the desired signal with the selected levels (Atienza et al., 2005; Burger et al., 2007; Daubechies, 1992; Samar et al., 1995; Wang et al., 2009). Determining the number of levels to decompose the raw signal can be based on the principle that the number of samples should be equal to two to the power of the optimal number of levels for the decomposition on the signal (Tikkanen and Sellin, 1997; Wang et al., 2009). We also use this rule hereinafter for WLD. Then, the problems are to determine the type of wavelet for WLD and the levels to reconstruct the desired signal. Currently, the most used methods for this are: 1) calculate the correlation among the selected wavelet coefficients and the assumed desired signal (Burger et al., 2007), 2) calculate the frequency band of each level (Wang et al., 2009). If the desired signal was known, the first procedure could be very effective. However, this assumption is too strong to be available in practice. The second method is according to the next criterion— the bandwidth at different levels in WLD can be defined through the association between the sampling frequency and two to the power of the corresponding frequency levels (Wang, et al., 2009). This method does not take the information of the wavelet into account. In fact, for different wavelets, the frequency bands and the spectral structures of the output of WLD under the same level may be different. As Basar et al. (2001) suggested, the frequency information of the desired signal should be well known before the wavelet related analysis. Thus, the design of WLD should be based on the spectral features of the desired signal. This is the basic principle for application of WLD for the study of MMN.

Another important data processing method for ERPs is ICA. This was applied in 1996 to extract ERPs by Makeig and colleagues (1996) through exploitation of the spatial independence among different electrical sources of the brain. Since then, many researchers have been attracted by this topic. EEGLAB with ICA is commonly used in EEG and ERP studies (Delorme and Makeig, 2004; Jung et al., 2009; Makeig et al., 2004 and 2002; Mars et al., 2008; McMenamin et al., 2009; Miyakoshi et al., 2010). The classic ICA is the linear transformation model which compliments the EEG recordings. The advantages of ICA decomposition are that it exploits the spatial independence of different sources and does not require other prior knowledge of sources, such as, the temporal or frequency information. Moreover, its algorithms are usually adaptive. On the other hand, ICA also has few disadvantages. For example, the ICA algorithm sometimes may not converge to the global optimum. However, the shortcomings do not prevent ICA becoming an excellent method in the study of ERPs (Vigario & Oja, 2008). The application of ICA to study the neuronal activity usually includes three steps: 1) to perform the ICA decomposition on the multichannel EEG recordings to extract the independent components, 2) to select the desired component for the further analysis, 3) to project the selected component back to electrodes to recover the amplitude of the extracted component with the unit of micro volt. How to design the proper procedure for each step is critical to the application of ICA.

In summary, different methods are based on the different features of MMN. DW is according to the temporal feature; the digital filter makes use of the frequency information; WLD exploits the temporal and frequency characteristics; and ICA depends on the spatial independence of sources. It is evident that MMN features are not entirely used in any of the above four methods. Consequently, it is worth considering the design of a new method to extract MMN trace by exploiting the temporal, spectral, time-frequency and spatial features of MMN together and investigating whether the new procedure may contribute MMN with better properties.

Indeed, although WLD and ICA have been used to extract MMN, there are still some open questions to be answered. For example, regarding WLD, which wavelet should be chosen for the decomposition? Which levels are appropriate for the reconstruction to extract MMN? Are the single-trial recordings, concatenated-trial recordings or the averaged traces more appropriate to ICA? What kind of the pre-processing will benefit ICA decomposition? Which ICA algorithm is appropriate to extract MMN source component reliably? How is the desired MMN component chosen from among all the extracted components? Can the back projection of the desired component entirely correct its variance and polarity indeterminacy in the electrode field? What will be finally obtained through the ICA based procedure? This study will design an easily implemented procedure to answer these questions based on the features of MMN. As the core technique to decompose the EEG recordings in this study is to combine the single channel method-WLD and the multichannel method-ICA together, the proposed method is denoted as wICA hererinafter.

Furthermore, unlike the digital or wavelet filter, ICA does not possess the superposition rule (Mitra, 2005). Theoretically, this means that the estimation of ICA on the averaged trace is not equal to the average over the estimation of ICA on recordings of single-trials. Thus, this study also attempts to examine whether the single-trial based ICA and averaged trace based ICA perform differently.

3.2.2 Extraction of time-frequency represented MMN

As discussed earlier, the time-frequency representation of MMN can provide more information than does the peak amplitude and latency. There are two possible procedures to achieve such representation of the pure MMN activity of the brain.

One procedure is to extract the MMN from the averaged trace, and then to perform the time-frequency analysis on the extracted MMN. Such methods have been introduced in the previous subsection. Particularly, ICA has the theoretical assumption that the electrical sources of the brain are independent of each other and the practical assumption that the number of samples for the ICA decomposition should be several times the squared number of estimated sources (Makeig et al., 1997 and 1999). Such requirement may limit the performance and application of ICA in practice.

The other procedure is first to perform the time-frequency analysis on the averaged trace at every channel and then to decompose the multichannel time-frequency representation for extracting the MMN component. Nonnegative matrix factorization (NMF) and nonnegative tensor factorization (NTF) are such methods and have already been applied to study the time-frequency represented biomedical signals (Lee et al., 2007 and 2009; Li and Zhang, 2010; Lohmann et al., 2007; Miwakeichi et al., 2004; Morup et al., 2007 and 2006; Sajda et al., 2004). NMF and NTF do not require the source independence assumption and are not as strictly restricted to the number of samples for the decomposition as ICA. Concering ICA decomposition, basis functions are ranked by the non-gaussianities; while to NMF/NTF decomposition, basis functions are not ranked, but represent intrinsic properties of the data set. From the perspective of data analysis, NMF and NTF are more attractive because they take into account the spatial, temporal and spectral information of EEG recordings and the electrical sources of the brain more accurately than does ICA and they usually provide sparse common factors or hidden (latent) components with physiological meaning and interpretation (Lee and Seung, 1999).

This study will perform NMF and NTF to achieve the time-frequency represented MMN and P3a components to exploit more information between typically developing children and clinical children.

4 PROPOSED METHODS TO EVALUATE AND EXTRACT MISMATCH NEGATIVITY THROUGH ITS FEATURES

This chapter will discuss how methods are derived through features of MMN for its evaluation and extraction from EEG recordings.

4.1 Evaluation of MMN

4.1.1 Representation of MMN

Reference:

Cong, F., Sipola, T., Huttunen-Scott, T., Xu, X., Ristaniemi, T., & Lyytinen, H. (2009). Hilbert-Huang versus morlet wavelet transformation on mismatch negativity of children in uninterrupted sound paradigm. Nonlinear Biomedical Physics, 3:1.

Cong, F., Sipola, T., Xu, X., Huttunen-Scott, T., Lyytinen, H., & Ristaniemi, T. (2010). Concatenated trial based Hilbert-Huang transformation on event-related potentials. Proc. International Joint Conference on Neural Networks 2010 (IEEE World Congress on Computational Intelligence), Barcelona, Spain, July 18-23, 2010, pp. 1379-1383.

In this thesis, two paradigms for the application of HHT to represent MMN are discussed: One is to perform HHT on the averaged trace and the other is that EMD is executed on the trace of the concatenated-trial and the Hilbert transformation is implemented on the averaged IMF trace.

The first paradigm is based on the averaged trace. This is because an ERP could be obtained through averaging and filtering over a number of trials (Picton et al., 2000b). The idea is first to generate the ERP and then to analyze its time-frequency properties. However, the duration of the averaged trace in the ERP study is in general, merely hundreds of milliseconds within one experiment segment/trial and the number of recorded samples within such a short time interval is usually limited to several hundreds. As a result, the decomposition of these recordings into oscillations may not be sufficient. Regarding the current applications of HHT, the signal often possesses a great number of samples, such as, the satellite dataset, speech and underwater acoustic recordings to achieve sufficient decomposition in the application of HHT (Huang et al., 1998).

Thus, a second paradigm is invented for the application of HHT to MMN in this study in order to overcome the bottleneck mentioned above. Firstly, the recordings of some single trials are concatenated together; then, EMD is performed on the connected trial to obtain IMFs; next, each IMF can be disjoined into IMF based single-trials and the averaging over these IMF based single-trials may be implemented to achieve the averaged IMF trace; finally, Hilbert transformation is calculated for each averaged IMF trace and the instantaneous frequencies are calculated to achieve HHT for MMN.

In contrast to the averaged trace based HHT, the concatenated-trace based HHT can decompose the recordings into more oscillations. Indeed, one oscillation represents one frequency band. Thus, the latter paradigm of HHT can provide the time-frequency representation with higher resolutions, which is often desired for the time-frequency analysis.

From the view of the time-frequency representation, the ROI of the proposed paradigm for HHT can represent better temporal and spectral properties of MMN than does the conventional wavelet transform. This results from the definition of frequency in HHT. It is derived through difference operation over two adjacent instantaneous phases of an IMF, i.e., the frequency defined by the Hilbert transformation is obtained straightly from the raw signal. However, the frequency defined by wavelet transformation is through the convolution of a Fourier related basis and a local period of the raw signal. Thus, in contrast to wavelet transformation, HHT may better reveal the dynamic brain activities.

4.1.2 Inspection of correlation of recordings among single trials

Reference:

Cong, F., & Ristaniemi, T. (2008). Second-order improperness in frequency-domain colored signal model. Proc. IEEE Workshop on Machine Learning for Signal Processing, Cancun, Mexico, October 16-19, 2008, pp. 321-326.

Cong, F., Ristaniemi, T., & Lyytinen, H. (2010) A potential real-time procedure to evaluate correlation of recordings among single trials (CoRaST) for mismatch negativity (MMN) with Fourier transformation. Manuscript submitted to *Clinical Neurophysiology* for publication (in second round review).

The fast inspection of the correlation of recordings among single trials is critical to the study of MMNs. This task can be fulfilled through the Fourier

Transformation based paradigm, which may be considerably quicker than is achieved by the wavelet transformation based ITC.

Four steps comprise the new paradigm:

1) Set the frequency band of MMN.
2) Perform Fourier Transformation on the recordings of every trial to achieve the transformed data (complex-valued) at each frequency bin within the frequency band of MMN.
3) Formulate the frequency-domain MMN model (Cong and Ristaniemi, 2008b). This model is represented by a complex-valued vector including the Fourier transformed data for all trials at the same frequency bin. Then, two real-valued vectors at each frequency bin are available: one is the real-part vector including the real part of the complex-valued vector and the other is the imaginary-part vector consisting of all the imaginary parts of the complex-valued elements of the vector.
4) Calculate the correlation coefficient of the two vectors at each frequency bin.

The rationale of this new paradigm results from the composition of the real-part and imaginary-part vectors. This has been illustrated by Cong and Ristaniemi (2008b). Please refer to the corresponding publication for details.

4.2 Extraction of MMN

4.2.1 Extraction of MMN from averaged traces

Reference:

Cong, F., Kalyakin, I., Huttunen-Scott, T., Li. H., Lyytinen, H., Ristaniemi, T. (2010). Employing timing, frequency and spatial information to extract mismatch negativity of children. Reports of Department Mathematical Information Technology, Series B. Scientific Computing, No.B4/2010 (31 pages), University of Jyväskylä, Finland .

Cong, F., Kalyakin, I., Ristaniemi, T., & Lyytinen, H. (2008). Drawback of ICA procedure on EEG: polarity indeterminacy at local optimization. In A. Katashev, Y. Dekhtyar & J. Spigulis (Eds.), NBC 2008, IFMBE Proceedings, 20 (4), pp. 202-205, 2008. Springer-Verlag Berlin Heidelberg 2008.

Cong, F., Kalyakin, I., & Ristaniemi, T. (2010). Can back-projection fully resolve polarity indeterminacy of ICA in study of ERP? Biomedical Signal Processing and Control, DOI: 10.1016/j.bspc.2010.05.006 (in press).

4.2.1.1 Averaged trace for wICA

MMN has been extracted by ICA from the recordings of concatenated single trials (Marco-Pallarés et al., 2005) and from the averaged recordings over single trials (Kalyakin et al., 2008; Kalyakin et al., 2009). The former paradigm supplied more samples to ICA and benefited the convergence of the ICA algorithm; however, the latter procedure fed ICA with a better structured MMN waveform. In reality, both methods implicitly assume that the cognitive processes stay identical from one trial to another. Another application of ICA to extract an ERP out is directly from the EEG recordings of a single trial (Iyer & Zouridakis, 2007).

For MMN, particularly with regard to the EEG recordings from children, MMN activity usually cannot be significantly observed from EEG recordings of concatenated single trials or EEG recordings of a single trial. This is because MMN is very small, and the SNR in the single trial is too low. The goal to apply ICA in this study is to extract the MMN component out, i.e., the extracted component at least should possess the well-structured MMN waveform. However, in practice, the ICA algorithm 'pays attention' to the relatively large activity in the data (Makeig et al., 2002-). Therefore, the ICA decomposition on EEG recording of MMN from children in the type of the concatenated single trials or a single trial may be too difficult to obtain the desired MMN component.

ERPs are usually achieved through averaging and filtering over a number of single trials (Picton et al., 2000b), as is MMN (Näätänen, 1992). Provided that there are sufficient single trials, MMN activity can at least be roughly observed in the average trace. Then, ICA decomposition on the averaged traces may be easier in contrast to the EEG recordings of a single trial or the concatenated trials. Subsequently, this study performs wICA on the averaged traces of each participant to extract the MMN component

4.2.1.2 Preprocessing for wICA—WLD on MMN

For ICA, as stated in the EEGLAB tutorial, data quality is critical in order to obtain good ICA decomposition (Makeig, et al., 2002-). The averaging may improve the SNR (Harmony, 1984). However, this may be unsatisfactory. Sometimes, the MMN component is not yet evident in the averaged trace and is still buried in the EEG. Thus, before the application of ICA, the single-channel method-- WLD can be used for the denoising.

The problem concerning WLD in our study is to design a special paradigm to include the information of the wavelet when choosing the appropriate wavelet for decomposition and the proper levels for reconstruction to extract MMN.

To resolve this problem, WLD can be regarded as a special band pass filter. The spectrum of the output of this filter should be able to conform to the spectral properties of MMN. Consequently, the problem as mentioned above, turns to how to acquire the spectral feature of the output of the wavelet decomposition. Thus, the new developed methodology is based on analysis of the frequency response of a band pass filter and consists of four steps: 1) the unit impulse is decomposed into levels by a wavelet, 2) each level is used for the reconstruction, 3) calculate the Fourier transformation of the reconstructed signal to obtain the frequency responses at each level, 4) select the proper levels for the reconstruction of the desired signal with reference to the spectral features of the desired signal. Moreover, the selected coefficients should possess the temporal feature of MMN. This compensates the drawback of the spectral features. In this way, the proper wavelet and levels for the reconstruction can be found.

In this study, the wavelet of reversal biothogonal of order 6.8 and seven levels were chosen for the decomposition and the same wavelet and coefficients under the fifth and sixth levels were selected for the reconstruction. This was because the frequency responses of such a wavelet filter met the frequency property of MMN, i.e., the optimal frequency band of MMN was from 2-8.5Hz (Kalyakin et al., 2007) and the main power of the MMN could lie below 5Hz (Picton et al., 2000a).

4.2.1.3 Estimating MMN source from averaged traces with ICASSO for wICA

In the second chapter, Fig.6 has demonstrated that only the EEG recordings are known under the linear transformation model of the latent variables. Therefore, the target of ICA is how to separate the sources of the brain out from the EEG recordings. Fig.7 depicts such a process. This is the inverse process described in Fig.6.

As shown in Fig.7, the core of ICA is to find the separation matrix. After this matrix is obtained, the multiplication of the multichannel recordings and this matrix produces the ICA components, i.e., the estimation of the sources. In contrast to the sources in Fig.6, it should be noted that the ICA components in Fig.7 are only the randomly scaled version of the corresponding sources and the order of the ICA components is arbitrary. Consequently, in theory, the estimated components by ICA in Fig.7 can only reflect the structure of the true sources in Fig.6. The indeterminacy of the variance can be resolved in theory and will be discussed in the coming subsections.

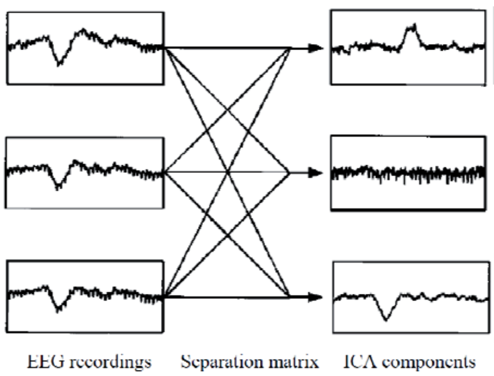

FIGURE 7 Separation process of ICA (Adapted from Makeig et al., 1997)

In order to find the separation matrix, a cost function is usually designed to make the ICA components conform to some special statistical requirement

(Comon, 1994). For example, ICA assumes the sources are independent of each other and then the criterion of the cost function is to make the ICA components independent of each other (Comon, 1994). Nevertheless, Daubechies and colleagues (2009) have recently declared that ICA can work well in cases where sources are sparse and are not necessarily independent of each other. In the study of biomedical signals, InfoMax ICA (Lee et al., 1999) and FastICA (Hyvärinen, 1999) are the most used (Daubechies et al., 2009). InfoMax ICA tends to require numerous samples to achieve good convergence (Lee et al., 1999). Since the averaged traces are chosen for the ICA decomposition, InfoMax ICA is not appropriate to this study, therefore FastICA is set for the basis of the separation.

Because FastICA is an adaptive algorithm and multichannel EEG recordings are usually of high dimensional space, the output of single-run FastICA may possibly be of high uncertainty (Groppe et al., 2009; Himberg et al., 2004; Zeman et al., 2007). Fortunately, ICASSO can somewhat resolve this problem (Himberg et al., 2004). ICASSO is the software to reliably extract components from multichannel recordings. One procedure of ICASSO is to perform FastICA many times through initializing the unmixing matrix for every run. Thus, the same number of components can be extracted every time. Subsequently, all the components are clustered to find the common components in so many runs. As a result, the output from FastICA based ICASSO is more robust than the single-run FastICA. For details of ICASSO, see the study of Himberg et al. (2004).

4.2.1.4 Facilitating wICA decomposition through concatenating recordings of different deviants

ICA has a special requirement regarding the number of samples of recordings. This is usually at least several times larger than the squared number of sources (Makeig et al., 1997 and 1999). In general, the number of sources may be assumed equal to the number of channels (Delorme and Makeig, 2004). For example, suppose there are nine channels' recordings and then nine sources will be suggested to be extracted. According to the rule mentioned above, there should be at least 162 samples for the ICA decomposition. However, there may be fewer recordings than this required number in one averaged trace. Therefore, one way to resolve this problem is to concatenate the averaged traces of different experiment conditions together for each channel (Kalyakin et al., 2008 and 2009, Vakorin et al., 2010). This could possibly release the limitation of the number of samples for the ICA decomposition.

Such connection of averaged traces under different conditions may be reasonable. For example, during the elicitation of MMN, different deviants could have different magnitudes of deviance to the repeated stimuli under the same deviant type or could be different deviant types. Nevertheless, whatever they are, different deviants usually appear arbitrary during the elicitation (Näätänen, 1992; Näätänen et al., 2004) and the cognitive or perception processes for different trials have been regarded to be identical. To this end, connecting the averaged traces under different deviants is acceptable.

4.2.1.5 Choosing the MMN component for wICA through support to absence ratio

After the sources are estimated by ICA, the desired components are usually chosen for further processing. As introduced by Tie et al. (2008), methods used to choose the desired components are usually based on spatial patterns, map polarities, temporal characteristics, spectral criteria, and so on. For example, the MMN peak amplitude is positive in the mastoid and negative in the frontal and central areas under the reference to the tip of the nose (Näätänen, 1992); MMN is time-locked and should appear in the time frame from 50ms to 200ms after the deviation offset in the procedure through one continuous sound (Huttunen et al., 2007); the optimal frequency band of MMN is between 2Hz and 8.5Hz in our dataset (Kalyakin et al., 2007).

Based on the time-frequency feature of MMN, this study has designed a new paradigm to choose the desired component. The intrinsic idea is to retrieve the extracted component best representing MMN information in the time and frequency domains. Four steps compose the procedure:

1) every extracted component is transformed into the time-frequency representation by the conventional wavelet transformation;
2) the same ROI is located for every time-frequency represented component through temporal and spectral features of MMN;
3) calculate the SAR of every time-frequency represented component;
4) choose the component with the largest SAR as the desired MMN component.

With reference to the ICA components in Fig.7, SAR can definitely distinguish the upper and bottom component. The property of SAR has been introduced in the second chapter and is not repeated here.

4.2.1.6 Projecting the desired component(s) back to electrodes

As mentioned earlier, the components estimated by ICA have scaling indeterminacy, i.e, the variance and polarity (positive or negative) of such components are random (Comon, 1994). They should be corrected when MMN peak amplitudes (magnitude and polarity) are important for further studies. In order to achieve this goal, the selected component is usually projected back to the electrodes and the projection is acquired through the outer product between the corresponding column of the inverse of the separation matrix and the selected component (Makeig et al., 1997 and 1999).

However, even under the global optimized ICA decomposition (Comon, 1994), such back projection can not produce the real brain source, but the multiplication of the real brain source and its transfer function from the location of the source of the brain to any point on the scalp (Cong and Ristaniemi, 2008a). With the global optimization of ICA decomposition, each component only contains the information of one source (Comon, 1994; Cong and Ristaniemi, 2008a). In practice, this is rarely achieved. This is because the ICA decomposition is, in practical terms, locally optimized in the study of EEG (Groppe et al., 2009; Himberg et al., 2004; Zeman et al., 2007). Thus, several components may have the property that only one source of information is represented, but any other component may contain the information of a few sources. As a result, the scaling problem cannot be fully corrected (Cong and Ristaniemi, 2008a).

Usually, the polarity of an ERP for certain electrodes can be hypothesized. Therefore, after the selected component is projected back to the electrodes, it is necessary to check whether the polarity of the projected component for a certain electrode meets the theoretical expectation. If not, the polarity should be corrected. This is the post processing for the projected ICA component in the electrode field. Actually, it is out of the ICA concept already. The target is to make the whole procedure produce more reasonable results. For example, assuming that the polarity correction step would not be implemented, polarities of the peak amplitudes on the same channel for different participants could be randomly different for the same ERP. This would not be good for further statistical tests.

Moreover, if two or more selected ICA components are required to be projected to electrodes simultaneously, the parallel projection of these components is theoretically equal to the sum of the sequential projection of each component. Practically, as the polarities of the projected components are possibly random at the electrodes, this parallel projection may produce some mistakes. For example, two components are to be projected back to electrodes, respectively, and the component-1 may have the polarity reversal at a certain electrode, but component-2 does not possess this at that electrode. In the parallel projection, only the sum of the individual projection of two components can be obtained. Thus, it becomes impossible to correct the polarity reversal of component-1 at that electrode. Therefore, the parallel projection may not be precise. Fortunately, the sequential projection of each component back to electrodes may provide the opportunity to correct the polarity reversal.

It should be noted that, if all the ICA components are projected back to the electrodes, raw recordings are produced. Obviously, this is not the goal for further study.

After the desired component is projected back to the electrodes, the MMN peak amplitude could be measured in the unit of a microvolt. Its latency can be measured from the ICA component or from the projected ICA component in the electrode field and there is no difference between the two methods.

4.2.1.7 Summary

Subsections 4.2.1.1 to 6 are the complete steps to extraction of a MMN component and facilitation of the measurement of the MMN peak and latency under the wICA. In summary, Fig.8 describes the whole procedure. Under the global optimized ICA decomposition, what can be achieved by this methodology, theoretically, are the component extracted by ICA and the projection of those components at the electrode field. The former is the random scaled version of one brain source and the latter is the multiplication of the brain source and its transfer function from the location of the source of the brain to the point on the scalp. Thus, the real source of the brain is not yet available. In practice, the estimation approximates this resource within the theoretical expectation. Moreover, when the ICA decomposition approaches the global optimization, the difference between the practical estimation and the theoretical expectation becomes smaller.

In order to demonstrate the procedure in Fig.8, Fig.9 takes the examples of six sources and EEG recordings of six channels for the simulation. Fig.9-1 shows the sources, EEG recordings, and components extracted by ICA. In this example, the second and third sources are the desired sources and the second and the fourth extracted components correspond to these. The two extracted components are quite similar to the counterparts of sources 2 and 3, respectively. However, both have arbitrary variance and polarities. Moreover, the order of the extracted components is random and neither is it identical to that of the sources. The upper row of Fig.9-2 depicts the second real brain source and its theoretical projection, the practical projection of the second extracted component and the corrected practical projection; the middle row illustrates the similar information for the third real brain source and its counterpart—the fourth extracted component; and the bottom row expresses the theoretical projection of the second and third real sources, the parallel projection of the second and fourth extracted components and the sum of the sequential projection with the abnormal polarity correction of each extracted component. To one source, the theoretical projection is the multiplication of the real brain source and the corresponding transfer function. To the projection of one extracted component in the electrode field, the corrected projection is the multiplication of the practical projection with the abnormal polarity and '-1'. This simulation designates that the theoretical projection and the practical projection are quite similar to each other at most electrodes, which is the contribution of the ICA based paradigm stated in Fig.8. Meanwhile, this demo also describes three kinds of differences: 1) the difference between one real source in the brain and its theoretical projection at the scalp may be significant because of the volume conduction; 2) the difference between the theoretical projection of one source and its corrected practical projection of the corresponding ICA component becomes smaller than that between a theoretical projection and the practical projection with the abnormal polarity in the electrode field; 3) the difference between the theoretical projection of two sources and the sum of the sequential projection with the abnormal polarity modification of the corresponding ICA components transpires as smaller than that between the theoretical projection and the parallel projection.

To correct the abnormal polarity, this study simply implements a procedure that '-1' is multiplied to the projected component in the electrode field. Indeed, such correction does not change the sign of the 'actual' sources of the brain. Under the local optimization, the estimation of ICA procedure on EEG is the approximation of theoretical expectation under the global optimization. This means there are errors between the estimation and the theoretical expectation. Such errors merely originate from the separation matrix in ICA. Under the global optimization, the separation matrix can guarantee that one estimated component only corresponds to one source. However, under the local optimization, the separation matrix cannot guarantee that one estimated component only contains the information of one source. Furthermore, since the projection matrix is the inverse of the separation matrix, it must also take errors. The correction made in this study is indeed the post processing after ICA and can also be regarded as the further processing on certain elements of the projection matrix. Thus, the correction does not change the real source of the brain.

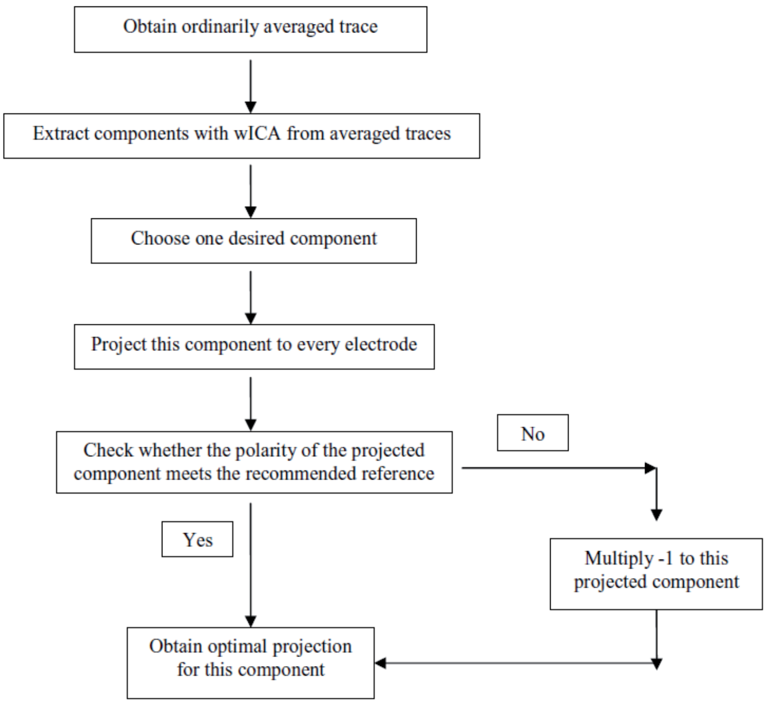

FIGURE 8 Diagram of the complete steps to extract MMN component and to facilitate the measurement of the MMN peak and latency under the wICA

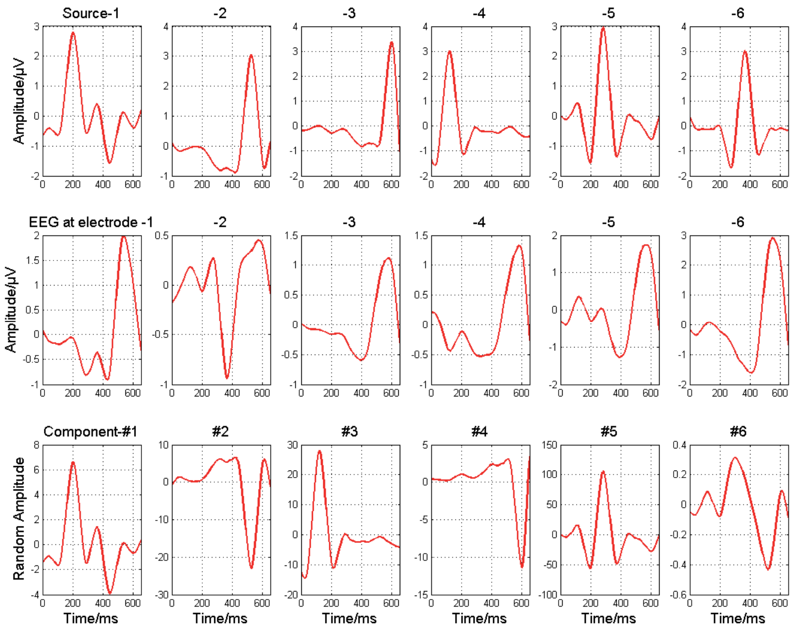

FIGURE 9-1 Simulated sources, EEG recordings, and ICA components

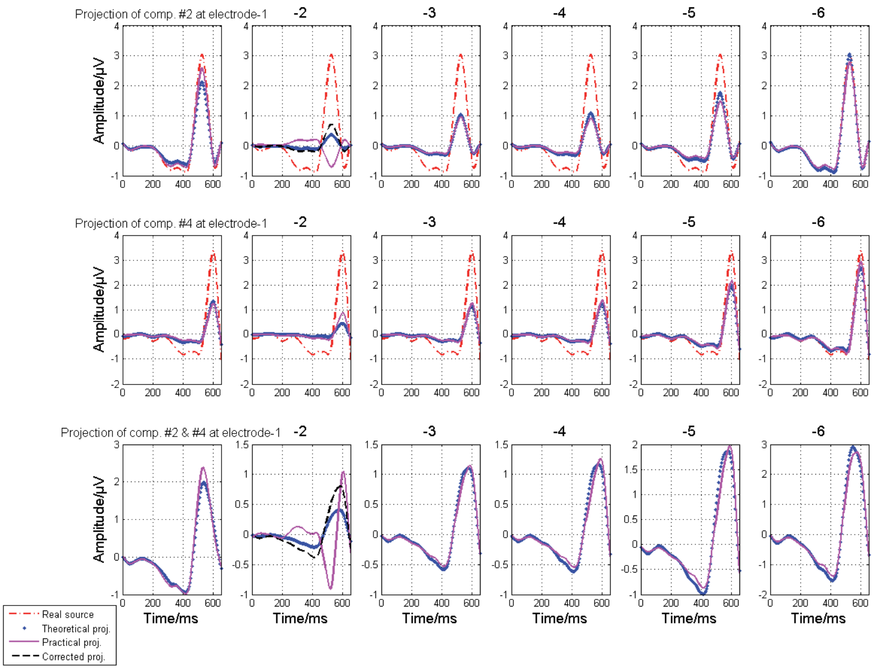

FIGURE 9-2 Real sources, theoretical projection, practical projection and corrected projection of component-2 and component-4 under the parallel and sequential manners

4.2.2 Extraction of MMN from recordings of single trials

Reference:

Cong, F., Kalyakin, I., Huttunen-Scott, T., Li. H., Lyytinen, H., & Ristaniemi, T. (2010). Single-trial based independent component analysis on mismatch negativity of children. International Journal of Neural Systems, 20(4), 279-292.

Unlike the digital or wavelet filter, ICA does not possess the superposition rule (Mitra, 2005). This means that, in theory, the estimation of ICA on the averaged trace is not equal to the average over the estimation of ICA on recordings of single-trials. Hence, it is worth considering performing ICA on the single-trial recordings to achieve the ICA based single-trial recordings, and then make an average for those new trials to generate MMN. This can be very time consuming, but it may be interesting to observe new results. The method is termed single-trial based ICA (sICA) in this study. The paradigm can be implemented as follows:

1). perform the denoising source separation (DSS) (Särelä and Valpola, 2005) based ICASSO on single-trial recordings;

2). select the estimated component with the largest SAR;

3). project the selected component back to the electrodes;

4). apply WLD on recordings of that raw single-trial to achieve the polarity for reference;

5). correct the polarity indeterminacy with the reference derived from WLD at each electrode to obtain the ICA-based single trial;

6). repeat steps 1-5 for all trials;

7). average over the ICA-based single trials for each participant;

8). implement the digital filter on the sICA based averaged trace to remove the low frequency noises generated by the averaging over many trials.

To sICA, DSS is adopted for ICASSO instead of FastICA in the first step. This is because the averaged trace could be free of sensor noises and then the classic ICA model is appropriate. For the single-trial recording, the sensor noise usually exists significantly, thus denoising is necessary. DSS can combine the denoising and FastICA together, so it is used in this study. The fourth and the fifth steps are to correct the abnormal polarity of the projected ICA component in the electrode field. The reference of the polarity is achieved from the wavelet filtered trace, not from prior knowledge of MMN. This is because MMN is always defined through the averaged trace and it is not reasonable to settle the polarities of all the single-trial recordings on the same channel to be identical. After the raw recordings are filtered, the evolution of the waveform can be found and then the polarity of the peak within the time frame representing the temporal feature of MMN can be retrieved. The last step is necessary to sICA. This is because averaging is actually a low pass filter and the low drift frequency may be generated through averaging over a number of trials. Such a filter may reduce the influence of the low frequency drift to the waveform.

In summary, the intrinsic of sICA is to improve the SNR in every single-trial. Then, averaging may contribute MMN with better properties.

4.2.3 Extraction of time-frequency represented MMN

Reference:

Cong, F., Zhang, Z., Kalyakin, I., Huttunen-Scott, T., Lyytinen, H., & Ristaniemi, T. (2009). Non-negative matrix factorization vs. FastICA on mismatch negativity of children. Proc. International Joint Conference on Neural Networks, Atlanta, Georgia, USA, June 14-19, 2009, pp. 586-590.

Cong, F., Kalyakin, I., Phan, A. H., Cichocki, A., Lyytinen, H., & Ristaniemi, T. (2010). Extract mismatch negativity and P3a through two-dimensional nonnegative decomposition on time-frequency represented event-related potentials. In L. Zhang, J. Kwok, and B.-L. Lu (Eds.): ISNN 2010, Part II, Lecture notes in computer science, 6064, pp. 385–391, 2010, Springer-Verlag Berlin Heidelberg 2010

The feasibility of NMF/NTF and the linear transformation model of EEG have been illustrated in the second chapter. For simplicity, it is not stated here.

Like ICA, NMF and NTF can also be targeted to find the separation matrix. However, NMF and NTF depend on the cost function under the constraints to nonnegativity and sparsity, not the spatial independence among sources (Cichocki et al., 2009). Raw EEG recordings do not conform to the requirement of nonnegativity. To facilitate NMF and NTF, the time-frequency representation of EEG recordings is first achieved and then NMF and NTF decompose the time-frequency represented EEG to obtain the desired time-frequency represented components (Lee et al., 2007 and 2009; Li and Zhang, 2010; Lohmann et al., 2007; Miwakeichi et al., 2004; Morup et al., 2007 and 2006; Sajda et al., 2004) . This study follows this line.

NMF and NTF also belong to the adaptive algorithms. In order to guarantee satisfactory convergence, a hierarchical and multistage procedure has been developed (Cichocki and Zdunek, 2006 and 2007). This consists of a sequential factorization of nonnegative matrices and is composed of many layers from which multi-start initialization can be utilized for each layer.

Five steps comprise the application of NMF and NTF on MMN. These are as follows:

1) perform the conventional wavelet transformation on the averaged trace to obtain its time-frequency representation;

2) decompose the multichannel time-frequency representation through NMF/NTF with the multilayer manner;

3) locate the same ROI for every time-frequency represented component through temporal and spectral features of MMN;

4) calculate the SAR for each time-frequency represented component;

5) choose the component with the largest SAR as the time-frequency represented MMN component.

In summary, what can be achieved through NMF/NTF is the time-frequency represented MMN component (Cong et al., 2010, 2009b). Like the ICA component, it has the variance indeterminacy in contrast to the real brain source. The contribution of NMF/NTF is to extract the structure of time-frequency represented MMN source from the time-frequency representation of an ordinary averaged trace. SAR can be used to denote the feature of the time-frequency represented MMN component for further analysis.

4.3 Author's contribution to joint publications

For all the articles, the author of this dissertation has been the principal and corresponding author, has presented the main idea of every article, has conducted the data analysis, and has written the article. The coauthors have given comments and suggestions on every article.

5 CONCLUSIONS AND DISCUSSIONS

This thesis has designed data processing methods to evaluate and extract mismatch negativity (MMN), a negative event-related potential (ERP) from EEG recordings and these procedures have been derived from the temporal, spectral, time-frequency and spatial features of MMN. Through the study of the real multichannel recordings of MMN from children, the effectiveness of these proposed methods are validated.

To represent MMN, the nonlinear time-frequency analysis method—Hilbert-Huang Transformation (HHT) (Huang et al., 1998) can contribute a more sparse, sharper, more dynamic and reasonable time-frequency representation in contrast to the conventional wavelet transformation (Burrus, 1998; Daubechies, 1992). As a result, HHT can more effectively represent the temporal and spectral features of MMN for further analysis. Particularly, from a psychological perspective, the application of HHT could reveal a special property of children with attention deficit hyperactivity disorders, i.e., they may have more temporally, spectrally, and spatially distributed brain activities than do the control children.

To ensure fast measurement of the correlation of recordings among single trials for MMN activity is very important during the experiment. The proposed frequency domain MMN model derived from Fourier transformation can facilitate achievement of this goal. The proposed method with Fourier transformation only takes less than one percent of the computing time of inter-trial coherence (ITC) with wavelet transformation. This means that the proposed method has the potential to measure the correlation of recordings among single trials in a real-time manner during the MMN experiment.

From the averaged recordings, the proposed method-wICA exploiting the temporal, frequency and spatial information of MMN source can extract MMN with better-defined properties than those estimated by the methods using parts of these features, for example, difference wave (DW) using the temporal feature, optimal digital filter (ODF) using the frequency feature (Kalyakin et al., 2007), independent component analysis (ICA) using the spatial feature (Kalyakin et al. 2008 and 2009). The superior properties in this study are referred to as the characteristics that a larger deviant may elicit an MMN peak with larger amplitude and shorter latency (Näätänen, 1992).

Moreover, the single-trial based ICA and averaged trace based ICA perform differently, i.e., extract different MMNs from the same dataset. This is because ICA does not possess the superposition rule (Comon, 1994; Mitra, 2005). Although the single-trial based ICA is very time consuming, it is still worth investigating the estimation from the EEG recordings, simply for the potential that the single-trial based ICA can conform to the dynamic model of EEG (EEG models may vary along different trials).

Furthermore, nonnegative matrix factorization (NMF) and nonnegative tensor factorization (NTF) can release the strong assumption of independence among sources required by ICA, can extract the time-frequency represented MMN and P3a simultaneously and facilitate the statistical tests on P3a, compensating the visual inspection of P3a through the waveforms. In this way, more information between typically developing children and children with reading disability can be exploited and may be helpful for the furtherment of clinical research.

Regarding ICA for ERP studies, there are still many open questions to be answered. For example, how to interpret in theory that the wavelet decomposition helps to achieve the reliable and robust ICA decomposition from the view of linear transformation model of EEG recordings. Do the ICA models of two deviants remain identical in the experiment? How are the ICA models of single trials evaluated in the experiment? What is the minimum number of trials required to produce MMN with good properties? What can we learn from the linear transformation model of EEG? How can better ICA algorithms be designed according to the features of ERPs? These questions are difficult to answer, but they are critical to the attainment of a more precise and more reliable estimation of brain activity. In practice, the computing of ICASSO is very expensive and it is difficult for the real-time application. Subsequently, how to reduce the complexity of computing is also challenging.

This thesis discusses the feasibility to study MMN and P3a components together with the standard NMF or row-wise column NTF algorithms (Cichocki et al., 2009) since ICA cannot achieve this goal in our dataset. Surprisingly, both such basic algorithms under two-dimensional nonnegative decomposition could extract the MMN and P3a components. Moreover, the coupling feature of MMN and P3a has been revealed by the simple NTF method. In fact, both NMF and NTF have better algorithms (Cichocki et al., 2009) and it will be necessary and promising to study which algorithms will be better to study MMN in theory and in practice, i.e., better in revealing the psychological knowledge of MMN which cannot be observed through the study of the MMN trace. This will be significant in the clinical study of MMN with NMF or NTF. Moreover, the conventional wavelet transformation helps to facilitate NMF and NTF in this study. Since HHT outperforms it to transform the MMN trace into time-frequency domain, it will be interesting to perform the NMF and NTF on the HHT based time-frequency represented MMN recordings in the future.

Although this study is only focused on the study of MMN elicited by one paradigm, the outlines of methods developed in this study can also be used in the research of MMNs elicited by other paradigms and other ERPs. This is because other MMNs and ERPs also have similar temporal, spectral, time-frequency and spatial features to the MMN used in this study.

YHTEENVETO (FINNISH SUMMARY)

Tämä tutkimus keskittyy poikkeavuusnegatiivisuuden (MMN) erottamiseen aivosähkönauhoituksista käyttäen ajallisia, spektraalisia, aika-taajuus- ja tilapiirteitä.

Arviointi sisältää MMN:n esitysmuodon ja laadun määrittelyn. Hilbert-Huang-muunnos (HHT) on aika-taajuusanalyysimenetelmä, jolla tutkitaan epälineaarisia ja epästationaarisia signaaleja, ja sitä voidaan käyttää MMN:n esittämiseen. Perinteiseen wavelet-muunnokseen verrattuna HHT esittää tehokkaammin MMN:n ajalliset ja spektraaliset piirteet. Yksittäisten kokeiden nauhoituksien korrelaation määrittelemiseksi esitetään malli MMN:stä taajuustasossa Fourier-muunnoksen avulla. Ehdotetun CoRaST-menetelmän hyöty tässä tutkimuksessa on se, että se vaatii vähemmän kuin prosentin laskenta-aikaa kuin perinteinen kokeiden välinen koherenssi. Tämä mahdollistaa CoRaSTin toteuttamisen reaaliaikajärjestelmissä.

MMN-komponentin erottamiseksi aivosähkönauhoituksesta ajan suhteen esitetään robusti ja luotettava menetelmä käyttäen hyväksi MMN:n aika-, taajuus- ja tilainformaatiota. Tämän uuden menetelmän hajotelmaosuus sisältää wavelet-muunnoksen ja riippumattomien komponenttien analyysin (ICA). Niinpä sitä kutsutaan wICA:ksi. wICA on hyödyllinen tilanteessa,jossa aivoissa on vain yksi aktiivinen toiminto, muut toiminnot eivät ole aktiivisia, ja tämä aktiiviinen toiminto kuvautuu aivojen sisältä päänahalle. Ehdotettu wICA-menetelmä voi suoriutua paremmin MMN:n erottamisessa aivosähkökäyrästä kuin perinteiset erotusmenetelmät, jotka käyttävät ajallista tietoa, MMN:n tunnettua taajuuskaistaa käyttävät optimaaliset digitaalisuotimet tai tilatietoon perustuva ICA.

Jotta aika-taajuustasossa esitetty MMN-komponentti saataisiin selville, epänegatiivinen matriisifaktorisointi (NMF) ja epänegatiivinen tensorifaktorisointi (NTF) hajottavat monikanavaisen aivosähkön aika-taajuusesityksen. NMF ja NTF tuottavat P3a:n arvion yhtäaikaisesti ja helpottavat P3a:n tilastollista analyysia. Tämä on lisäys P3a-aaltomuotojen silmämääräiseen tarkasteluun.

Vaikka tämä tutkimus on keskittynyt vain yhden koeasetelman tuottamaan MMN:ään, kehitettyjen menetelmien perustaa voidaan käyttää myös muulla tavoin tuotettujen MMN:ien ja herätepotentiaalien (ERP) tutkimiseen. Syy tähän on se, että muut MMN:t ja ERP:t ovat samankaltaisia kuin tämän tutkimuksen MMN ajallisesti, spektraalisesti, aika-taajuuden osalta sekä tilatasossa.

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