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Igor Kalyakin

Extraction of Mismatch Negativity from Electroencephalography Data

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ABSTRACT

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In this thesis, we consider three procedures to extract the mismatch negativity, a component of event-related potential, from electroencephalography data: optimal digital filtering, wavelet decomposition, and independent component analysis decomposition procedures. The procedures are compared on two different datasets, stressing their advantages over the conventional difference wave procedure. The main results of the thesis support the use of the wavelet decomposition and independent component analysis decomposition procedures to reveal the experimental effects which are expected from the literature, but not distinguishable through the traditional procedure, and show that these developed procedures may allow us to reduce the duration of an experimental session. Also, we discuss some practical issues related to the use of independent component analysis-based procedures in the extraction of the mismatch negativity. Finally, we consider a method for spatial denoising in multi-channel electroencephalography data, which can be used as a preprocessing step prior to the extraction of the mismatch negativity or any event-related potential as well.

Keywords: electroencephalography, event-related potential, mismatch negativity, difference wave, optimal digital filtering, wavelet decomposition, independent component analysis, signal-to-noise ratio, support-to-absence ratio

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Igor Kalyakin

ABBREVIATIONS

BSS	Blind source separation
DSS	Denoising source separation
DW	Difference wave
EEG	Electroencephalography
ERP	Event-related potential
FA	Factor analysis
FFT	Fast Fourier transform
IC	Independent component
ICA	Independent component analysis
MMN	Mismatch negativity
MRA	Multiresolution analysis
NMF	Non-negative matrix factorization
ODF	Optimal digital filtering
PC	Principal component
PCA	Principal component analysis
SAR	Support-to-absence ratio
SOA	Stimulus onset asynchrony
SNR	Signal-to-noise ratio
WLD	Wavelet decomposition

CONTENTS

LIST OF INCLUDED ARTICLES

I Kalyakin, I., González, N., Joutsensalo, J., Huttunen, T., Kaartinen, J., & Lyytinen, H. (2007). Optimal Digital Filtering versus Difference Waves on the Mismatch Negativity in an Uninterrupted Sound Paradigm. *Developmental Neuropsychology*, *31*(*3*), 429–452.

II Cong, F., Kalyakin, I., Huttunen-Scott, T., Li, H., Huang, Y., Guttorm, T., Ristaniemi, T., & Lyytinen, H. *Wavelet Decomposition on Mismatch Negativity of Children in Uninterrupted Sound Paradigm*. Manuscript submitted for publication.

III Kalyakin, I., González, N., & Lyytinen, H. (2008). Extraction of the Mismatch Negativity on Two Paradigms Using Independent Component Analysis. *Proceedings of the CBMS 2008*. In S. Puuronen, M. Pechenizkiy, A. Tsymbal, & D. J. Lee (Eds.), *21st IEEE International Symposium on Computer-Based Medical Systems*, *CBMS 2008* (pp. 59–64). Los Alamitos, CA: IEEE Computer Society Conference Publishing Services.

IV Kalyakin, I., González, N., Kärkkäinen, T., & Lyytinen, H. (2008). Independent Component Analysis on the Mismatch Negativity in an Uninterrupted Sound Paradigm. *Journal of Neuroscience Methods*, *174*(*2*), 301–312.

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VI Cong, F., Kalyakin, I., Ristaniemi, T., & Lyytinen, H. (2008). Drawback of ICA Procedure on EEG: Polarity Indeterminacy at Local Optimization. *IFMBE Proceedings*, *20(4)*. In A. Katashev, Y. Dekhtyar, & J. Spigulis (Eds.), *14th Nordic-Baltic Conference on Biomedical Engineering and Medical Physics*, *NBC 2008* (pp. 202–205). Berlin, Heidelberg, Germany: Springer-Verlag.

VII 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. *IJCNN 2009 Conference Proceedings*. *The 2009 International Joint Conference on Neural Networks*, *IJCNN 2009* (pp. 586–590). Eau Claire, WI: Documation LLC for IJCNN [CD-ROM].

VIII Ivannikov, A., Kalyakin, I., Hämäläinen, J., Leppänen, P. H. T., Ristaniemi, T., Lyytinen, H., & Kärkkäinen, T. (2009). ERP Denoising in Multichannel EEG Data Using Contrasts between Signal and Noise Subspaces. *Journal of Neuroscience Methods*, *180*(2), 340–351.

1 INTRODUCTION

It is evident that, during the last four decades, a new branch of science, cognitive neurophysiology, has been developing rapidly. This branch of science attempts to answer one of the most basic questions of humanity — the underlying neuronal mechanisms of human mental activity — more concretely and directly than before. The noninvasive study of human brain activity under normal conditions has a relatively limited arsenal of available methods and techniques. So far, the most widely used method is electroencephalography (EEG) — the measurement of the electrical activity generated in the brain with electrodes attached to the scalp. The EEG activity can be registered under spontaneous passive conditions or as responses to some external stimuli. The latter responses are often called event-related potentials (ERPs) to emphasize that they reflect the electrical activity in the brain associated with information processing.

So far, a large amount of articles devoted to the study of different ERPs has been published. Among them, the mismatch negativity (MMN) studies of the central auditory function have recently become very popular. There are several reasons for this wide interest in one of the smallest component of ERP. The MMN has created an unparalleled tunnel to the central auditory processing and underlying neural mechanisms. This tunnel provides the way to achieve a totally new level of understanding of the brain processes, which underlie central auditory perception, and the different types of auditory memory. At the same time, it allows for a better understanding of the attentional processes which control the access of auditory sensory input to conscious perception and other higher forms of memory.

Despite the aforementioned attractive perspectives in favor of the use of MMN, several pitfalls may emerge on the stage of signal processing of the collected data. The main problem comes from the fact that the MMN deflection is a relatively small signal compared to ongoing spontaneous EEG activity and noise, which are always present during a recording session. Usually, for more or less reliable evaluation of the basic quantitative characteristics of the MMN, hundreds of trials need to be averaged to allow an MMN peak to emerge. Moreover, in most cases, the so-called difference wave (DW) procedure needs to be applied to further clean up the MMN peak from irrelevant ERPs. Due to the nature of this procedure, where two different time intervals (sweeps) of a trial are subtracted from each other, the resulting MMN traces may contain up to two times more noise than before the subtraction. In practice, this is often the case as noise in these time intervals is only partly uncorrelated and, thus, is an additive quantity. The DW procedure is simple and, thus, widely used. However, due to the aforementioned noise increase in this procedure, new signal processing procedures need to be developed to avoid necessity of the subtraction.

In this thesis, we propose three procedures for the extraction of the MMN: optimal digital filtering (ODF), wavelet decomposition (WLD; both are single-channel methods), and independent component analysis (ICA) decomposition (multi-channel method) procedures. These procedures are considered to be alternative ways to extract the MMN from EEG data, supplementing the results obtained with the conventional DW procedure and making them more precise. It should be noted that the studies with application of the ICA-based procedures to extract the MMN are quite infrequent in the literature in contrast to the relatively large number of studies devoted to their application to extract other ERPs, thus being candidates for increased attention of the research community. Moreover, we briefly consider some practical issues of application of the ICA-based procedures to the MMN data when the so-called abnormal polarity reversal may arise as the result of the local optimization in a stochastic ICA algorithm. Also, we compare the ICA decomposition procedure with the non-negative matrix factorization (NMF), assuming weaker requirements of the latter to the MMN data under study, which may have a positive impact on the performance of the separation of the MMN from other irrelevant ERPs. Finally, we consider an ERP denoising procedure which uses the spatial information from multi-channel EEG data and, thus, may provide better results than simple single-channel averaging methods. Such denoising procedures may be used in particular as the preprocessing step prior to the extraction of the MMN or any other ERP as well.

The thesis is divided into two parts. The first part is the summary of the collection of the original papers which are then presented in the second part. The included articles are listed before this introductory chapter. The rest of the summary is organized as follows: Chapter 2 presents the basic topics of neurophysiology, which are necessary for the understanding of the results of the thesis; in Chapter 3, we consider the traditional and recently proposed procedures for the extraction of the MMN from EEG data; Chapter 4 contains summaries of the articles included in this thesis; and finally, in Chapter 5, the main results of the thesis are summarized, limitations of the research and further work are discussed.

2 OUTLINE OF NEUROPHYSIOLOGY: ELECTRICAL BRAIN SIGNALS

In this chapter, we present some basic topics of neurophysiology, which are necessary to understand the results of the thesis. In this context, the concepts exposed are not intended to provide a complete background on neurophysiology. On the contrary, here we only focus on describing EEG, and its derivative, ERPs. Finally, we introduce MMN, its technical characteristics, and why this small electrical brain response is important in clinical neurophysiology. Despite the relatively wide application of these topics, some fundamental issues are still controversial and, thus, need to be shortly described.

2.1 Electroencephalography

Originally, EEG was developed as a method for investigating mental processes. Soon, it started to be used in clinical applications, mostly in the study of epilepsy. The EEG recordings became even more popular with the introduction of ERPs (see Section 2.2) where it correlates with sensory and cognitive brain processing.

Research in EEG can be traced back to 1875, to the work of Richard Caton who first recorded electrical brain activity in exposed brains of rabbits and monkeys. In 1929, Hans Berger (Berger, 1929) discovered the so-called alpha rhythm in the ongoing EEG activity in man and this was considered as the first measurement of electrical brain activity in humans. Visual patterns, which are available through recording of the EEG signals, were correlated with various states, functions, dysfunctions, and diseases of the brain and central nervous system. Thus, it became one of the most important tools in neurophysiology to study these functions and diagnose diseases.

The EEG can roughly be defined as the recording of the mean electrical activity of the brain in different sites of the head. More specifically, it is the sum of the extracellular current flows of a synchronously active group of nerve cells. In turn, the electrical activity elicited by single nerve cells stems from the electrochemical processes underlying the generation of “action potentials”, essential for information transfer between nerve cells. These processes can have excitatory or inhibitory nature, respectively causing a reduction or increase of the membrane potential. The summed “action potentials” are the primary origins for the electrical potentials recorded from the scalp (Başar, 1980).

The EEG recording is obtained by placing electrodes on the scalp. A conductive gel or paste is normally used to improve the contact between these electrodes and the scalp. It is usually done after preparing the scalp area under electrodes by light abrasion, which removes dead skin cells, in order to reduce impedance. A recording system for the EEG usually consists of electrodes, amplifiers, filters, and a recording unit. The most widely used placement of electrodes is the so-called 10–20 international system (Reilly, 1993). It consists of up to 20 electrodes which are uniformly distributed along the head. Measurements of the electrical brain potentials can be recorded between pairs of active electrodes (bipolar recordings) or with respect to a supposed passive electrode called reference (monopolar recordings). Different electrode placements may be used as the reference, e.g., the tip of the nose or two earlobes. High-density (up to 256 electrodes) systems of electrode placement are also used.

Conventionally, EEG activity presented in spontaneous conditions can be characterized by the brain oscillations or rhythms. Brain oscillations are divided into frequency bands that are related with different brain states, functions, or pathologies, i.e., alpha (7.5–l2.5 Hz), beta (12.5–30 Hz), theta (3.5–7.5 Hz), delta (0.5–3.5 Hz), and gamma (30–60 Hz) rhythms (Niedermeyer, 1993; Steriade, 1993). Their contribution to the overall brain activity is changed in different situations, particularly with the level of vigilance, e.g., alertness, relaxation, sleep, etc.

2.2 Event-related potential

Spontaneous EEG activity can be altered by some stimulation. It can be internal (omission of an expected stimulus in a sequence of repeated stimuli) or external (sound tone, light flash, etc.) stimulation. The alteration of ongoing EEG activity caused by this stimulation is called ERP, and, in the case of external stimuli, also called evoked potential (EP). Thus, the EPs are a class of ERPs, which require the physical presence of a stimulus. The EPs are originated at the brainstem level and related to the execution of basic functions of perception, e.g., forming an internal representation of a stimulus and passing the retrieved information to the cortex centers involved in the execution of cognitive functions.

More technically, the ERPs are small voltage fluctuations (peaks) resulting from neural activity evoked by a stimulus in the EEG activity. The amplitude of the ERP peaks is usually under 5 μV and rarely exceeding 15 μV. This makes the ERPs much smaller than the spontaneous EEG activity which has a typical amplitude of 20–200 μV. Owing to this fact, it is a commonly applied practice to perform averaging of as many responses as available during the recording session to visualize the ERP of interest. The rationale behind the averaging is that the ERPs are time-locked to the stimulation event and have a similar pattern of response throughout repetitive homogeneous stimulation and that noise has a zero mean with symmetrical marginal distributions (Başar, 1980; Harmony, 1984). The averaging tends to decrease the influence of random EEG activity (i.e., spontaneous or non-event related fluctuations) while maintaining the consistent event related activity. Due to its simplicity and high efficiency, this procedure is by far the fundamental approach in the study of the ERPs.

There are mainly three modalities of stimulation (Regan, 1989): auditory (e.g., the stimuli are tones, clicks, etc.), visual (e.g., the stimuli are light flash, reversal of a pattern, etc.), and somatosensory (e.g., the stimuli are elicited by electrical stimulation of peripheral nerves, pain, senses, etc.).

By convention the ERP waveforms are divided into several parts or components which are the positive and negative-going fluctuations (Cacioppo et al., 2000). The components that occur prior to 100 ms after the stimulation onset are thought to reflect the information processing in the early sensory pathway. Cognitive scientists are mostly interested in the so-called long-latency ERPs which include P1, P2, N1, N2, and P3 (or P300) components. The long-latency ERPs are associated with cognitive processes, e.g., execution of memory, language, changes in the mental state, attention tasks, etc. These components are named by their polarity (P for positive and N for negative) and either their ordinal position after stimulus onset (P1 is the first positive peak), or their latency after stimulus onset (P300 is a positive-going component peaking at 300–400 ms). In general, the long-latency components which occur prior to 200 ms are thought to reflect late sensory and early perceptual processes while those after 250 ms or later are thought to reflect higher-level cognitive processes (e.g., memory, language, etc.). The ERP components can also be classified to either exogenous or endogenous components. The exogenous responses (mostly those prior to 200 ms) are elicited by sources clearly outside the processing system and reflect the physical features of the stimuli while the endogenous responses (mostly those after 200 ms) are internally paced (Näätänen, 1992).

2.3 Mismatch negativity

The MMN is a component of ERP. It occurs under any modality of stimulation described in the previous section, but has most frequently been studied for audition and vision. The oddball paradigm is most often used in the experiments to record the MMN. For example, in the auditory modality of stimulation, it consists in presentation of an infrequent and unpredictable irregularity (target or deviant stimulus) within a relatively long sequence of repetitive sounds (non-target or standard stimuli) (Näätänen, 1992; Näätänen et al., 1978). Such an irregularity can consist in a deviation from the standard stimuli in a first-order feature such as frequency, intensity, location, or duration of a sine or harmonic tone. However, it can also consist in a deviation from the standard stimuli in higher-order features, for example, a tone that differs from the preceding series of stimuli in the conjunction of two of its features (Gomes et al., 1997). The MMN is elicited regardless of whether the subject is paying attention to the auditory stimuli. The MMN peaks at 100–200 ms after deviation onset with the amplitude of peaks being up to –3 μV (rarely, up to –10 μV). The main intra-cerebral sources of the MMN are located in the auditory cortices of the temporal lobe (Näätänen, 1992). It has the fronto-centrally predominant scalp distribution and, when the nose reference is used, it reverses the polarity at leads positioned below the Sylvian fissure (Deacon et al., 2000). The polarity reversal may be absent with deviations in higher-order features (Gomes et al., 1997), however these types of stimulation are uncommonly used. Various kinds of physical changes in the auditory stimuli (intensity, duration, frequency, rise time, sound location, etc.) elicit the MMN (for a review, see Näätänen, 1992). Additionally, experimental variables, such as the probability of the deviant stimuli, magnitude of the deviation, and length of stimulus onset asynchrony (SOA), affect the basic characteristics of the MMN (Schröger, 1998; Sinkkonen & Tervaniemi, 2000). The SOA is usually defined as the time interval between the onset of two successive stimuli and, in extreme case, can be equal to the duration of a stimulus, e.g., an uninterrupted sound paradigm with no silence between the stimuli (Pihko et al., 1995; Winkler & Schröger, 1995).

Let us emphasize the main quantitative measures which can be used to characterize the MMN deflection from the signal processing point of view. The MMN can be quantified mainly through its peak amplitude and latency (Schröger, 1998; Sinkkonen & Tervaniemi, 2000). The polarity of the MMN corresponds to the sign of voltage of the MMN peak and is often incorporated to the peak amplitude measure. Calculation of signal-to-noise ratio (SNR) and support-to-absence ratio (SAR) is also useful, since these measures can serve as indicators of quality of the MMN data and success of the application of the procedures under study. The peak amplitude of the MMN is usually defined as a single data point most distant from the baseline value. The latency of the MMN is defined as a time interval corresponding to the MMN peak amplitude and calculated starting from the onset of the deviant stimulus. The single trial SNR of any ERP can be calculated using several procedures (Elberling & Don, 1984; Furst & Blau, 1991; Möcks et al., 1988; Rohde et al., 2002; Schimmel et al., 1974; Özdamar & Delgado, 1996). The most widely used procedure was originally reported in the study by Möcks et al. (1988). In short, the signal power estimate is the variance of the averaged trace of all available single trials of one type of deviant stimuli. The noise power estimate is the mean value of the variances of all available single trials minus the signal power estimate. The division of these two estimates results in the single trial SNR estimate based on these available single trials. The estimation of the SNR becomes more accurate with increasing the number of single trials involved in this estimation. Finally, the SAR of any ERP, recently proposed quality measure of ERP data (Cong et al., 2008a, b), is the quantity which reflects the relations between different time-frequency parts of a signal under study. In short, the time-frequency representation of an ERP needs to be calculated, providing a data matrix with the dimensions of time by frequency. In this matrix, the frequency range corresponds to the spectrum feature of the ERP of interest. In the time domain, the time range of a trace where the ERP is present is named as its support and residuals are named as its absence (Harmony, 1984). For the case of the MMN, the SAR reflects the relative power of the MMN time-frame to other parts of the recording within a trial through the time and frequency information simultaneously. This feature is considered to be the advantage of the SAR compared to the single trial SNR measure as the latter only uses information from the time domain. Since the support and absence are analyzed within the same frequency band, this parameter is particularly useful in reflecting the separation performance of overlapped ERPs. When the overlapped ERPs are removed, the support signal should become more evident and, thus, the SAR is improved. The larger the SAR is, the better the support signal is obtained. However, the main disadvantage of the SAR is the necessity to know a priori the frequency content of the ERP of interest, which often is not available.

One important and well-known characteristic of the MMN, supported by a substantial number of publications, is that the more deviant stimulus elicits a more pronounced MMN whose peak amplitude is larger and whose latency is shorter than for the less deviant stimulus (for a comprehensive review, see Näätänen, 1992). However, the decrease of the MMN latency is considered to be a more sensitive correlate of the increase of the magnitude of deviation than the increase of the MMN peak amplitude. This was recently confirmed in the study by Horváth et al. (2008) who showed that a larger magnitude of deviation did not necessarily result in a larger MMN in the paradigm with minimized confound of other ERPs, but these did result in an earlier MMN.

At present, the MMN provides the best known objective measure of the accuracy of the central auditory function in the human brain associated with the detection of changes in the auditory environment (Näätänen et al., 2007). There is no comparable measure in cognitive neuroscience, not even among those provided by the most modern brain-imaging technologies. The MMN does not require attention and is task independent. This makes it appropriate for testing the differences, e.g., between clinical populations. It can also be used in the assessment of individuals such as infants who are unable to respond in a test situation by speaking. It can be measured in sleep and coma. Moreover, the MMN allows us to study the accuracy of auditory discrimination independently for any acoustic feature (e.g., frequency, intensity) and for learned categories (e.g., language phonemes). Also, with the MMN, there is a possibility to estimate the duration of sensory memory. This can be done by measuring the decay of the MMN amplitude as a function of the interval between two successive stimuli. The measurement of the MMN is inexpensive and easy. Ontologically, it is the first “cognitive” ERP component with relatively well know generators and their functional significances. Due to its several advantages, the MMN has numerous existing and potential applications, both clinical and other. The most important of them are listed bellow (Näätänen & Escera, 2000).

- Pediatrics and Neuropediatrics: newborns, preterm infants.
- Developmental disorders: dyslexia, dysphasia, autism.
- Speech and language: aphasia, early language development.
- Audiology: cochlear implants.
- Psychiatry: schizophrenia, depression, somatization, alcoholism.
- Neurology: aging, Alzheimer's and Parkinson's diseases, coma (monitoring and prognosis), frontal-lobe damage, thalamic infarctions, neglect and auditory extinction.
- Others: anesthesia, drug effects (alcohol, antihistamine, cholecystokinin, and so on), learning (native language, foreign language), musicality, noise effect, and hypnosis.

The fast detection of the MMN has significant importance in the training of auditory/speech perceptual ability in clinical and other populations (Lyytinen et al., 2005). Auditory discrimination, which is evidenced by the MMN, can be assessed by computation and evaluation of the simple peak amplitude and latency measurements of this ERP. The human brain can be trained on the auditory discrimination following an online procedure. This procedure may consist in changing the type of stimulation (e.g., reducing the magnitude of deviation) and assessing if the auditory discrimination is improved with training. The human brain trained under these conditions is theoretically able to discriminate very small changes between the auditory stimuli even during sleep. This has a high psychophysiological relevance for different brain studies. However, until the present day, there is a limited amount of computational ways to follow perceptual learning on the basis of ERPs (in particular, MMN) responding to changes in the auditory environment. Since the MMN responses are averaged over a number of trials in order to obtain a reliable measure of the peak amplitude and latency of these responses and then further inefficiently processed (the DW procedure; see Section 3.1), it may be too slow for the online assessment of learning. In this context, the online computation and evaluation of the basic parameters of the MMN is a highly essential step forward to be able to train the human brain in such a manner. However, due to a very low amplitude of the MMN peaks compared to spontaneous EEG activity, the first step towards such online assessment procedure requires the development of the reliable procedures which will evaluate the basic quantitative characteristics of the MMN in a fewer number of trials than the traditional techniques.

3 METHODS FOR EXTRACTION OF MISMATCH NEGATIVITY

In this chapter, we present the traditional and recently proposed procedures for the extraction of the MMN from EEG data: DW, ODF, WLD, and ICA decomposition procedures.

3.1 Difference wave

Due to the fact that the physical characteristics of standard and deviant stimuli are quite similar to each other, both of them may elicit some identical exogenous ERP components that may, similarly to the MMN, be sensitive to the irregularities in repetitive auditory stimulation (e.g., P1, N1; Näätänen, 1992). However, only the deviant stimulus elicits the MMN. The conventional approach to remove the common exogenous processing is to apply the DW procedure (Schröger, 1998). It consists in the subtraction of the ERPs elicited by the standard stimulus (standard sweep) from that elicited by the deviant stimulus (deviant sweep). This procedure only leaves a clean MMN if these common ERPs are indeed identical. It means that these ERPs do not depend on the difference between the standards and deviant stimuli. However, in practice, this is not always the case, leading to an under- or overestimation of the MMN (Horváth et al., 2008; Jacobsen & Schröger, 2003). Additionally, the DW procedure reduces the SNR because noise in the standard sweep is added to that in the deviant sweep, that is, in practice, often the case, since noise in these sweeps is only partly uncorrelated. Thus, if a paradigm eliciting practically flat responses to the standard stimuli is available, the responses to the deviant stimuli can be used without application of the DW procedure (Sinkkonen & Tervaniemi, 2000). In fact, mainly N1 component, a negative deflection peaking at 50–150 ms after stimulus onset and, thus, partly overlapping the time window of the MMN, contributes to common exogenous processing (Näätänen, 1992). The N1 consists of at least three components, two of which are sensitive to the SOA, becoming smaller with shortening the SOA (for a review of component structure of the N1, see Näätänen & Picton, 1987).

Due to its simplicity and high efficiency, the DW procedure is so far the standard frame of reference for quantification of the MMN. However, as it reduces the SNR in the resulting MMN traces, alternative procedures which will avoid the necessity of the subtraction should be developed and paradigms eliciting nearly flat responses to the standard stimuli should preferably be used.

3.2 Time-frequency methods

3.2.1 Optimal digital filtering

Any time signal, including EEG recordings, can be represented in different ways depending on the interest in visualizing certain characteristics. Among these, the frequency representation is the most powerful and conventional one. It allows for the visualization of the periodicities of EEG signals, which often helps to understand the underlying physical phenomena. That is the main advantage over the time representation. Frequency analysis was developed by Jean Baptiste Fourier (1768–1830). The Fourier transform is computationally very attractive as it can be calculated by using an efficient algorithm called fast Fourier transform (FFT; Cooley & Tukey, 1965; Yuen & Fraser, 1979).

Regardless of the experimental design employed to elicit the MMN, increasing the SNR of recordings is necessary, especially if the MMN is considered to be used for the assessment of individuals. The noise level can be reduced by digital filtering which can be implemented, for example, using the FFT algorithm. The rationale behind linear filtering is that certain frequencies of EEG data completely consist of meaningless variations and can thus be discarded (Sinkkonen & Tervaniemi, 2000). This applies to both very low frequencies, which may slowly shift the baseline (reference voltage in EEG recordings), and very high frequencies, which, if present at longer latencies, may likely be independent of the stimulus.

The frequency range of the MMN is a question still under speculation in the literature (Picton et al., 2000; Sabri & Campbell, 2002; Sinkkonen & Tervaniemi, 2000). An analog band-pass of 0.1–30 Hz is often used during recording of the MMN. However, these are probably not the optimal filter settings with respect to the SNR, since the MMN has most of its energy in the 2–5 Hz frequency range (Picton et al., 2000). Sinkkonen and Tervaniemi (2000) noted that a band-pass filter in the frequency range of 1–20 Hz is, in most cases, acceptable for visualization of the MMN, but this is not optimal to perform quantitative amplitude and latency analyses of the MMN. In this context, they proposed to apply the optimized low-pass filter (e.g., a cosine slope of 5–10 Hz width centered at 10 Hz) and then measure the amplitude and latency of the MMN peak. The numerical values of the MMN amplitude obtained after such a filtering do not behave on the scale of the original responses as this filtering smoothes the shape of the MMN peak. Using these values for comparisons between experimental conditions, groups, or individuals is preferable due to the increased SNR (Sinkkonen & Tervaniemi, 2000). In fact, this approach may be preferred in the treatment of data from paradigms that are unlikely to produce other significant activities at the nearby latencies. This is so, because such an optimized filter spans a wider time interval than the response itself to account for the temporal correlation of data. However, considerations about the high-pass filter settings are limited in the literature. The MMN can significantly be distorted by slow ERPs and low-frequency background EEG activity, which should be eliminated by a suitable high-pass filter.

The aforementioned optimized filter, but with some variations in choice of the cut-off frequencies, was used in several studies. For example, Tervaniemi et al. (1999) used the band-pass digital filter of 1–30 Hz for data illustration and of 2–10 Hz (24 dB/octave in both) for the subsequent amplitude and latency analyses of the MMN; Sabri and Campbell (2002) proposed to use the band-pass digital filter with the cut-offs not narrower than 3–12 Hz. These studies use different experimental designs to elicit the MMN. This fact may explain the differences in the settings of the band-pass digital filter.

It should be noted that the main purpose of any filter applied to MMN data is to reduce background noise, reject other irrelevant ERP activities, and, in the process, not to distort the actual MMN. However, distinguishing between the signal and unwanted activities is not always easy, since this requires some knowledge about their frequency contents. The frequency content of the MMN may be overlapped with that of the unwanted activities and, thus, the settings for the optimized digital filter should be adjusted in an experimental paradigm under study.

3.2.2 Wavelet decomposition

The Fourier transform consists in expressing the signal of interest as a linear function of complex sinusoids of different frequencies. However, it gives no information about time and requires stationarity of the signal. By "windowing" the complex sinusoidal functions of the Fourier transform, a time evolution of the frequencies can be obtained when the windows are slid throughout the signal. This procedure is called Gabor transform. The Gabor transform gives an optimal time-frequency representation for the chosen size of the window. However, one critical limitation appears when windowing the data, due to the uncertainty principle (Chui, 1992). If the window is too narrow, the frequency resolution will be poor, and if the window is too wide, the time localization will not be so precise. EEG data, which may involve slow activities, will require wide windows and, on the other hand, for EEG data with fast transients (high frequency fluctuations) a narrow window will be more suitable. Thus, due to its fixed window size, the Gabor transform is not suitable for the analysis of EEG signals involving different ranges of frequencies.

Grossmann and Morlet (1984) introduced wavelet transform in order to overcome this problem. The main advantage of the wavelet transform is that it provides a varying window size, being wide for the slow frequencies and narrow for the fast frequencies. In turn, it leads to an optimal time-frequency resolution in all frequency ranges (Chui, 1992; Mallat, 1989). Furthermore, owing to the fact that windows are adapted to the transients of each scale, wavelets do not impose stationarity of the signal. Due to this advantage, a band-pass digital filter based on the wavelet transform may provide better results compared to that based on the Fourier transform. The latter removes the frequency content of a certain frequency range. Its output is the reconstruction based on the whole period of the original data within a certain frequency band. As a result, it cannot separate the ERPs overlapped in the frequency domain (see above), and the filter coefficients do not reflect any particular information of the ERPs in the time domain. The MMN is time-locked to the deviant stimuli and should appear at a certain time interval and certain frequency band according to the experimental paradigm. Consequently, to separate the MMN from the overlapped ERPs in the time and frequency domains simultaneously, it is necessary to somehow exploit the time and frequency information of the MMN. This can be achieved by using the WLD (Burrus et al., 1998). The core of the WLD is to apply the appropriate wavelet ("mother wavelet") to decompose the signal into different levels and then to find the proper levels to reconstruct the desired parts of the original signal. This decomposition and reconstruction can be implemented using a hierarchical scheme called multiresolution analysis (MRA; Chui, 1992; Mallat, 1989). Under this scheme, contracted versions of the wavelet function match the high frequency components of the original signal and, on the other hand, dilated versions match the low frequency oscillations. By projecting the original signal into wavelet functions of different sizes, it is possible to obtain the details of the signal on different scale levels. In other words, with the MRA, higher temporal resolutions at higher frequencies and lower temporal resolutions at lower frequencies can be obtained. The optimal mother wavelet to be applied to a certain signal can be chosen based on its mathematical properties or just based on visual features that can more or less be suitable for the analysis of a certain signal.

The WLD has already been used in the analysis of EEG signals with different wavelets (Adeli et al., 2003; Bartnik et al., 1992; Bertrand et al., 1994; Bostanov & Kotchoubey, 2006; Jongsma et al., 2006; Kalyakin et al., 2003; Quian & Garcia, 2003; Rossoa et al., 2006; Wilson, 2004; Zhang & Zheng, 1997). Some of these studies use the WLD as a preprocessing technique for digital filtering of the ERPs of interest and report better results than those obtained with Fourier-based techniques, especially when applied to non-stationary signals. As in the case of Fourier-based digital filtering, the main goal of WLD-based digital filtering is to extract the ERPs of interest by eliminating the contribution of ongoing EEG activity and other irrelevant ERP components. The WLD-based digital filters were implemented in some MMN studies, e.g., for denoising in MMN data of adults using a biorthogonal wavelet (Atienza et al., 2005), for the decomposition of the MMN of children using Coifman wavelets (Burger et al., 2007), etc. These two studies use different types of wavelets and analyze different MMN datasets (adults and children). Thus, the MMN patterns differ between these two datasets, explaining the use of different mother wavelets.

3.3 Source separation methods (ICA)

In general, the methods for ERP signal processing can be divided into two groups. The first group is the single-channel methodologies, such as a digital filtering, WLD, etc., and the second group is the multi-channel methodologies, for example, principal component analysis (PCA), factor analysis (FA), ICA, etc. (Sanei & Chambers, 2007). The multi-channel methods usually require much more computations compared to the single-channel methods. Due to this requirement, the multi-channel methods are often uneconomical and hardly implemented in fast real-time data processing systems. However, they can provide better results due to the utilization of spatial information about the ERPs of interest among recordings from different electrode locations.

So far, among these multi-channel methodologies, the most widely used approach is ICA (Hyvärinen et al., 2001). The ICA is a particular class of methods to solve the relaxed blind source separation (BSS) problem. In general, the BSS problem consists of recovering unobserved signals or "sources" from several observed mixtures. Usually, the observations are obtained at the output of a set of sensors, where each sensor receives a different combination of the source signals. The term "blind" means that the source signals are not observed and no information is available about the mixture. The lack of prior knowledge about the mixture can be compensated by a statistically strong but often physically plausible assumption of independence between the source signals (the relaxed BSS problem). This independence assumption is used by the ICA.

The linear BSS model can be expressed formally, where a set of m linear and instantaneous mixtures $x_1(t),\ldots,x_m(t)$ of some n original unknown source signals $s_1(t),\ldots,s_n(t)$ is observed and the goal is to determine the source signals given only their mixtures. That is, given the equation:

$$\mathbf{x} = \mathbf{As}\,, \tag{1}$$

where $\mathbf{x} = (x_1(t),\ldots,x_m(t))^T$, $\mathbf{A} = [\mathbf{a}_1,\ldots,\mathbf{a}_m]$ is the unknown $m \times n$ mixing matrix and $\mathbf{s} = (s_1(t),\ldots,s_n(t))^T$. The aim is to estimate a demixing matrix $\mathbf{B} \approx \mathbf{A}^{-1}$ such that the mixing process $\mathbf{A}$ can be inverted and the source signals $\mathbf{s}$ recovered:

$$\hat{\mathbf{s}} = \mathbf{Bx} = \mathbf{BAs} \approx \mathbf{s}\,, \tag{2}$$

where $\hat{\mathbf{s}}$ denotes the estimated source signals.

In order to solve the relaxed BSS problem, the ICA assumes the source signals to be non-Gaussian mutually independent and identically distributed (i.i.d.) processes and the mixing matrix $\mathbf{A}$ to be full rank with $m \geq n$ (i.e., there are at least as many mixtures as source signals). Under these assumptions, mixing matrix **A** can be estimated up to a row permutation and scale factor. The estimated source signals in the case of the ICA are called independent components (ICs). Considering the case of the separation of ERPs, if the ICs with indexes in some set Ω are found to be ERPs of interest (e.g., MMN), these can easily be projected back to the electrode locations by:

$$\mathbf{x}_{ICAsep}(t) = \sum_{j \in \Omega} \hat{\mathbf{a}}_j \hat{\mathbf{s}}_j(t). \tag{3}$$

This effectively cancels activities irrelevant to MMN (other ERPs, background electrical brain and non-brain fluctuations, artifacts, etc.) and considerably increases the SNR of the experimental data.

The source separation methods can be classified into four groups by the a priori information or criteria used to find a solution (Cichocki & Amari, 2002):

ICA-based methods: as mentioned above, the source signals are assumed to be i.i.d processes, thus, only statistical (distributional) properties of the observable mixtures are used, discarding time autocorrelation within each sensor observation of these mixtures. The main differences among algorithms in this group consist of the definition of a suitable contrast function measuring independence (non-Gaussianity, mutual information, marginal entropies, maximum likelihood, cumulants, etc.) and the optimization procedure (gradient-based or algebraic methods) used to find the extremum of the contrast function. The well-know algorithms from this group are FastICA, Infomax ICA, JADE, etc. (for a review, see Hyvärinen et al., 2001).

Temporal/spectral structure: the criteria of this category exploit the fact that, if the source signals have a temporal/spectral structure, then they also have non-zero autocorrelations. In this case, the statistically very strong assumption of independence between the source signals can be relaxed to the assumption of their uncorrelatedness. As a consequence, the separation can be achieved by using simple second-order statistics in contrast to the ICA-based methods from the first group, which use higher-order statistics. The well-know algorithm from this group is TDSEP (Ziehe & Müller, 1998).

Diversities of the signals: these include different discriminating a priori known properties of the signals in temporal, spatial, and frequency domains or in combinations of these domains. Thus, the source signals are initially divided into several categories by their discriminative properties in the chosen domains. The separation algorithm should be aware of this division and automatically classifies estimated components into defined groups. For example, Särelä and Valpola (2005) proposed an algorithmic framework called denoising source separation (DSS) which incorporates some prior knowledge to the source separation algorithm by means of denoising of the source signal estimates.

Non-stationarity: the second-order non-stationarity is usually considered within this category. This means that the variance of signals changes in time. The source separation problem under the variance non-stationarity assumption can be solved, for example, by perfoming second-order decorrelation.

Additionally, combinations of the methods from these four groups can also be used. For example, JADETD algorithm is a straightforward combination of higher-order statistics and temporal information. It performs the BSS by simultaneous diagonalization of a set of cumulant matrices and a set of time-delayed correlation matrices, achieving comparable performance to JADE or TDSEP as long as their respective assumptions are fulfilled and clearly outperforming them otherwise (Müller et al., 1999).

In this thesis, we mostly focus on solving the relaxed BSS problem by the ICA-based procedures, i.e., the first group of methods (see Sections 4.1.3–4.1.6). However, some BSS approaches from the other groups are also considered in two our studies (see Sections 4.1.7–4.1.8). We discuss below some problems with the ICA-based methods and present the main applications of these methods to EEG (ERP) signals.

An important problem with some ICA algorithms is that they are stochastic. This means that the results of one run of the algorithm may differ from those of another run. Thus, an ICA algorithm gives a specified number of ICs but it may be unclear which of these are stable and can be considered relevant. For example, marginal distribution-based ICA algorithms try to find the global extremum of a contrast function (e.g., likelihood, mutual information, negentropy). The probability of finding this extremum may be very low, especially in a high dimensional space (for a discussion, see Hyvärinen et al., 2001). Himberg et al. (2004) presented an approach to investigate the algorithmic and statistical reliability of the ICs obtained after the FastICA algorithm (Hyvärinen, 1999). Their method is based on estimating a large number of IC candidates by running the FastICA algorithm many times and visualizing their clustering in the signal space. This approach was implemented in the ICASSO software package (Himberg et al., 2004). Another important problem with the ICA, as in any other parameter estimation problem, is overfitting (for a review, see Särelä & Vigário, 2003). In general, ICA overfitting occurs when the number of parameters to be estimated from the data is too large with respect to the number of data samples. In the BSS problem, ICA overfitting leads to completely wrong ICs which show poor reliability. In the case of marginal distribution-based ICA algorithms, such estimated ICs have a single spike or bump and are practically zero elsewhere. These ICs can easily be interpreted as non-existent ERPs.

The ICA is widely used in biomedical applications and, in particular, to study EEG (ERP) signals (for a review, see Albera et al., 2010). These applications assume that several conditions are verified, at least approximately: the existence of statistically independent sources of brain signals, their instantaneous linear mixing at the electrode locations, stationarity of the mixing, and stationarity of the ICs. It should be noted that the ICA can be seen as an extension to the PCA and FA. However, it is considered as a much more powerful technique which is capable of estimating the underlying sources when these classic methods completely fail (e.g., see Jung et al., 2000b).

The first line of application of the ICA to EEG signals is the separation of artifacts (Jung et al., 2000a, b; Vigário, 1997; Vigário et al., 1998; Zvyagintsev et al., 2008). Artifacts mean signals not generated by brain activity, but some other external disturbances, such as ocular, muscular activity, cardiac cycle, etc. The

ICA, in contrast to the PCA, gives a method for artifact removal where an accurate model of the process that generated the artifacts is not needed. This is the blind aspect of the method. Moreover, specified observation intervals that contain mainly the artifact and additional inputs are also not needed. This is the unsupervised aspect of the method. It turns out that the artifacts are quite independent from the rest of the signal and, thus, even this requirement of the model is reasonably well fulfilled.

The second line of application of the ICA to EEG signals is the separation of the ERP components. Makeig et al. (1996) presented the first application of blind decomposition to the biomedical time series. They applied the Infomax ICA algorithm to decomposition of the ERP data and reported the use of the ICA to monitor alertness. Successive comprehensive studies from this research group (Makeig et al., 1999a, b) demonstrated the success of the ICA in the separation of some early (e.g., N1–P1 complex) and late positive (e.g., P3 complex) ERPs during visual spatial attention tasks. Vigário et al. (1999) compared the PCA and ICA in the quality of the decomposition of different ERPs and showed that the PCA often could not really separate the independent signals. In fact, after computing the principal components (PCs) of these signals, most of them still represented a mixture of the ERPs, making it difficult for any kind of interpretation. In contrast, after computing the ICs, the psychologically plausible ERP components could be visible and separated.

The studies with application of the ICA to the analysis of the MMN are relatively infrequent in the literature. By saying the "analysis of the MMN", we consider here the second line of application of the ICA to EEG and ERP signals, namely the separation of the ERP components from each other. Indeed, cleaning the initial EEG data, which involves the separation of the ERPs from ocular, muscular artifacts, etc. and denoising, may (and should) be considered as a preprocessing step prior to the separation of the MMN from other irrelevant ERPs. In this connection, the publications devoted to cleaning the MMN data from artifacts are not present here.

Marco-Pallarés et al. (2005) designed a two-step approach to uncover the spatiotemporal pattern of brain activations underlying the MMN. They separated statistically independent sources by preprocessing the data with ICA and subsequently identified the cerebral sources of each IC using low-resolution tomography (LORETA). The authors found six main ICs using 30 electrode locations that accounted for more than 67% of data variance in the time window of the MMN defined as 100–300 ms from the onset of the deviant stimuli. They argued correspondence of the sources associated with these ICs to those proposed in the classical MMN literature.

Hill et al. (2005) used support vector machine classification and recursive channel elimination on the ICs of the averaged ERPs after application of the FastICA algorithm to show that untrained user's ERP (MMN) data can be classified with a high level of accuracy. However, they noted that application of the DW procedure reduced the SNR of the MMN, in turn, yielding poorer classification accuracy. They argued that an auditory paradigm eliciting the MMN could be used as a basis for brain–computer interfaces.

4 THESIS CONTRIBUTION

In this chapter, we provide a brief summary of each article included in the thesis and discuss the main results obtained in each corresponding article. Also, contribution of the author of the thesis for joint publications is presented.

4.1 Summary of the included articles

4.1.1 "ODF vs. DW on MMN in uninterrupted sound"

Reference: Kalyakin, I., González, N., Joutsensalo, J., Huttunen, T., Kaartinen, J., & Lyytinen, H. (2007). Optimal Digital Filtering versus Difference Waves on the Mismatch Negativity in an Uninterrupted Sound Paradigm. *Developmental Neuropsychology*, *31*(*3*), 429–452.

In this study, we investigate and illustrate an alternative way of the quantification of the MMN, the ODF procedure, and compare it with the traditional DW procedure. To begin with, we briefly introduce the MMN, the experimental variables, which may affect its elicitation, and the traditional way to remove common exogenous ERPs, i.e., the DW procedure. The latter involves the subtraction of the ERP responses elicited by the standard auditory stimuli (standard sweep) from that elicited by the deviant auditory stimuli (deviant sweep). Then, we discuss that, in some experimental paradigms, e.g., in an uninterrupted sound paradigm, this subtraction may have a negative impact on the quantification of the MMN as the common exogenous ERPs may differ in the standard and deviant sweeps. Moreover, the subtraction reduces the single trial SNR of the MMN in any paradigm. For our experiments, we use the stimulation procedure originally reported in the study by Pihko et al. (1995) and slightly modified in the study by Huttunen et al. (2007). Such a stimulation procedure was initially designed to obtain a large number of trials (350 for each of two types of deviant stimuli) over a short time (15 min). We hypothesize that, in this paradigm, the DW procedure is not the most efficient way to quantify the MMN, and we provide several reasons to acknowledge this statement. At the same time, we assume that the ODF procedure may behave more efficiently in the context of the extraction of the MMN. Similarly to the case of the DW procedure, we provide the reasons which underlie our assumptions. We review the literature where the frequency range of the MMN is discussed, and digital filtering is performed on the data collected under different experimental paradigms. We apply these two procedures separately to the same ERP data and then compare statistically the peak amplitude, latency, and single trial SNR of the MMN to ascertain any advantages of application of the ODF procedure over the DW procedure.

After a brief description of the procedure of the recording and the design of the experimental paradigm itself, the ODF procedure is considered in detail. It consists of a set of low- and high-pass digital filters which are used to determine the digital filter settings for the optimal extraction of the MMN. We use FFT-based digital filters with zero padding to increase the resolution in the frequency domain. Repeated measures ANOVAs are used in the statistical analyses.

By performing all necessary calculations, analyses, and comparisons, we demonstrate that the ODF procedure performs better than the DW procedure in the quantitative MMN analyses in the experimental paradigm under study. It increases the single trial SNR and has no effect on the temporal characteristics of the MMN. An increased single trial SNR means that a smaller number of trials can be collected when applying such a filtering to obtain the same single trial SNR than when applying the DW procedure (about 250 trials instead of the original 350 trials). This shortens the experimental session, which is especially relevant when the participants are children. However, the proposed procedure reduces the MMN peak amplitude, which may be explained by the biased baseline level in the DW procedure and the low frequency drift presented in the recordings. Neither the ODF or DW procedures extract the MMN whose quantitative characteristics are supported by the literature, i.e., the more deviant stimulus should produce an MMN with a larger peak amplitude and earlier latency than the less deviant stimulus. The possible explanations are given. The frequency range for the optimal extraction of the MMN in the paradigm under study is 2–8.5 Hz. This finding is used in the subsequent studies where the same dataset is utilized by the author of this thesis and colleagues. Finally, we discuss in detail why the DW procedure produces an unclean MMN in this particular paradigm. The two main reasons are a partial lack of the time synchronization between the responses to the corresponding repeated stimuli in the standard and deviant sweeps and the difference at the amplitude of these responses. Also, we provide the considerations about the digital filters which may be used in the ODF procedure and about the methods for the SNR estimation of ERPs.

It should be noted that this study is the principal study of this thesis as it raises the most important research question concerning the MMN extraction from EEG data, which have subsequently been tried to be answered in the following studies. In this context, in the following four studies, the research question remains the same, namely, to obtain a cleaner MMN with some new procedure than with the referenced DW procedure, whose quantitative characteristics are supported by the literature.

4.1.2 "WLD on MMN in uninterrupted sound"

Reference: Cong, F., Kalyakin, I., Huttunen-Scott, T., Li, H., Huang, Y., Guttorm, T., Ristaniemi, T., & Lyytinen, H. *Wavelet Decomposition on Mismatch Negativity of Children in Uninterrupted Sound Paradigm*. Manuscript submitted for publication.

This study introduces another single-trial methodology, the WLD procedure, an alternative way of the quantification of the MMN. This procedure is compared to the ODF and DW procedures considered in the previous study on the same dataset to ascertain whether it contributes with a cleaner MMN than the other two procedures. As mentioned in Section 3.2.2, wavelets have a varying window size adapted to each frequency range. Thus, wavelet-based filtering of some frequency bands does not affect the morphology of the others. This is not the case for Fourier-based filters where filtering the high frequencies of EEG data affects the morphology of the low frequencies. As a consequence, the shape of the ERP spikes may be modified, thus, obscuring important details. In general, Fourier-based filtering gives a smoother signal than that obtained by using wavelets (MRA) due to the nearly optimal time-frequency resolution of wavelet transform for every scale. Thus, wavelet-based filtering leads to a better resolution of the ERP responses compared to Fourier-based filtering. These considerations explain the choice of the WLD procedure to extract the MMN.

The core of the WLD procedure is to apply the appropriate wavelet to decompose the signal of interest into different levels and then to find the proper levels to reconstruct the desired parts of the original signal. Thus, we choose several types of wavelets and analyze their frequency responses in order to define the most appropriate wavelet for the extraction of the MMN in the experimental paradigm under study. Then, we choose the corresponding levels for the decomposition and reconstruction of the MMN. By conducting a series of simulations, the chosen mother wavelet is a reverse biorthogonal wavelet of order 6.8 (rbio6.8). In the MRA, we use seven levels for the decomposition (D1–D7) and two levels for the reconstruction of the MMN, namely D5 (6.25–3.125 Hz) and D6 (3.125–1.5625 Hz), as these two levels correspond as close as possible to the frequency range of the ODF procedure, i.e., 2–8.5 Hz, defined in the previous study. The implementation of the DW and ODF procedures is the same as in the previous study.

The results show that the WLD procedure extracts a cleaner MMN than the other two procedures. It extracts the MMN whose quantitative characteristics are supported by the literature. The more deviant stimulus produces an MMN with a larger peak amplitude (however, only in quantitative values; surprisingly, no statistical significance) and earlier latency (statistically significant) than the less deviant stimulus. After application of the WLD procedure, contribution of other ERPs to the resulting traces is the smallest compared to the referenced procedures (especially compared to the DW procedure). However, the peak amplitude of the MMN is also reduced. This may be explained by stronger filter settings in the WLD procedure. The ODF procedure has a longer latency of the MMN than that for both the WLD and DW procedures. There is no difference in the latency of the MMN between the WLD and DW procedures.

The WLD procedure is recommended for the extraction of the MMN from EEG data in the studies which use single-channel methods and the time-frequency representation of data. However, it should be noted that some methodologies used in this study, namely the choice of the appropriate wavelet based on its frequency response and the desired levels for the reconstruction in the MRA, require prior knowledge of the MMN frequency content, which, in general, is unknown. For the experimental paradigm under study, we define this range in the previous report and directly use it in this study. However, in other experimental designs, such information may not be available and needs to be somehow obtained, e.g., through the MMN spectrum analysis, prior to the use of the aforementioned methodologies. This is a limitation of the approach.

4.1.3 "ICA on MMN in two sound paradigms"

Reference: Kalyakin, I., González, N., & Lyytinen, H. (2008). Extraction of the Mismatch Negativity on Two Paradigms Using Independent Component Analysis. *Proceedings of the CBMS 2008*. In S. Puuronen, M. Pechenizkiy, A. Tsymbal, & D. J. Lee (Eds.), *21st IEEE International Symposium on Computer-Based Medical Systems, CBMS 2008* (pp. 59–64). Los Alamitos, CA: IEEE Computer Society Conference Publishing Services.

In this short pilot study, we develop, implement, and preliminarily test a new procedure for the extraction of the MMN, which utilizes a multi-channel methodology. The procedure is based on ICA and, thus, called the ICA decomposition procedure. The goal is to evaluate whether it extracts a cleaner MMN and produces an increased SNR, when compared to the conventional DW procedure. Such an approach is tested in two slightly different experimental paradigms, employing uninterrupted and interrupted sounds.

After a brief introduction to the ICA and how it can be used to separate the ERPs, the core of the procedure is described. It consists of four consecutive steps: (1) decomposition of the original traces into ICs, (2) validation of the obtained ICs, (3) division of the validated ICs to the MMN-like and non-MMN-like ICs, and (4) projection of the MMN-like and non-MMN-like ICs back to the electrode locations separately. Each step is considered in detail to explain the chosen methodology. The FastICA algorithm and the ICASSO software package are used.

The obtained results show that the ICA decomposition procedure performs better than the DW procedure in the extraction of the MMN in both studied experimental paradigms. It extracts a cleaner MMN and facilitates improvement of the single trial SNR compared to the DW procedure. Due to this improvement, it may allow for shorter recording sessions of the MMN. However, in this pilot study, we use the ERP data from only one participant from each of the two paradigms. Thus, the obtained results should be validated through performing a series of statistical tests. This is done in the following two studies.

4.1.4 "ICA on MMN in uninterrupted sound (extended)"

Reference: Kalyakin, I., González, N., Kärkkäinen, T., & Lyytinen, H. (2008). Independent Component Analysis on the Mismatch Negativity in an Uninterrupted Sound Paradigm. *Journal of Neuroscience Methods*, *174*(2), 301–312.

The purpose of this study is to compare the efficiency of the ICA decomposition procedure against the ODF and DW procedures in the quantitative analyses of the MMN elicited in an uninterrupted sound paradigm. To begin with, we briefly introduce the MMN, the particular paradigm for its elicitation, and discuss the results of application of the ODF and DW procedures to the ERP data obtained in our previous study (see Section 4.1.1). We raise the main drawbacks of their application, which motivated us to develop a new procedure. Then, the ICA is introduced in the context of how it may improve the results of the extraction of the MMN. The potential problems of application of marginal distribution-based ICA algorithms (i.e., stochasticity, overfitting) as well as types of the ICA (BSS) algorithms are discussed. We hypothesize that the MMN and other irrelevant ERP and non-ERP activities are elicited from spatially different sources in the brain and are independent from each other. Thus, a marginal distribution-based ICA algorithm can separate them. We assume that this procedure would allow us to extract a cleaner MMN and obtain an increased single trial SNR compared to the referenced procedures mentioned earlier. We apply each of these three procedures separately to the same ERP data. Then, we compare statistically the peak amplitude, latency, and single trial SNR of the MMN to ascertain any advantages of application of the ICA decomposition procedure over the two referenced procedures.

After a brief description of the procedure of the recording and the design of the experimental paradigm itself, an extended description of the ICA decomposition procedure compared to the previous pilot study is given. The implementation of the two referenced procedures is the same as in our study in Section 4.1.1. Repeated measures ANOVAs are used in the statistical analyses.

By performing all necessary calculations, analyses, and comparisons, we demonstrate that the ICA decomposition procedure performs better than the ODF and DW procedures in the quantitative analyses of the MMN in the present paradigm employing an uninterrupted sound. The statistical comparisons among the three procedures show that the ICA decomposition procedure significantly improves the single trial SNR compared to the DW procedure. Also, it produces a similar single trial SNR compared to the ODF procedure that does not support our hypothesis of a better single trial SNR after application of the ICA decomposition procedure. Nevertheless, application of the ICA decomposition and ODF procedures would require fewer experimental trials to obtain the same single trial SNR than application of the DW procedure, about 265 and 281 trials, respectively, instead of 350 trials for one type of deviant stimuli. This may shorten the experimental session. Reduction at the MMN peak amplitude is significant after application of both the ICA decomposition and ODF procedures compared to the DW procedure. The main reason is a biased baseline in the DW procedure as a result of the subtraction. The MMN peak amplitude is similar after application of the ICA decomposition procedure compared to the ODF procedure. Finally, the temporal characteristics of the MMN are not affected by any of the procedures under study.

The ICA decomposition procedure allows for the extraction of a cleaner MMN whose characteristics are in agreement with most of the literature. The MMN elicited by the more deviant stimulus is significantly larger at the peak amplitude and earlier in the latency compared to the less deviant stimulus. In contrast, the peak amplitude and latency of the MMN for the two deviant stimuli do not differ significantly between deviants when extracted through the ODF or DW procedures.

The main limitation of this study is the number of available electrode locations. The collected ERP data contain only nine electrode locations that may not be sufficient for the ICA to separate enough of the MMN from other ERPs. However, the obtained results seem to be reasonable and, thus, the proposed ICA decomposition procedure is recommended to be used for interpretation of the MMN component in ERP studies, supplementing the conventional DW procedure. This is especially relevant for the cases when the experimental effects which are expected from the literature are not distinguishable through the DW procedure alone. We also suggest that the proposed procedure can be used to study the MMN in experimental paradigms similar to this uninterrupted sound paradigm with small modifications.

4.1.5 "ICA on MMN in interrupted sound (extended)"

Reference: Kalyakin, I., González, N., Ivannikov, A., & Lyytinen, H. (2009). Extraction of the Mismatch Negativity Elicited by Sound Duration Decrements: A Comparison of Three Procedures. *Data & Knowledge Engineering*, *68*(*12*), 1411–1426.

The purpose of this study is to compare statistically the performance of the conventional DW, ODF, and recently proposed ICA decomposition procedures in the quantitative analyses of the MMN. The comparison is performed in the context of the experimental paradigm, employing a more prototypical MMN protocol with a silence between the stimuli. The employed paradigm with duration decrement deviants is a small modification of the uninterrupted sound experimental paradigm used in our previous studies (see Sections 4.1.1–4.1.4). This modification allows us to test the sensitivity of the ODF and ICA decomposition procedures to small variations in the stimulus setup. Each of the three aforementioned procedures is separately applied to the same ERP data. Then, the results obtained after application of these procedures are statistically compared on the peak amplitude, latency, and single trial SNR of the MMN to ascertain the most suitable procedure for the quantitative analyses of the MMN, which can then be used in similar paradigms with sound duration decrements. This study extends the results described in the study in Section 4.1.3.

After a brief description of the procedure of the recording and the design of the experimental paradigm itself, the DW, ODF, and ICA decomposition procedures are considered, stressing differences in their implementation compared to the previous studies. The main difference is the use of an alternative approach to obtain DW traces, which is called the DW procedure with an average standard sweep. This approach may reduce up to three times (corresponding to the number of types of deviant stimuli) the noise variance in the average standard sweep to be subtracted from each single trial deviant sweep. In turn, this should provide cleaner DW traces and lead to an improved single trial SNR of the MMN. Repeated measures ANOVAs are used in the statistical analyses.

In general, the obtained results are comparable with those obtained in our previous study with an uninterrupted sound paradigm (see Section 4.1.4). However, the procedures differ in the performance of the MMN extraction. Application of the DW procedure is reasonable in this paradigm, since it removes common exogenous processing, but not endogenous processing (P3a component), and keeps the MMN unchanged. In contrast, application of the ODF procedure with the frequency range of 2–8.5 Hz used for the extraction of the MMN is not efficient, since this produces the residuals of both the exogenous and endogenous processing, which partly overlap the MMN and bias the baseline (e.g., exogenous P1 component). The best performance among the three procedures is achieved by application of the ICA decomposition procedure, where no residuals of any exogenous responses with negligible residual of the P3a responses are observable.

The main statistical comparisons among the three procedures show that reduction at the MMN peak amplitude is significant after application of both the ICA decomposition and ODF procedures compared to the DW procedure. The MMN peak amplitude is lower after application of the ICA decomposition procedure compared to the ODF procedure. This finding can be explained by the biased baseline in the case of the ODF procedure. The temporal characteristics of the MMN are not affected by any of the procedures under study. Finally, application of the ODF procedure significantly improves the single trial SNR compared to the DW and ICA decomposition procedures. However, as mentioned earlier, the ODF procedure produces a mixture of the MMN and residuals of some exogenous responses. The ICA decomposition procedure numerically requires a smaller number of trials than the DW procedure, but only for the two most deviating stimuli. Statistically, these values are non-significant. The lack of a significant effect in the single trial SNR between these two procedures can be explained by the use of an alternative method to obtain the DW traces, i.e., the DW procedure with an average standard sweep (see above), which, as the results show, performs better than the ordinary DW procedure for the MMN extraction. We recommend usage of the DW procedure with an average standard sweep when an experimental paradigm involves more than one type of deviant stimulus. In particular, if this number is greater than two, the DW traces become much cleaner.

After performing the ICA decomposition, the MMN for the most deviant stimulus is significantly larger at the peak amplitude and earlier in the latency than for the second (by magnitude of deviation) deviant stimulus. These results are in agreement with well-known characteristics of the MMN, supported by a substantial number of publications. However, there is no statistically significant difference in the latency of the MMN between the third and second deviant stimuli, whereas the difference at the peak amplitude is present. One possible explanation of these results can be that the difference between the standard stimulus and the third deviant stimulus is too small to elicit a reliable effect in the latency of the MMN, rather than an inability of the ICA decomposition procedure to extract a genuine MMN. The DW and ODF procedures show statistically significant differences at the peak amplitude of the MMN for all pairs of types of deviant stimuli (except one pair in the DW procedure), but not in the latency of the MMN. Despite the lack of a significant effect between deviants in the latency of the MMN (probably due to a lack of power in the statistical tests), it should be noted that the values of the latency of the MMN for the DW procedure are also in agreement with the expected characteristics of the MMN, but this is not the case for the ODF procedure where reversed inter-relations are observed. The lack of an effect on latency, while an effect on amplitude is obtained, may mean that the DW procedure is not sufficiently powerful to reveal a clean MMN with the current sample size compared to the ICA decomposition procedure with its different mathematical background.

The main results obtained in this study support the use of the ICA decomposition procedure as a supplementary tool to validate the results obtained with the DW procedure. They also show the insensitivity of the ICA decomposition procedure to variations in the experimental design. At the same time, such variations drastically affect the performance of the ODF procedure whose application is limited by a paradigm it is developed for.

4.1.6 "Polarity indeterminacy at local optimization in ICA"

Reference: Cong, F., Kalyakin, I., Ristaniemi, T., & Lyytinen, H. (2008). Drawback of ICA Procedure on EEG: Polarity Indeterminacy at Local Optimization. *IFMBE Proceedings, 20(4)*. In A. Katashev, Y. Dekhtyar, & J. Spigulis (Eds.), *14th Nordic-Baltic Conference on Biomedical Engineering and*

Medical Physics, NBC 2008 (pp. 202–205). Berlin, Heidelberg, Germany: Springer-Verlag.

This study considers the case of finding the local extremum of an optimization function in a stochastic ICA algorithm which may use various gradient descent methods. When such an ICA algorithm is applied to some multi-channel EEG data, it is usually the case of a high-dimensional signal space. The probability to find the global extremum of the optimization function in this ICA algorithm is relatively low. Thus, the ICA may extract some ICs at the local optimization, which, as shown in this study, produce the artificial polarity indeterminacy at some electrode locations when projected back to the signal space.

The polarity of a peak is an important characteristic of ERP responses. It is often used to correctly identify ERPs observed during a recording session. This is also the case for the MMN. As mentioned in Section 2.3, when all electrode locations are referred to the tip of the nose, the MMN has a negative amplitude on the frontal, central, and parietal electrode locations and positive amplitude on the mastoid electrode locations. This polarity reversal property of the MMN is used to automatically identify the MMN-like ICs in the ICA decomposition procedure (see our previous studies where the latter is applied).

By performing the numerical simulations, we show that the artificial polarity indeterminacy may occur in approximately 10% of cases of the locally optimized function. We propose to correct the sign in the ERP traces obtained after the projection of the chosen ICs back to the electrode locations in these 10% of cases. However, this correction is possible only when prior knowledge of the polarity of the desired ERP at different electrode locations is available. This information is usually known for the MMN and mostly defined by the electrode placement used as the reference.

Undoubtedly, the main intention in the studies where stochastic ICA algorithms are used should be to achieve a global solution in an optimization function of the algorithm rather than simply to correct the sign at the local inaccurate solution. To find the global solution, other methodologies can be considered, e.g., testing of different ICA optimization algorithms which may incorporate some prior knowledge of the signal of interest, different approaches for data preprocessing, dimensionality reduction, etc. However, this simple sign correction should not be left aside and may be used with careful control of the possible negative effects which may be caused by the inaccurate estimation of an ERP component under study.

4.1.7 “NMF vs. FastICA on MMN in uninterrupted sound”

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. *IJCNN 2009 Conference Proceedings. The 2009 International Joint Conference on Neural Networks, IJCNN 2009* (pp. 586–590). Eau Claire, WI: Documation LLC for IJCNN [CD-ROM].

Recently, the NMF has begun to be applied in different scientific fields, including EEG data processing. The NMF does not require the assumption about independence of the source signals and is not restricted to the length of data, as compared to the ICA. In this method, the basis functions are not strictly ranked, but represent intrinsic properties of data, in contrast to the ICA where the basis functions are ranked, e.g., by their non-Gaussianity. Application of the NMF looks promising as it takes into account spatial and temporal correlations between variables in a more accurate fashion than the ICA does.

In this short study, we estimate whether the NMF provides better separation of the MMN from other irrelevant ERPs than that achieved by the ICA. The SAR, a new recently proposed quantity (see Section 2.3), is calculated to estimate the performance of the separation. The FastICA algorithm is used in this study. Repeated measures ANOVAs are used in the statistical analysis of the SAR values in both procedures under study.

After averaging all of the single trials in each electrode location, type of deviant stimuli, and subject separately, time-frequency representations of the traces are obtained. This step transforms the data into non-negative values which are required by the NMF procedure. Finally, the NMF of this time-frequency representation of the data is applied, providing the estimated NMF components. The obtained results show that the SAR of the MMN component is 49.0 dB, 33.6 dB, and 30.5 dB for the NMF, ICA, and ordinary averaging procedures, respectively. The difference between any two procedures is significant. Both the NMF and ICA extract a cleaner MMN compared to the ordinary averaging procedure, and the NMF statistically outperforms the ICA.

It should be noted that calculation of the SAR requires prior knowledge of the frequency content of the MMN, which, in general, is unknown. We use this information from our previous study in Section 4.1.1. However, in other experimental designs, the spectrum analysis of the MMN should be performed prior to the calculation of the SAR. This is a limitation of the approach.

4.1.8 “ERP denoising in multi-channel EEG data”

Reference: Ivannikov, A., Kalyakin, I., Hämäläinen, J., Leppänen, P. H. T., Ristaniemi, T., Lyytinen, H., & Kärkkäinen, T. (2009). ERP Denoising in Multichannel EEG Data Using Contrasts between Signal and Noise Subspaces. *Journal of Neuroscience Methods*, *180*(2), 340–351.

This study introduces a new procedure for ERP denoising in multi-channel EEG data. The procedure consists in the separation of ERP and noise subspaces in multidimensional EEG data, using the spatial information of the data. The separation is performed by a linear transformation with a subsequent dimension reduction, involving the rejection of the noise components during inverse transformation to the original signal space. The goal of this study is to develop, implement, and validate the ERP denoising procedure, and then to compare statistically its performance with the traditional averaging procedure.

We hypothesize that the proposed denoising procedure should provide better results in terms of the SNR than the averaging procedure as it should benefit from the spatial information contained in the multidimensional EEG data. High-density EEG data (128 channels) from 52 children are used in this study. Repeated measures ANOVAs are used in the statistical analysis.

The main criteria used for validation of the proposed procedure are the amount of remaining noise power in the denoised ERP estimate and the possible signal loss during denoising. Both quantities affect the SNR and, thus, should be controlled separately. Denoising can be considered successful when an increased SNR value is obtained after application of the procedure and simultaneously the signal loss is insignificant. Maximization of the SNR is also the criterion used in the optimization procedure (the core of denoising) to find the linear projections of the signal and noise subspaces.

The obtained results show that the proposed procedure outperforms the averaging procedure in a small and medium number of trials (2–150 in average over participants), whereas the averaging procedure performs slightly better than the proposed procedure for larger numbers of trials (more than 150). The possible explanation is below. As carefully discussed in this study, in practice, the signal and noise subspaces cannot be fully separated due to the violation of some theoretical assumptions. Thus, a loss of energy of the signal when rejecting the noise subspace takes place. In the case of a small number of trials, noise removal by the denoising procedure dominates more than the negligible signal loss. This provides better performance of the proposed procedure compared to the averaging procedure. On the other hand, in the case of a larger number of trials, noise removal by the denoising procedure is not sufficient enough to compensate the signal loss in this procedure, thus, providing lower SNR values than those in the averaging procedure. Despite this, the obtained results are encouraging. The proposed procedure performs better than the averaging procedure in terms of the SNR on small and medium number of trials. It may reduce the duration of a recording session. These results are confirmed by the statistical test which is conducted for the case of medium number of trials (100 trials). This test shows that the proposed procedure significantly improves the SNR compared to the averaging procedure.

It should be noted that, in this study, we try to establish a framework for the class of the methods for ERP denoising as well. The proposed procedure is one of several realizations of ERP denoising within this class of methods. Regarding the case of the extraction of the MMN, this denoising procedure is definitely beneficial. Indeed, in the analysis of the MMN, the standard frame of reference is the DW procedure. The standard and deviant sweep should be clean enough prior to the subtraction in the DW procedure to minimize the effect of the increase of noise after the subtraction. Such denoising may also be useful prior to application of the ICA decomposition procedure. In this case, dimensionality of the resulting ERP traces obtained after the rejection of the noise subspace is reduced. Thus, the performance of the ICA decomposition procedure in the separation of the MMN from other irrelevant ERPs should be improved.

4.2 Author’s contribution to joint publications

The present introductory part has been written solely by the author who has received comments and suggestions concerning its content and structure from the supervisors and reviewers of the thesis.

In Article I, the author of this thesis is the principal and corresponding author who has proposed the main idea of the study, developed the methodology, implemented all signal processing procedures under study by means of MatLab, and conducted the necessary statistical analyses. Documentation of the results of the study has been performed by the author of this thesis with subsequent correction of the terms and language by the co-authors. The development of the experimental paradigm and EEG data collection have been performed by the co-authors. Preprocessing of the raw EEG data and their conversion to MatLab-readable format have been done by the author of the thesis. These data have subsequently been used in Articles II, III, IV, and V. The article has been refereed by two international reviewers and published as a regular journal paper (in special issue).

In Article II, the author of this thesis is the second author who has implemented one of the three signal processing procedures under study, given comments and suggestions to the principal author, and contributed to documentation and revision of the study. The article has been refereed by two international reviewers and already re-submitted after the major revision as a regular journal paper.

In Article III, the author of this thesis is the principal and corresponding author who has proposed the main idea of the study, developed the methodology, and implemented all signal processing procedures under study by means of MatLab. The development of the experimental paradigm, EEG data collection (part of the data), and conversion of these data to MatLab-readable format have also been performed by the author of this thesis with contribution of the colleagues on the stage of data collection. The converted EEG data have subsequently been used in Article V. Documentation of the results of the study has been performed by the author of this thesis with subsequent correction of the terms and language by the co-authors. The article has been refereed by two international reviewers and published in the proceedings of international conference. The results of the study have been presented at the conference personally by the author of this thesis.

In Article IV, the author of this thesis is the principal and corresponding author who has proposed the main idea of the study, developed the methodology, implemented all signal processing procedures under study by means of MatLab, and conducted the necessary statistical analyses. Documentation of the results of the study has been performed by the author of this thesis with subsequent correction of the terms and language by the co-authors. In this study, the same converted EEG data as in Article I have been used. The article has been refereed by two international reviewers and published as a regular journal paper.

In Article V, the author of this thesis is the principal and corresponding author who has proposed the main idea of the study, developed the methodology, implemented all signal processing procedures under study by means of MatLab, and conducted the necessary statistical analyses. Documentation of the results of the study has been performed by the author of this thesis with subsequent correction of the terms and language by the co-authors. In this study, the same converted EEG data as in Article III have been used. The article has been refereed by two international reviewers and published as a regular journal paper (in special issue).

In Article VI, the author of this thesis is the second author who has given comments and suggestions to the principal author on the stage of data simulation, and contributed to documentation and revisions of the study. The article has been published in the proceedings of international conference. The results of the study have been presented at the conference by the principal author.

In Article VII, the author of this thesis is the third author who has implemented one of the three signal processing procedures under study, given comments and suggestions to the principal author, and contributed to documentation and revision of the study. The article has been refereed by four international reviewers and published in the proceedings of international conference. The results of the study have been presented at the conference by the principal author.

In Article VIII, the author of this thesis is the second author who has performed preprocessing of the raw EEG data and their conversion to MatLab-readable format, developed the design for statistical analyses of the results obtained after application of the procedure under study, given comments and suggestions to the principal author, and contributed to documentation and revision of the study. The article has been refereed by two international reviewers and published as a regular journal paper.

5 CONCLUSIONS

In this thesis, we have considered three procedures for the extraction of the MMN, a component of ERP, from EEG data: ODF, WLD, and ICA decomposition procedures. We have shown that these procedures can provide alternative ways of quantification of the MMN which is conventionally analyzed through the calculation of DWs. We have shown that, in some experimental paradigms, the DW procedure was not the most optimal way for the extraction of the MMN. Moreover, this procedure reduced the SNR as it required the subtraction of different time intervals of the ERP traces. In contrast, no subtraction was needed in the ODF, WLD, and ICA decomposition procedures, which, in turn, made their application more attractive. However, in the analysis of ERP data collected under two different experimental paradigms, we have shown that the performance of the extraction of the MMN was different between all proposed procedures. Let us emphasize the main differences of these procedures compared to the DW procedure.

The ODF procedure: is a single-channel method; has originally been developed for an uninterrupted sound paradigm; is very sensitive to changes in the experimental design; reveals no difference between types of deviant stimuli; provides an increased single trial SNR; may reduce the duration of a recording session. This procedure is recommended to be used only in the paradigm to which the procedure is developed for.

The WLD procedure: is also a single-channel method; has originally been developed for an uninterrupted sound paradigm; requires prior knowledge about frequency content of the MMN; reveals significant difference in the latency (but not at the peak amplitude) of the MMN between types of deviant stimuli; provides an increased single trial SNR; may reduce the duration of a recording session. This procedure is recommended to be used in the paradigms where the frequency range of the MMN is known a priori.

The ICA decomposition procedure: is a multi-channel method; has been developed regardless of any particular experimental paradigm; is insensitive to changes in the experimental design; reveals significant difference both at the peak amplitude and in the latency of the MMN between types of deviant stimuli; provides an increased single trial SNR (compared to the ordinary DW procedure, see Section 4.1.4; but similar SNR compared to the improved DW procedure, see Section 4.1.5); may reduce the duration of a recording session. This procedure is recommended to be used when the quantitative characteristics of the MMN, which are expected from the literature, are not distinguishable through the DW procedure alone.

As a resume, it should be noted that the WLD and especially ICA decomposition procedures are computationally sophisticated methods. The standard frame of reference for the MMN component is the DW procedure. Although the DW procedure will continue to be used as a reference to interpret the MMN component in ERP studies, the WLD and ICA decomposition procedures, as the results of this thesis have shown, can certainly supplement it. With their use, our initial goal — to reduce the duration of a recording session by collecting fewer number of trials without loss in the performance of the extraction of the MMN component — seems to be realistic and reachable. For example, the ICA decomposition procedure required about 265 trials instead of 350 original trials needed for the DW procedure to obtain the same single trial SNR. In this particular case, the achieved improvement is equal to 24.3% and is definitely a step forward towards the online procedure for training the auditory/speech perceptual ability in clinical and other population (for more details, see Section 2.3). In this context, the questions of the relative complexity of these two developed procedures can easily be solved by the use of modern equipment which, at present, is computationally powerful enough for such tasks.

The main limitations of this thesis are the use of a limited set of available methods or their combinations for the separation of the ERPs, a limited set of parameters to manipulate within each of the procedures under study, as well as a limited set of MMN datasets.

Under this set of methods, we mean the use of more sophisticated single-channel procedures, e.g., the weighed averaging instead of the ordinary averaging, and different multi-channel methodologies. The latter ones include different source separation methods which use different a priori information or criteria to find a solution, e.g., ICA (considered in this thesis), temporal/spectral structure, diversities of the signals, non-stationarity, or their combinations. One of these source separation methods with different assumptions compared to the ICA is NMF (see Section 4.1.7). Combinations of these single- and multi-channel methodologies can also be considered, including those proposed in this thesis. For example, the ICA decomposition procedure can be applied subsequently after the WLD procedure. This combination may provide better performance than each of these procedures separately (unpublished results). Of course, ERP denosing procedures, one of which has been considered in Section 4.1.8 and showed better results than the ordinary averaging, should be applied to clean up the data prior to the use of the procedures to separate the ERPs (MMN). In this context, it should be noted that the ODF and WLD procedures can be considered as the latter approaches, i.e., for the separation of ERPs from each other. However, they can simultaneously be considered as the approaches for denoising, i.e., removing low- and high-frequency noise and preserving ERPs as well. At the same time, the ERP denoising procedure described in Section 4.1.8

was namely designed to remove noise, but not to separate ERPs. Nevertheless, the ICA decomposition procedure can be applied after any of these procedures regardless of their conditional division. Concatenation of the procedures should result in a much cleaner MMN analysis as mentioned above.

Under this set of parameters, we mean different types of filters in the ODF procedure; different mother wavelets, levels of decomposition, the use of wavelet packets in the WLD procedure; different contrast functions (e.g., maximization of non-Gaussianity, information-theoretic measures, maximum likelihood estimation, tensorial methods) and optimization algorithms (gradient-based or algebraic methods), the number of electrode locations and, subsequently, the number of the MMN-like and non-MMN-like ICs, the use of data mining techniques to classify the ICs in the ICA decomposition procedure.

Under this set of datasets, we mean that only two MMN datasets have been analyzed in this thesis. Both of them contained only duration deviants. A number of other experimental paradigms have been developed so far, including both the traditional oddball paradigms with frequency, intensity, rise/fall time deviants, etc. and recent "optimal" paradigms. Paradigms belonging to the second category aim at reducing the duration of recording sessions without reducing the reliability of the MMN (Näätänen et al., 2004). Application of the procedures developed in this thesis to data from these optimal paradigms looks very promising in the context of reducing the duration of recording sessions.

These limitations can directly be addressed in future research. Some of them are currently being considered and will be reported in future scientific contributions.

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YHTEENVETO (FINNISH SUMMARY)

Tämän "Poikkeavuusnegatiivisuuden erottaminen EEG-signaalista" otsikoidun väitöskirjatutkimuksen tavoitteena on ollut kehittää, kokeilla ja validoida uusia signaalinkäsittelyratkaisuja poikkeavuusnegatiivisuutena (mismatch negativity, MMN) tunnetun herätevaste-(event-related potential, ERP-)komponentin erottamiseksi elektroenkefalografisesta (EEG-)signaalista.

MMN-tutkimuksia, joilla voidaan kartoittaa aivojen kuulomodaliteettiin liittyviä funktiota, on viime aikoina tehty enenevässä määrin. MMN tarjoaa keinon ymmärtää uudella tasolla niitä aivojen prosesseja, joihin kuulohavainnot ja erityyppiset kuulomuistin ilmiöt perustuvat. MMN:n nopealla tunnistuksella on potentiaalisesti tärkeä rooli auditorisen ja/tai puheen havaintokyvyn harjoittamisessa sen ollessa esimerkiksi kliinisistä syistä tarpeen. MMN:n ilmaisemaa auditorista diskriminaatiota voidaan arvoida ERP:stä yksinkertaisia amplitudi- ja latenssiarvoja laskemalla. Niiden tulkinta on kuitenkin erityisen ongelmallista siksi, että MMN on suhteellisen heikko signaali spontaaniin EEG:hen ja kohinaan verrattuna. Lisäksi useimmissa tapauksissa on käytettävä erotuskäyrän (difference wave, DW) laskentamenettelyä MMN:n erottamiseksi irrelevantista herätevastevaihtelusta. Kuitenkin DW menetelmän edellyttämän kahdesta aikaikkunasta eristetyn signaalin erotuksen laskemisesta seuraa, että tuloksena saatu MMN-käyrä voi sisältää jopa kaksi kertaa enemmän kohinaa kuin mitä signaalissa oli ennen erotuksen laskua.

Tässä väitöskirjatutkimuksessa ehdotetaan kolmea MMN:n eristämismenettelyä: optimaalista digitaalista suodatusta (ODF), wavelet-hajotelmaa (WLD) ja riippumattomien komponenttien analyysiin (ICA) perustuvaa erottelua. DW-laskennasta poiketen nämä menettelyt eivät edellytä kahden käyrän erotuksen laskentaa. Kahden ensin mainitun etuna on se, että niissä arvioidaan MMN:ä taajuusalueella. ICA erottelun etuna on DW-menettelyyn nähden taajuusalueen informaation käyttö MMN:stä. Menettelyjä arvioidaan vaihtoehtoisina ja tarkentavina keinoina eristää MMN EEG-aineistosta täydentämään tuloksia, joita voidaan saada perinteisellä DW-menettelyllä.

Työn päätulokset tukevat wavelet- ja ICA-pohjaisia menettelyjä siinä, että ne paljastavat MMN:n amplitudeissa ja latensseissa kirjallisuuden perusteella näkyväksi odotettuja kokeellisia vaikutuksia, joita ei saada selville yksinomaan erotuskäyrää hyväksi käyttämällä. Tulokset ovat myös osoittaneet, että kehitetyillä menettelyillä voidaan lyhentää MMN:n tunnistamisen edellyttämää mittausaikaa. Tämä on erityisen huomionarvoista lasten ja potilaiden mittauksissa. Lisäksi tarkastelun kohteina on käytännöllisiä kysymyksiä, jotka liittyvät ICA-pohjaisiin MMN:n tunnistuskeinoihin. Lopuksi tuodaan esiin monikanavaisen EEG:n spatiaalisen häiriönpoiston keinoja, joita voidaan käyttää MMN:n tai minkä tahansa ERP:n eristämisen esikäsittelyvaiheessa.

INCLUDED ARTICLES

I

OPTIMAL DIGITAL FILTERING VERSUS DIFFERENCE WAVES ON THE MISMATCH NEGATIVITY IN AN UNINTERRUPTED SOUND PARADIGM

Kalyakin, I., González, N., Joutsensalo, J., Huttunen, T., Kaartinen, J., & Lyytinen, H. (2007)
Developmental Neuropsychology, *31*(3), 429-452

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II

WAVELET DECOMPOSITION ON MISMATCH NEGATIVITY OF CHILDREN IN UNINTERRUPTED SOUND PARADIGM

Cong, F., Kalyakin, I., Huttunen-Scott, T., Li, H., Huang, Y., Guttorm, T.,
Ristaniemi, T., & Lyytinen, H.
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III

EXTRACTION OF THE MISMATCH NEGATIVITY ON TWO PARADIGMS USING INDEPENDENT COMPONENT ANALYSIS

Kalyakin, I., González, N., & Lyytinen, H. (2008)
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IV

INDEPENDENT COMPONENT ANALYSIS ON THE MISMATCH NEGATIVITY IN AN UNINTERRUPTED SOUND PARADIGM

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Journal of Neuroscience Methods, 174(2), 301–312

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V

EXTRACTION OF THE MISMATCH NEGATIVITY ELICITED BY SOUND DURATION DECREMENTS: A COMPARISON OF THREE PROCEDURES

Kalyakin, I., González, N., Ivannikov, A., & Lyytinen, H. (2009)
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VI

DRAWBACK OF ICA PROCEDURE ON EEG: POLARITY INDETERMINACY AT LOCAL OPTIMIZATION

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VII

NON-NEGATIVE MATRIX FACTORIZATION VS. FASTICA ON MISMATCH NEGATIVITY OF CHILDREN

Cong, F., Zhang, Z., Kalyakin, I., Huttunen-Scott, T., Lyytinen, H., &
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VIII

ERP DENOISING IN MULTICHANNEL EEG DATA USING CONTRASTS BETWEEN SIGNAL AND NOISE SUBSPACES

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