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Fast parametric evaluation of central speech-sound processing with mismatch negativity (MMN)

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ABSTRACT

The aim of this study was to develop a paradigm for obtaining a multi-feature profile for central auditory processing of different magnitudes of prosodic and phonetic changes in speech sounds. We recorded the MMNs to three vowel identity changes, three magnitudes of changes in intensity, and vowel duration as well as to two magnitudes of pitch changes from semi-synthetic vowels in 34 min. Furthermore, we examined how the type and magnitude of deviation affect the size and timing of the MMN. All sound changes elicited statistically significant MMN responses, with the MMN amplitudes increasing with an increase in sound deviance. Importantly, the MMN amplitudes for the vowel changes reflected the differences between the phonemes, as did the MMNs to vowel-duration changes reflect the categorization of these sounds to short and long vowel categories, which are meaningful in the Finnish language. This new multi-feature MMN paradigm is suitable for investigating the central auditory processing of different magnitudes of speech-sound changes and can be used, for instance, in the investigation of pre-attentive phoneme categorization. The paradigm is especially useful for studying speech and language disorders in general, language development, and evolution of phoneme categories early in life, as well as brain plasticity during native or second language learning.

1. Introduction

The mismatch negativity (MMN) component of the electroencephalogram (EEG) has become increasingly popular in the studies of central auditory processing and sound discrimination. The MMN is elicited in a situation where an auditory regularity is violated in a perceptible manner. At its simplest, this violation can be a change in one sound feature, such as pitch (Sams et al., 1985; Paavilainen et al., 1993; Tiitinen et al., 1994) or intensity (Näätänen et al., 1989; Woldorff et al., 1991), within an otherwise homogenous stream of sounds. It can also be a more complex one, such as a repetition of a sound in a descending pitch trend (Tervaniemi et al., 1994), an omission of sound in an otherwise steady sound sequence (Nordby et al., 1994; Yabe et al., 1997), or even a change in a complex spectro-temporal rule (Paavilainen et al., 2007). Initially, the MMN was interpreted to represent a comparison process where the current auditory input is compared to and found deviating from, i.e., mismatching with, the memory trace representing the preceding auditory input (Näätänen et al., 1978). Later on, the theory has been revised so that the memory trace includes not only the information of the previous auditory input but also predictions of future auditory events in the form of rules or trends (Näätänen and Winkler, 1999; Näätänen et al., 2010). According to the most recent theories, the MMN is generated when the predictive models of the auditory environment fail, with the main function of the MMN-generating process being that of adjusting the neural model to better describe the regularities of the auditory environment (Winkler et al., 1996, 2009).

Typically, the MMN is extracted by subtracting the averaged response to the "standard" sounds, which represent the auditory regularity, from the average response to the regularity-violating "deviant" sounds. In this difference signal, the MMN is most often seen between 100 and 250 ms from the onset of deviation. When the nose is used as a reference site, the polarity of the MMN is negative at the frontal electrodes and inverts to positive at the mastoids (Alho et al., 1993). The principal generator of the MMN, and its magnetic equivalent MMNm (recorded with the magnetoencephalogram, MEG), have been localized to the supratemporal planes of both left and right temporal lobes, to the vicinity of the primary auditory cortices (e.g., Hari et al., 1984; Alho

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et al., 1993; Alho, 1995; Frodl-Bauch et al., 1997). This temporal component is mainly responsible for the actual modelling of the auditory events, namely the comparison process between the perceived and predicted input (Näätänen et al., 1993). Further, it has been proposed as the first level of auditory object formation (Ritter et al., 2000; Winkler et al., 2009). In addition to the temporal component, several studies suggest also the existence of a frontal subcomponent, possibly functionally related to the modulation of attention to the auditory events (for a review, see Deouell, 2007). Furthermore, when presenting speech stimuli, also a third subcomponent, overlapping with the two aforementioned ones, has been proposed. It is elicited for changes in the phonemes of one's own native (Näätänen et al., 1997) or later-learned foreign language (Winkler et al., 1999), and it is usually lateralized to the language-dominant hemisphere (typically left; Näätänen et al., 1997; Shestakova et al., 2002, 2003). This third MMN component has been interpreted to represent the activation of long-term memory traces for familiar speech sounds (Näätänen et al., 1997; Winkler et al., 1999; Shestakova et al., 2002, 2003).

When using paradigms that do not carefully control for the refractoriness differences between the repetitive standard and more rare deviant stimuli, such as the oddball and the multi-feature paradigms, the MMN amplitude directly correlates with the relative magnitude of the regularity violation, and usually, to the actual perception of the difference between the expected and the occurred auditory events (for a review, see Kujala and Näätänen, 2010). In oddball and multi-feature paradigms, larger violations elicit higher MMN amplitudes in proportion to smaller violations of similar type (e.g., a small pitch change elicits a smaller MMN amplitude than a larger pitch change; Sams et al., 1985; Tiitinen et al., 1994; Pakarinen et al., 2007). The MMN amplitude correlates with the behavioural detection accuracy of the violations (Amenedo and Escera, 2000; Pakarinen et al., 2007), and an increase in the MMN amplitude coincides with the increased behavioural detection accuracy as a result of discrimination training (Näätänen et al., 1993; Tervaniemi et al., 2001; Kujala et al., 2001; for a review, see Kujala and Näätänen, 2010). Moreover, the MMN is typically not elicited when the sound change is not perceived (Winkler et al., 1999; see however van Zuijen et al., 2006; Paavilainen et al., 2007). The few findings of significant group or experimental-condition differences for MMN amplitudes in the absence of concomitant differences in behavioural discrimination (Bradlow et al., 1999; Jaramillo et al., 2001; Kozou et al., 2005) can probably be attributed to both methodological (e.g., statistical power) and/or content-related (e.g., the extent to which they tap sensory discrimination or also other discrimination-related processes such as response strategy or motivation) dissimilarities between the MMN and behavioural measurements.

As with the amplitude, the average latency of the MMN varies for different types of violations, in that the MMN is usually peaking earlier, for instance, for duration, than for location changes (Pakarinen et al., 2007). When the violation magnitude is varied within the deviation type, as in presenting different magnitudes of pitch changes in an oddball or in a multi-feature paradigm, the latency is typically shorter for the large as compared with smaller sound changes, though this variation may depend on the type of sound changes used (Pakarinen et al., 2007). For instance, the MMNs peak earlier for larger and later for smaller pitch changes, and the latencies directly correlate to the behavioural detection speed of these changes, whereas the MMN latencies for different magnitudes of duration changes may not significantly differ from each other (Pakarinen et al., 2007).

However, some other studies, in which the differences in neural refractoriness between the standard and the deviant stimuli are very carefully controlled for, suggest that the MMN itself would be more of an all-or-none type of a response (Winkler et al., 2001; Horváth et al., 2008). According to these studies, the amplitude and latency effects that are seen in the MMNs recorded in the oddball and multi-feature paradigms, result partly from the variation in the overlapping refractoriness-dependent N1-response (Winkler et al., 2001; Horváth et al., 2008). In addition, some of the amplitude enhancement that occurs with an increase of the deviation magnitude seems to be explained by the fact that when the sound change is larger, the MMN is elicited more often (e.g., Winkler et al., 2001), resulting in a higher mean amplitude when averaging over several trials or subjects, or both. Thus, the traditionally measured MMN parameters, which indeed well predict the subjective perception of the sound changes, are most likely a combination of the N1 and MMN signal, though, also in this manuscript, referred to as MMN only, for simplicity.

One of the major advantages in recording the MMN comes from the fact that it can be recorded in a passive listening situation without the subject's attention to the stimulation. Thus, it can be easily recorded even from subjects who cannot be examined with the more traditional behavioural methods of sound discrimination. The MMN has indeed been successfully applied in a multitude of clinical studies, for instance with patients with schizophrenia (Michie et al., 2000; Michie, 2001) or an attention deficit (Oades et al., 1996; Kemner et al., 1996; Sawada et al., 2010), and even with patients in a vegetative state (Kane et al., 1993, 1996; Fischer et al., 1999, 2010; Wijnen et al., 2007). The MMN is also commonly used in studies of normal development and ageing, as well as their disorders, such as developmental language disorders (e.g., specific language impairment and dyslexia; for reviews see Kujala et al., 2007a, 2007b; Bishop, 2007) and neurodegenerative diseases (e.g., Parkinson's and Alzheimer's diseases; Pekkonen, 2000; Brønnick et al., 2010). Moreover as the MMN can be obtained also from foetuses in the uterus (MMNm, recorded with MEG; Huotilainen et al., 2005; Draganova et al., 2005, 2007), newborns during sleep (Morr et al., 2002; Huotilainen et al., 2003; Novitski et al., 2007; Draganova et al., 2007; Vestergaard et al., 2009), as well as preterm babies (Fellman et al., 2004; Mikkola et al., 2007), it provides means to evaluate the development, both the maturational as well as the learning-related changes in central auditory processing at very early, often critical, stages in development.

One of the downsides of the MMN recordings has been the relatively long recording time. This has recently been overcome with the development of new multi-feature recording paradigms (e.g., Näätänen et al., 2004; Pakarinen et al., 2007). Since its discovery in 1978 (Näätänen et al., 1978), the MMN was recorded in an oddball paradigm, in which the majority of the tones were repetitive standards, occasionally intervened by rare (~10%) deviant tones. In the new fast multi-feature paradigms the different types of sound changes are presented within the same stimulus sequence, with every other tone as a standard and every other tone as one of the several deviants. Each of these deviants differs from the standard in only one respect (such as pitch, intensity, or duration), and the paradigm is based on the assumptions that the MMNs can be independently elicited for different auditory attributes, and that the deviant tones can strengthen the memory trace of the standard with respect to those stimulus attributes they have in common (Nousak et al., 1996). For instance, the durations of the pitch and intensity deviants are identical with the standard, thus strengthening the memory trace for the standard sound duration. As a consequence, the recording time has dramatically decreased, as the number of standard repetitions is considerably lower than in the classical oddball paradigm. Now parametric, multi-attribute profiles of the central auditory processing can be obtained within one single recording session. For instance, recording a discrimination profile for small, intermediate, and large changes in sound pitch, duration, intensity and location, a total of 12 MMNs, would require only a 30-minute recording time with the multi-feature paradigm. For comparison, recording the same profile with the oddball paradigm would require 6 h. Importantly, the MMNs recorded with the new paradigm do not differ from those recorded with the oddball paradigm (Näätänen et al., 2004; Pakarinen et al., 2009), and there is some evidence that they may even be more sensitive in detecting impairments of the central auditory processing than the MMNs recorded in the oddball paradigm (Kujala et al., 2006; Thönnessen et al., 2008).

In addition to tone stimuli, multi-feature paradigms employing speech sounds (Pakarinen et al., 2009; Lovio et al., 2009) and even pseudowords (Thönnessen et al., 2010) have been developed for assessing different aspects of linguistic processing. Though the processing of linguistic information is known to differ from a non-linguistic one (Jaramillo et al., 2001), there is also evidence that the central auditory processing may also be selectively impaired for different magnitudes of sound changes. For instance in dyslexia, discrimination may be impaired for minor sound differences only (Baldeweg et al., 1999). Therefore, the aim of this study was to develop a paradigm to parametrically assess the processing of speech sounds, including several magnitudes of sound changes. Moreover, this approach allows the assessment of phoneme categorisation; in this case the categorization of four different exemplars of vowel /i:/ (standard /i:/ and three deviants) that differ in their duration, to two distinct phoneme categories of either short /i/ or long /i:/, a highly relevant distinction in the Finnish language. This could be especially useful in the studies of normal and abnormal developments of phoneme categories early in life as well as during the second language learning.

2. Materials and methods

2.1. Subjects

Nineteen healthy adults with no reported hearing or language-related problems participated in the study after giving their written informed consent. Data of three subjects were discarded because of technical difficulties, and excessive artefacts. The remaining group of 16 subjects (mean age 23.1, SD 4.5 years, 2 left-handed) is composed of 12 females. The procedures employed in the study conformed to the Declaration of Helsinki, and the study was approved by the Ethical Committee of the Department of Psychology, University of Helsinki.

2.2. Stimuli and procedure

The stimuli were semi-synthetic Finnish-language vowels, created by using the Semisynthetic Speech Generation method (SSG; Alku et al., 1999). The duration of the standard tone /i:/ was 170 ms with a pitch of 100 Hz (Table 1). For formant frequencies, see Table 2.

The deviants differed from the standard /i:/ either in features that are related to semantics (vowel identity and vowel duration) or in features that are related to prosody (pitch and intensity). In addition, the degree of deviance was manipulated at several levels of magnitude. The three vowel deviants were /y:/, /e:/ and /a:/. For their formant frequencies, see Table 2. The small, intermediate and large vowel duration deviants were 135 ms, 100 ms and 70 ms in duration, respectively. For the intensity deviants, three magnitudes of change in two directions (softer and louder) were used (see Table 1). For the pitch changes, two fundamental frequencies (110 and 136 Hz) were used, with an internal control built to the 110-Hz sound, which was presented often enough to allow the comparison of internal coherence of the measurement.

Table 1
Stimulus parameters.

Stimulus parameters				
	Vowel	Duration (ms)	Intensity (dB)	Pitch (Hz)
			Soft/loud	
Std	/i:/	170	60	100
Small deviant	/y:/	135	55/64	110
Medium deviant	/e:/	100	53/66	
Large deviant	/a:/	70	51/68	136

Table 2
Formant frequencies of the vowels.

Formant frequencies (Hz)				
	/i:/	/y:/	/e:/	/a:/
F1	317	332	431	581
F2	2211	1939	2016	910
F3	2739	2388	2354	2078
F4	3599	3340	3641	3586

The stimuli were conducted to the ears through thin flexible silicon tubes and foam ear tips, by using STIM 10 Ω insert earphone kits (NeuroScan, Herndon, VA) with an intensity of 60 dB above the subjective hearing level, which was individually measured before the experiment by using the stimulus sequence. The sounds were presented as in the multi-feature paradigm with different deviation magnitudes (Pakarinen et al., 2007). Every other tone was a standard ($P = 0.5$) and every other one of the 11 deviants ($P \approx 0.04$ for each deviant except $P \approx 0.08$ for the small pitch change). The occurrence of the deviants within the sequence was pseudo randomized in a way that all 4 deviant types appeared once in an array of 8 successive stimuli and the same deviant type was never repeated in succession. Each deviant was presented a total of 200 times (except small pitch changes 400 times). The stimulus-onset asynchrony (SOA) is 430 ms, and the total recording time is 34 min.

2.3. ERP measurement

During the ERP recording, the subjects watched a subtitled film (sound off) and were instructed to ignore the stimuli. The EEG was recorded (sampling rate 500 Hz) from 11 Ag/AgCl electrodes according to the international 10–20 System of Electrode Placement (F3, F4, C3, Cz, C4, P3, P4, LM, RM, VEOG, HEOG). An electrode placed at the tip of the nose served as a common reference. The vertical electro-oculogram (VEOG) was recorded from below the left eye and the horizontal electro-oculogram (HEOG) from the outer canthus of the right eye. The continuous EEG was filtered offline (bandpass 1–20 Hz). Epochs of 600 ms including a 100-ms pre-stimulus period were separately averaged for the standard and each of the different deviants. The small pitch deviants were divided into two separate averages in order to examine the internal consistency of the data. The mean voltage of the pre-stimulus period served as a baseline for the amplitude measurements. In order to exclude the artefacts and the large responses elicited by the first stimuli of the sequences, epochs including voltage changes exceeding 150 μV and those for the first 5 stimuli of each sequence were omitted from the averaging.

In order to delineate the MMN, the average response to the standard was subtracted from those to the deviants, resulting in 12 different difference signals (4 deviant types with 2–3 magnitudes of changes, with two separate averages for the small pitch deviant). The MMN mean amplitudes were calculated as a mean voltage at a 60-ms period centred at the peak latency (within a 100–250-ms time window) in the grand average difference signal, separately determined for each deviant type and magnitude. One-tailed t-tests were conducted to determine whether the MMN mean amplitudes at Cz differed significantly from zero.

The MMN peak amplitudes and latencies were measured from the most negative peak occurring 100–250 ms post deviance-onset at the central electrode Cz (showing the largest MMN amplitude in most subjects), and from the most positive peak within the same time interval at the mastoid electrodes LM and RM. The MMN peak latencies for the vowel-duration changes were corrected in relation to the sound-change onset. For the vowel-duration change the deviance onset was at 135 ms for the smallest deviation, at 100 ms for the intermediate deviation, and at 70 ms for the large deviation, in relation to the sound onset, whereas for the other sound changes the deviance onset was at 0 ms, i.e., the same as the sound-onset. In order to statistically compare the size of the MMN responses at mastoid electrodes (positive in their polarity) to those at Cz (negative in their polarity), the mastoid amplitudes were multiplied by -1. The following analyses of variance, similar to those used in a similar study with sinusoidal tones (Pakarinen et al., 2007) were decided on a priori: Two three-way analyses of variance (ANOVA) for repeated measures were conducted to test the effects of electrodes (3: Cz, RM, LM), deviant type (4: vowel duration, pitch, intensity, and vowel change), and the magnitude of deviation (3: small, medium, large) on both the MMN peak amplitude and latency. These analyses were also separately carried out for the different deviant types (deviation magnitude: 3 levels and electrode: 3 levels). Greenhouse–Geisser corrections were applied where appropriate (the original degrees of freedom and p-values after the correction are reported). Least-significant difference (LSD) tests were carried out as post-hoc analyses.

3. Results

Fig. 1 presents the nose-referenced deviant-minus-standard difference signals (average of 16 subjects) at a central electrode Cz and at left mastoid (LM) for each deviant type (vowel duration, pitch, intensity, and vowel change) and deviation magnitude (small, medium, large). Fig. 2 presents the MMN peak amplitude and latency for the sound changes at Cz and LM as a function of stimulus deviance. The MMNs peaked between 100 and 250 ms from the deviance onset. In all 12 subtraction signals, statistically significant MMN responses were found at Cz ($t_{15}=-1.8--11.2$, $P<0.05$; Table 3.).

3.1. Amplitude

Across deviant types, the three-way ANOVA for repeated measures on MMN peak amplitude revealed that the electrode had an influence on the MMN amplitude ($F_{2,30}=24.03$, $P<0.001$). The MMNs were smaller at the mastoidal electrodes than at Cz (LSD: $P<0.001$ for Cz vs. RM and LM). The MMN amplitude differed also between the different deviant types ($F_{3,45}=36.44$, $P<0.001$). The MMNs for the prosodic pitch and intensity changes were smaller than those for the phonemic vowel duration and vowel changes (LSD: $P<0.001$ for pitch and intensity vs. duration and vowel). Also the deviation magnitude affected MMN amplitude ($F_{2,30}=13.47$, $P<0.001$; contrast for linear change as a function of the deviation magnitude $F_{1,15}=20.24$, $P<0.001$). The MMN was smallest for the small, intermediate for the medium and largest for the large sound change (LSD: $P<0.05$ for small vs. medium and large, and large vs. small and medium). An interaction of the electrode and deviation magnitude was found ($F_{4,60}=6.55$, $P<0.01$). The MMN amplitude was modulated by the deviation magnitude only at Cz, whereas at mastoids there was no difference between MMNs for different deviation magnitudes (LSD: $P<0.01$ for small, medium and large at Cz vs. all others).

Two-way ANOVAs for repeated measures, conducted separately for the intensity, duration, vowel, and pitch MMNs further highlight the influence of the electrode on the MMN amplitude for all deviant types (pitch $F_{2,\ 30}=14{,}67$, $P<0.01$; intensity $F_{2,\ 30}=17{,}71$, $P<0.001$; duration $F_{2,\ 30}=8{,}14$, $P<0.01$; vowel $F_{2,\ 30}=19{,}33$, $P<0.001$). The

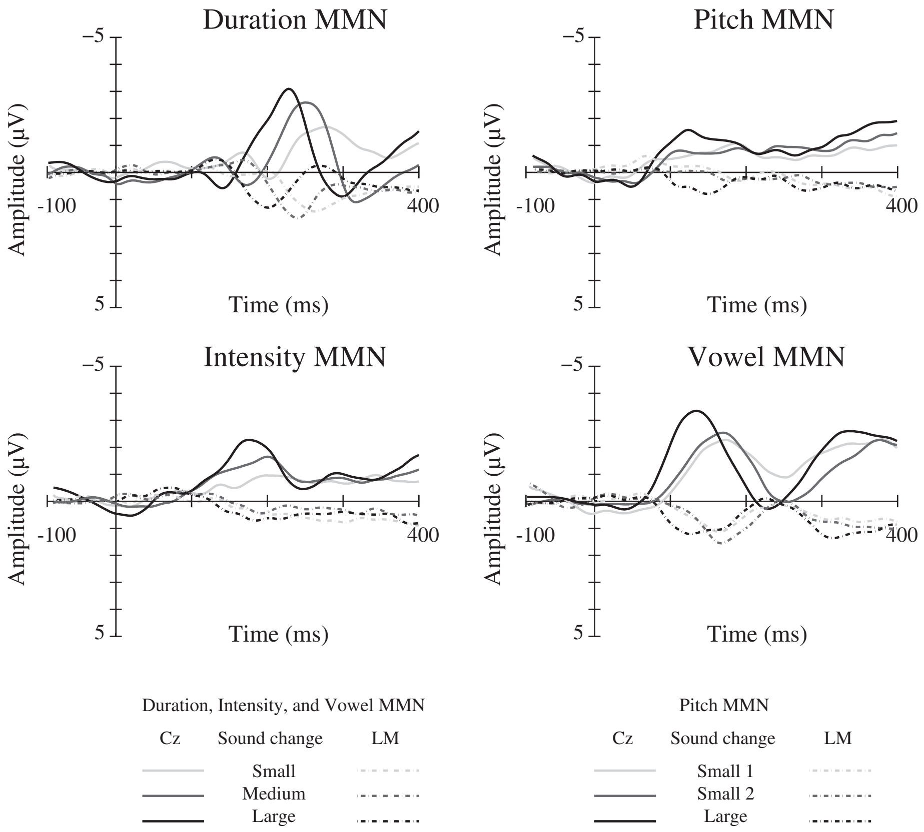

Fig. 1. MMN responses. Grand average deviant-minus-standard difference signals of 16 subjects for the small, intermediate and large sound changes in the vowel duration, intensity, and vowel identity changes, as well as for the two small and one large pitch changes. The solid lines denote the signals at Cz, and the dashed lines those at the LM. Sound onset is always at 0 ms.

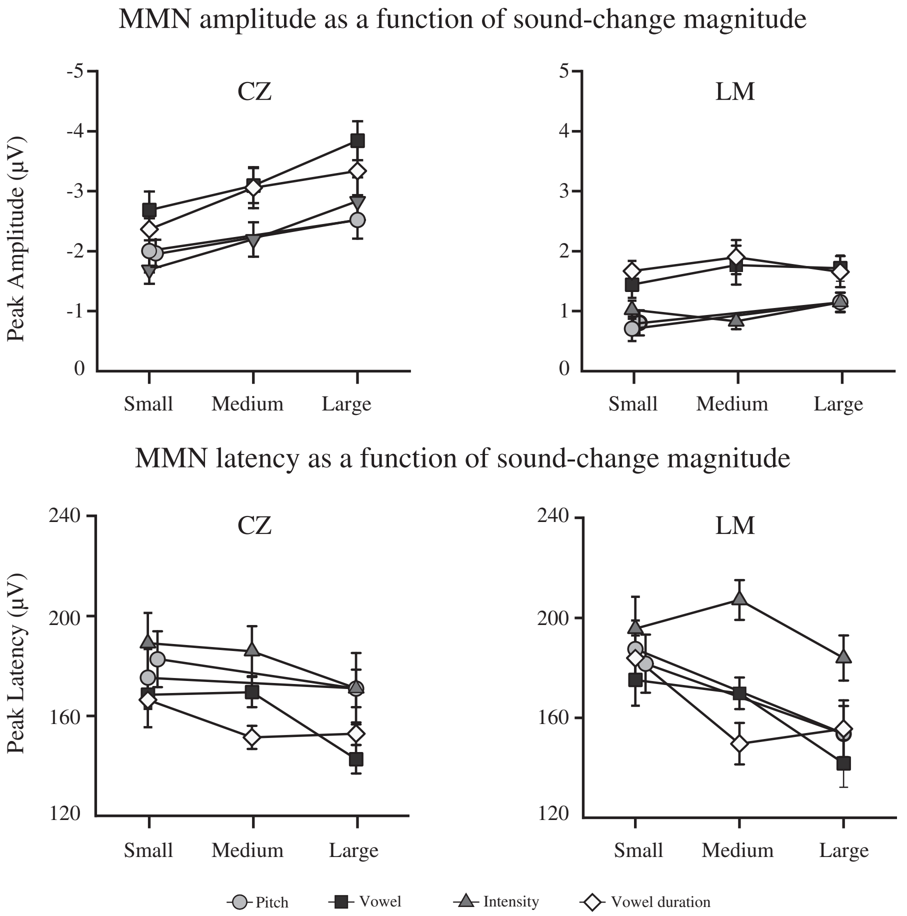

Fig. 2. MMN peak amplitudes and latencies. The MMN peak amplitude at Cz (upper left panel) and LM (upper right), and the MMN peak latency at Cz (lower left) and LM (lower right) as a function of stimulus deviance. Error bars denote the standard error of mean. The MMN latencies are presented in relation to the sound onset, except for the vowel-duration changes, which are presented in relation to the deviation onset.

MMNs were smaller at the mastoid electrodes than at Cz (LSD: pitch, intensity, vowel $P<0.01$, and duration $P<0.05$ for Cz vs. RM and LM). Also the magnitude of the deviation modulated the MMN amplitudes of all deviant types (pitch $F_{2,\ 30}=3{,}93$, $P<0.05$, contrast for linear change as a function of deviation magnitude $F_{1,15}=5.96$, $P<0.05$; intensity $F_{2,\ 30}=5{,}71$, $P<0.01$, contrast for linear change $F_{1,15}=8.86$, $P<0.01$; duration $F_{2,\ 30}=6{,}35$, $P<0.01$, contrast for linear change $F_{1,15}=7.39$, $P<0.05$; and vowel $F_{2,\ 30}=7{,}39$, $P<0.01$, contrast for linear change $F_{1,15}=11.21$, $P<0.01$). For the intensity changes the MMNs were larger for the large than for the other two sound changes (LSD: $P<0.05$ for large vs. small and medium) and for the vowel-duration and vowel changes the MMNs were smaller for the small than for the other two sound changes (LSD: duration, vowel $P<0.05$ for the small vs. the medium and large). Moreover, the MMN was larger for the large than for the two small pitch changes (LSD: $P<0.05$ for the large vs. the small1 and small2).

Table 3
The mean MMN amplitudes for the 4 types of deviations at different magnitudes of deviance. MMN mean amplitudes were measured at electrode Cz, and the data were referenced to the nose electrode.

Deviant type	Mean	t	Mean	t	Mean	t
	Small deviation		Medium deviation		Large deviation	
Vowel	−1.8 (.3)	-7.0^{***}	−1.8 (.2)	-9.7^{***}	−2.4 (.2)	-11.2^{***}
Intensity	−0.6 (.2)	-2.5^{**}	−1.2 (.3)	-4.2^{***}	−1.4 (.2)	-5.4^{***}
Duration	−1.4 (.3)	-5.4^{***}	−1.6 (.3)	-5.8^{***}	−1.6 (.3)	-5.3^{***}
	Medium deviation		Medium deviation		Large deviation	
Pitch	−0.6 (.3)	-1.8^{*}	−0.7 (.3)	-2.6^{**}	−1.0 (.2)	-4.3^{***}

Standard errors of means are in parentheses.
Results of one-tailed t-tests. * $P<0.05$, ** $P<0.01$, *** $P<0.001$.

3.2. Latency

Across deviant types, the three-way ANOVA for repeated measures on MMN peak latency revealed that the MMN latency differed between the different deviant types ($F_{3,45}=23.96$, $P<0.001$). The MMNs for the vowel-duration changes were earlier and those for the intensity changes later as compared with all other changes (LSD: $P<0.05$ for the duration vs. others and intensity vs. others). Also the deviation magnitude affected the MMN latency ($F_{2,30}=17.86$, $P<0.001$; contrast for linear change as a function of deviation magnitude $F_{1,15}=21.93$, $P<0.001$). The MMN was earlier for the large than for the small and medium deviations (LSD: $P<0.001$ for the large vs. the small and medium).

Two-way ANOVAs for repeated measures, conducted separately for the MMN latencies of different deviant types revealed that the magnitude of the deviation modulated the MMN latencies for pitch and vowel changes (pitch $F_{2,\ 30}=14.86$, $P<0.001$, contrast for linear change as a function of deviation magnitude $F_{1,15}=19.59$, $P<0.001$; and vowel $F_{2,\ 30}=9{,}46$, $P<0.01$, contrast for linear change $F_{1,15}=10.15$, $P<0.01$). For the vowel changes the MMNs were earlier for the large than for the small and medium sound changes (LSD: $P<0.01$, for the large vs. the small and medium). For the pitch changes, the MMNs peaked earlier for the large than for the two small sound changes (LSD: $P<0.001$ for the large vs. the small1 and small2).

4. Discussion

The aim of this study was to develop an MMN paradigm that allows a parametrical assessment of speech–sound processing in a short recording time (34 min). All sound changes: the small, intermediate, and large deviations in vowel intensity, duration, and identity, as well as the small and large changes in the pitch, elicited statistically significant MMN responses (Table 3). In general, the MMN amplitudes increased, and the latencies decreased with an increase in the deviation magnitude.

The MMN amplitude reflected both the physical and the phonological characteristics of the sound changes. The MMN amplitude for the vowel-duration changes reflected the physical difference between the sound deviations but also categorisation of the phoneme durations to short and long categories of /i:/. This is a highly relevant contrast in Finnish, a quantity language in which variations in the duration of, e.g., phoneme /i/ are interpreted as two categories, short /i/ and long /i:/, giving rise to the semantic differentiation in words. The MMN amplitude for the two largest vowel-duration changes i.e., to the 70-ms and 100-ms deviants which belong to the same phoneme category and are perceived (by a Finnish listener) as short /i/ did not differ from each other, despite their acoustical difference. Moreover, these MMNs differed from the MMN to the small 135-ms vowel-duration deviant, which is perceived as long /i:/ in the Finnish language. Thus, the MMN responses were more similar for the within-category, than for the between-category changes.

The MMN amplitude for the vowel changes from standard /i:/ to a rather close vowel /e:/, slightly further /y:/, and the clearly furthest /a:/ on the phoneme map was expected to directly reflect the distance between these different phoneme categories on the phoneme map. Indeed, there was a significant trend towards increasing MMN amplitude with an increasing phonemic deviance, although in the pairwise comparisons only the MMN to the smallest deviant /e:/ differed from the MMN amplitude to the vowels /y:/ and /a:/. A similar trend of increasing MMN amplitude with an increasing sound change was also found for the intensity changes, with the pairwise comparisons revealing larger amplitudes for the two large sound changes as compared with the smallest sound changes.

The MMN amplitude for the pitch changes reflected the degree of stimulus deviance. As expected, the MMN amplitudes for the two identical intermediate pitch changes did not differ from each other but were smaller than the MMN amplitude for the large pitch change. It should be noted however, that in the sequence, the small pitch changes were presented twice as often as the large pitch and the other sound changes ($P_{\mathrm{small\ pitch\ deviant}} = 0.08$; $P_{\mathrm{other\ deviants}} = 0.04$). As the MMN amplitude decreases with increasing deviant probability (Ritter et al., 1992), this may also have slightly reduced the MMN amplitude for the small, as compared with the large pitch changes. The MMN amplitude for the pitch changes, even for the large one, was relatively low compared to what one might expect on the basis of the previous literature (e.g., Tiitinen et al., 1994; Pakarinen et al., 2007). This may partly derive from the speech context: It is known that sound changes are differently processed in speech than in the non-speech contexts (Jaramillo et al., 2001) so that the frequency changes produce smaller MMN amplitudes in speech than in a non-speech context (Davids et al., 2009). Moreover, the pitch changes do not carry as much relevant information in the Finnish (quantity) language as they do in tonal languages, for instance. The relatively small MMN amplitude for the intensity changes, in turn, is a common finding in multi-feature paradigms (e.g., Pakarinen et al., 2007, 2010) and may be explained by the residual intensity variation in the stimulus sequence.

The MMN peaked earlier for the large vowel and pitch changes as compared with the smaller ones, whereas the latencies of the intensity and vowel-duration MMNs were not affected. The results are in concordance with a recent multi-feature study using non-speech sounds, showing that the latency of the MMN responses decreased with increasing pitch and location changes, with the peak latencies for the intensity and duration MMNs remaining unaffected (Pakarinen et al., 2007). In the aforementioned study (Pakarinen et al., 2007), only decrements (lower intensity) were used, and it was thought that the lower power of these stimuli may have delayed the N1 and thus affected the accuracy of the MMN latency estimation. However, the current study also used intensity increments, and yet the peak latencies for the different magnitudes of deviations remained unaffected, further attesting to the suggestion that the MMN latency (at least for the intensity changes) would not be sensitive to the deviation magnitude (Winkler et al., 2001; Horváth et al., 2008).

When all the deviants were examined together, the MMN amplitude modulation by deviation magnitude was seen only at the frontal and not at the mastoid electrode sites, possibly partially due to larger amplitudes, i.e., better signal-to-noise ratio at the frontal site. An alternative explanation would be, that the overlapping N1 response, which presumably contributes to the amplitude and latency modulation by the deviation magnitude (Winkler et al., 2001; Horváth et al., 2008), shows better on the frontal electrodes than on the mastoids. This difference between the electrode locations (frontal vs. mastoid) however, was not present when the different deviant types were separately examined. The MMN peak latency, in contrast, did not differ between the frontal and mastoid sites on any of the comparisons. As the mastoid amplitudes are rather small, and clearly smaller than the frontal ones, with the latencies being comparable, it would in many cases be more practical to reference the data to the mean of the mastoids in order to get a single integrated value of the entire MMN signal, instead of separately looking at the frontal and mastoid signals. Also, one could replace half of the small pitch deviants with an intermediate or even smaller pitch deviant to obtain a three-level pitch discrimination profile, if needed. One should however, be cautious when selecting the smallest deviations. As the processing of different deviation magnitudes (e.g., small vs. large intensity changes) is not as independent as it is for different deviation types (e.g., intensity vs. frequency changes), the comparability of the MMNs between subject groups may become limited if some of the subjects in either group do not discriminate all deviations. For instance, if a subject would not be able to discriminate the smallest intensity deviant presented in this study, the probabilities of the medium and large intensity deviants per se would remain unaffected (e.g., $\mathrm{P}_{\mathrm{intensity\_medium}} = 0.04$), but there would appear to be fewer intensity changes in general in the sequence (probability of the intensity deviants as a category: $\mathrm{P}_{\mathrm{intensity}} = \mathrm{P}_{\mathrm{intensity\_small}} + \mathrm{P}_{\mathrm{intensity\_medium}} + \mathrm{P}_{\mathrm{intensity\_large}} = 0 + 0.04 + 0.04$). This shift in probability might slightly affect the MMN amplitude for the medium and large intensity changes, making the comparison to those subjects who would discriminate also the smallest intensity deviants problematic. Therefore, for the maximum comparability, even the smallest deviations should be large enough to be perceived by all subjects.

The paradigm introduced here allows one to obtain a profile of central auditory speech sound discrimination of small, intermediate and large vowel, pitch, intensity, and vowel-duration changes in only a 34-minute recording time. Together with a 30-minute non-speech multi-feature paradigm with three magnitudes of deviations for pitch, intensity, duration, and location changes (Pakarinen et al., 2007) one could in just slightly over an hour recording time obtain a very extensive profile of the central auditory processing of both speech and non-speech sounds. Multi-feature paradigms with tones, indeed, have already been successfully applied in healthy children (Lovio et al., 2009) and newborns (Sambeth et al., 2000) as well as in several other studies including schizophrenia (Fisher et al., 2008; Thönnessen et al., 2008), epilepsy (Korostenskaja et al., 2010), post-traumatic stress disorder (Menning et al., 2008), adults with dyslexia (Kujala et al., 2006) and Asperger syndrome (Kujala et al., 2007a, 2007b), and the effects of mobile phone fields on adult and child brains (Kwon et al., 2009, 2010). Also the multi-feature paradigm with consonant–vowel syllables (Pakarinen et al., 2009) has already been applied to clinical studies with children at risk for dyslexia (Lovio et al., 2010) and children with Asperger syndrome (Kujala et al., 2010). In addition, a multi-feature MMN paradigm with pseudowords has been developed for studying auditory perception of emotions and prosody (Thönnessen et al., 2010). Furthermore, musical expertise and perception can be examined with a multi-feature paradigm where musically relevant sound changes are embedded within brief melodies (Vuust et al., 2011) and a multi-feature paradigm with clarinet sounds (Sandmann et al., 2010) has been used to study music perception of cochlear implant users. The paradigm presented here could provide new insights in evaluating whether the underlying problems, for instance in language disorders, are specific to language content or are more general in nature. One could also follow the development of the phoneme categories during the native language or second language learning and simultaneously examine whether these changes in speech processing are also generalized to the processing of non-speech sounds.

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References

Alho, K., 1995. Cerebral generators of mismatch negativity (MMN) and its magnetic counterpart (MMNm) elicited by sound changes. Ear and Hearing 16, 38–51.

Alho, K., Huotilainen, M., Tiitinen, H., Ilmoniemi, R.J., Knuutila, J., Näätänen, R., 1993. Memory-related processing of complex sound patterns in human auditory cortex: a MEG study. Neuroreport 4, 391–394.

Amenedo, E., Escera, C., 2000. The accuracy of sound duration representation in the human brain determines the accuracy of behavioural perception. The European Journal of Neuroscience 12, 2570–2574.

Baldeweg, T., Richardson, A., Watkins, S., Foale, C., Gruzelier, J., 1999. Impaired auditory frequency discrimination in dyslexia detected with mismatch evoked potentials. Annals of Neurology 45, 495–503.

Bishop, D.V., 2007. Using mismatch negativity to study central auditory processing in developmental language and literacy impairments: where are we, and where should we be going? Psychological Bulletin 133, 651–672.

Bradlow, A.R., Kraus, N., Nicol, T.G., McGee, T.J., Cunningham, J., Zecker, S.G., Carrell, T.D., 1999. Effects of lengthened formant transition duration on discrimination and neural representation of synthetic CV syllables by normal and learning-disabled children. The Journal of the Acoustical Society of America 106, 2086–2096.

Brønnick, K.S., Nordby, H., Larsen, J.P., Aarsland, D., 2010. Disturbance of automatic auditory change detection in dementia associated with Parkinson's disease: a mismatch negativity study. Neurobiology of Aging 31, 104–113.

Davids, N., van den Brink, D., van Turennout, M., Mitterer, H., Verhoeven, L., 2009. Towards neurophysiological assessment of phonemic discrimination: context effects of the mismatch negativity. Clinical Neurophysiology 120, 1078–1086.

Deouell, L.Y., 2007. The frontal generator of the mismatch negativity revisited. Journal of Psychophysiology 21, 188–203.

Draganova, R., Eswaran, H., Murphy, P., Lowery, C., Preissl, H., 2005. Sound frequency change detection in fetuses and newborns, a magnetoencephalographic study. NeuroImage 28, 354–361.

Draganova, R., Eswaran, H., Murphy, P., Lowery, C., Preissl, H., 2007. Serial magnetoencephalographic study of fetal and newborn auditory discriminative evoked responses. Early Human Development 83, 199–207.

Fellman, V., Kushnerenko, E., Mikkola, K., Ceponiene, R., Leipala, J., Naatanen, R., 2004. Atypical auditory event-related potentials in preterm infants during the first year of life: a possible sign of cognitive dysfunction? Pediatric Research 56, 291–297.

Fischer, C., Morlet, D., Bouchet, P., Luaute, J., Jourdan, C., Salord, F., 1999. Mismatch negativity and late auditory evoked potentials in comatose patients. Clinical Neurophysiology 110, 1601–1610.

Fischer, C., Luaute, J., Morlet, D., 2010. Event-related potentials (MMN and novelty P3) in permanent vegetative or minimally conscious states. Clinical Neurophysiology 121, 1032–1042.

Fisher, D.J., Labelle, A., Knott, V.J., 2008. The right profile: mismatch negativity in schizophrenia with and without auditory hallucinations as measured by a multi-feature paradigm. Clinical Neurophysiology 119, 909–921.

Frodl-Bauch, T., Kathmann, N., Möller, H.J., Hegerl, U., 1997. Dipole localization and test–retest reliability of frequency and duration mismatch negativity generator processes. Brain Topography 10, 3–8.

Hari, R., Hämäläinen, M., Ilmoniemi, R.J., Kaukoranta, E., Reinikainen, K., Salminen, J., et al., 1984. Responses of the primary auditory cortex to pitch changes in a sequence of tone pips: neuromagnetic recordings in man. Neuroscience Letters 50, 127–132.

Horváth, J., Czigler, I., Jacobsen, T., Maess, B., Schröger, E., Winkler, I., 2008. MMN or no MMN: no magnitude of deviance effect on the MMN amplitude. Psychophysiology 45, 60–69.

Huotilainen, M., Kujala, A., Hotakainen, M., Shestakova, A., Kushnerenko, E., Parkkonen, L., et al., 2003. Auditory magnetic responses of healthy newborns. Neuroreport 14, 1871–1875.

Huotilainen, M., Kujala, A., Hotakainen, M., Parkkonen, L., Taulu, S., Simola, J., et al., 2005. Short-term memory functions of the human fetus recorded with magnetoencephalography. Neuroreport 16, 81–84.

Jaramillo, M., Ilvonen, T., Kujala, T., Alku, P., Tervaniemi, M., Alho, K., 2001. Are different kinds of acoustic features processed differently for speech and non-speech sounds? Brain Research. Cognitive Brain Research 12, 459–466.

Kane, N.M., Curry, S.H., Butler, S.R., Cummins, B.H., 1993. Electrophysiological indicator of awakening from coma. Lancet 341, 688.

Kane, N.M., Curry, S.H., Rowlands, C.A., Manara, A.R., Lewis, T., Moss, T., et al., 1996. Event-related potentials — neurophysiological tools for predicting emergence and early outcome from traumatic coma. Intensive Care Medicine 22, 39–46.

Kemner, C., Verbaten, M.N., Koelega, H.S., Buitelaar, J.K., van der Gaag, R.J., Camfferman, G., et al., 1996. Event-related brain potentials in children with attention-deficit and hyperactivity disorder: effects of stimulus deviancy and task relevance in the visual and auditory modality. Biological Psychiatry 40, 522–534.

Korostenskaja, M., Pardos, M., Fujiwara, H., Kujala, T., Horn, P., Rose, D., et al., 2010. Neuromagnetic evidence of impaired cortical auditory processing in pediatric intractable epilepsy. Epilepsy Research 92, 63–73.

Kozou, H., Kujala, T., Shtyrov, Y., Toppila, E., Starck, J., Alku, P., et al., 2005. The effect of different noise types on the speech and non-speech elicited mismatch negativity. Hearing Research 199, 31–39.

Kujala, T., Näätänen, R., 2010. The adaptive brain: a neurophysiological perspective. Progress in Neurobiology 91, 55–67.

Kujala, T., Karma, K., Ceponiene, R., Belitz, S., Turkkila, P., Tervaniemi, M., et al., 2001. Plastic neural changes and reading improvement caused by audiovisual training in reading-impaired children. Proceedings of the National Academy of Sciences of the United States of America 98, 10509–10514.

Kujala, T., Lovio, R., Lepistö, T., Laasonen, M., Näätänen, R., 2006. Evaluation of multi-attribute auditory discrimination in dyslexia with the mismatch negativity. Clinical Neurophysiology 117, 885–893.

Kujala, T., Aho, E., Lepistö, T., Jansson-Verkasalo, E., Nieminen-von Wendt, T., von Wendt, L., et al., 2007a. Atypical pattern of discriminating sound features in adults with Asperger syndrome as reflected by the mismatch negativity. Biological Psychology 75, 109–114.

Kujala, T., Tervaniemi, M., Schröger, E., 2007b. The mismatch negativity in cognitive and clinical neuroscience: theoretical and methodological considerations. Biological Psychology 74, 1–19.

Kujala, T., Kuuluvainen, S., Saalasti, S., Jansson-Verkasalo, E., von Wendt, L., Lepistö, T., 2010. Speech-feature discrimination in children with Asperger syndrome as determined with the multi-feature mismatch negativity paradigm. Clinical Neurophysiology 121, 1410–1419.

Kwon, M.S., Kujala, T., Huotilainen, M., Shestakova, A., Näätänen, R., Hämäläinen, H., 2009. Preattentive auditory information processing under exposure to the 902 MHz GSM mobile phone electromagnetic field: a mismatch negativity (MMN) study. Bioelectromagnetics 30, 241–248.

Kwon, M.S., Huotilainen, M., Shestakova, A., Kujala, T., Näätänen, R., Hämäläinen, H., 2010. No effects of mobile phone use on cortical auditory change-detection in children: an ERP study. Bioelectromagnetics 31, 191–199.

Lovio, R., Pakarinen, S., Huotilainen, M., Alku, P., Silvennoinen, S., Näätänen, R., et al., 2009. Auditory discrimination profiles of speech sound changes in 6-year-old children as determined with the multi-feature MMN paradigm. Clinical Neurophysiology 120, 916–921.

Lovio, R., Näätänen, R., Kujala, T., 2010. Abnormal pattern of cortical speech feature discrimination in 6-year-old children at risk for dyslexia. Brain Research 1335, 53–62.

Menning, H., Renz, A., Seifert, J., Maercker, A., 2008. Reduced mismatch negativity in posttraumatic stress disorder: a compensatory mechanism for chronic hyperarousal? International Journal of Psychophysiology 68, 27–34.

Michie, P.T., 2001. What has MMN revealed about the auditory system in schizophrenia? International Journal of Psychophysiology 42, 177–194.

Michie, P.T., Budd, T.W., Todd, J., Rock, D., Wichmann, H., Box, J., et al., 2000. Duration and frequency mismatch negativity in schizophrenia. Clinical Neurophysiology 111, 1054–1065.

Mikkola, K., Kushnerenko, E., Partanen, E., Serenius-Sirve, S., Leipälä, J., Huotilainen, M., et al., 2007. Auditory event-related potentials and cognitive function of preterm children at five years of age. Clinical Neurophysiology 118, 1494–1502.

Morr, M.L., Shafer, V.L., Kreuzer, J.A., Kurtzberg, D., 2002. Maturation of mismatch negativity in typically developing infants and preschool children. Ear and Hearing 23, 118–136.

Näätänen, R., Winkler, I., 1999. The concept of auditory stimulus representation in neuroscience. Psychological Bulletin 125, 826–859.

Näätänen, R., Gaillard, A.W.K., Mäntysalo, S., 1978. Early selective-attention effect on evoked potential reinterpreted. Acta Psychologica 42, 313–329.

Näätänen, R., Paavilainen, P., Alho, K., Reinikainen, K., Sams, M., 1989. Do event-related potentials reveal the mechanism of the auditory sensory memory in the human brain? Neuroscience Letters 98, 217–221.

Näätänen, R., Schröger, E., Karakas, S., Tervaniemi, M., Paavilainen, P., 1993. Development of a memory trace for a complex sound in the human brain. Neuroreport 4, 503–506.

Näätänen, R., Lehtokoski, A., Lennes, M., Cheour, M., Huotilainen, M., Iivonen, A., et al., 1997. Language-specific phoneme representations revealed by electric and magnetic brain responses. Nature 385, 432–434.

Näätänen, R., Pakarinen, S., Rinne, T., Takegata, R., 2004. The mismatch negativity (MMN) — towards the optimal paradigm. Clinical Neurophysiology 115, 140–144.

Näätänen, R., Astikainen, P., Ruusuvirta, T., Huotilainen, M., 2010. Automatic auditory intelligence: an expression of the sensory-cognitive core of cognitive processes. Brain Research Reviews 64, 123–136.

Nordby, H., Hammerborg, D., Roth, W.T., Hugdahl, K., 1994. ERPs for infrequent omissions and inclusions of stimulus elements. Psychophysiology 31, 544–552.

Nousak, J.M., Deacon, D., Ritter, W., Vaughan Jr., H.G., 1996. Storage of information in transient auditory memory. Brain Research. Cognitive Brain Research 4, 305–317.

Novitski, N., Huotilainen, M., Tervaniemi, M., Näätänen, R., Fellman, V., 2007. Neonatal frequency discrimination in 250–4000-Hz range: electrophysiological evidence. Clinical Neurophysiology 118, 412–419.

Oades, R.D., Dittmann-Balcar, A., Schepker, R., Eggers, C., Zerbin, D., 1996. Auditory event-related potentials (ERPs) and mismatch negativity (MMN) in healthy children and those with attention-deficit or tourette/tic symptoms. Biological Psychology 43, 163–185.

Paavilainen, P., Jiang, D., Lavikainen, J., Näätänen, R., 1993. Stimulus duration and the sensory memory trace: an event-related potential study. Biological Psychology 35, 139–152.

Paavilainen, P., Arajärvi, P., Takegata, R., 2007. Preattentive detection of nonsalient contingencies between auditory features. Neuroreport 18, 159–163.

Pakarinen, S., Takegata, R., Rinne, T., Huotilainen, M., Näätänen, R., 2007. Measurement of extensive auditory discrimination profiles using mismatch negativity (MMN) of the auditory event-related potential. Clinical Neurophysiology 118, 177–185.

Pakarinen, S., Lovio, R., Huotilainen, M., Alku, P., Näätänen, R., Kujala, T., 2009. Fast multi-feature paradigm for recording several mismatch negativities (MMNs) to phonetic and acoustic changes in speech sounds. Biological Psychology 82, 219–226.

Pakarinen, S., Huotilainen, M., Näätänen, R., 2010. The mismatch negativity (MMN) with no standard stimulus. Clinical Neurophysiology 121, 1043–1050.

Pekkonen, E., 2000. Mismatch negativity in aging and in Alzheimer's and Parkinson's diseases. Audiology and Neuro-Otology 5, 216–224.

Ritter, W., Paavilainen, P., Lavikainen, J., Reinikainen, K., Alho, K., Sams, M., et al., 1992. Event-related potentials to repetition and change of auditory stimuli. Electroencephalography and Clinical Neurophysiology 83, 306–321.

Ritter, W., Sussman, E., Molholm, S., 2000. Evidence that the mismatch negativity system works on the basis of objects. Neuroreport 11, 61–63.

Sambeth, A., Pakarinen, S., Ruohio, K., Fellman, V., van Zuijen, T.L., Huotilainen, M., 2000. Change detection in newborns using a multiple deviant paradigm: a study using magnetoencephalography. Clinical Neurophysiology 120, 530–538.

Sams, M., Paavilainen, P., Alho, K., Näätänen, R., 1985. Auditory frequency discrimination and event-related potentials. Electroencephalography and Clinical Neurophysiology 62, 437–448.

Sandmann, P., Kegel, A., Eichele, T., Dillier, N., Lai, W., Bendixen, A., et al., 2010. Neurophysiological evidence of impaired musical sound perception in cochlear-implant users. Clinical Neurophysiology 121, 2070–2082.

Sawada, M., Iida, J., Ota, T., Negoro, H., Tanaka, S., Sadamatsu, M., et al., 2010. Effects of osmotic-release methylphenidate in attention-deficit/hyperactivity disorder as measured by event-related potentials. Psychiatry and Clinical Neurosciences 64, 491–498.

Shestakova, A., Brattico, E., Huotilainen, M., Galunov, V., Soloviev, A., Sams, M., et al., 2002. Abstract phoneme representations in the left temporal cortex: magnetic mismatch negativity study. Neuroreport 13, 1813–1816.

Shestakova, A., Huotilainen, M., Ceponiene, R., Cheour, M., 2003. Event-related potentials associated with second language learning in children. Clinical Neurophysiology 114, 1507–1512.

Tervaniemi, M., Maury, S., Näätänen, R., 1994. Neural representations of abstract stimulus features in the human brain as reflected by the mismatch negativity. Neuroreport 5, 844–846.

Tervaniemi, M., Rytkönen, M., Schröger, E., Ilmoniemi, R.J., Näätänen, R., 2001. Superior formation of cortical memory traces for melodic patterns in musicians. Learning & Memory 8, 295–300.

Thönnessen, H., Zvyagintsev, M., Harke, K.C., Boers, F., Dammers, J., Norra, Ch., et al., 2008. Optimized mismatch negativity paradigm reflects deficits in schizophrenia patients. A combined EEG and MEG study. Biological Psychology 77, 205–216.

Thönnessen, H., Boers, F., Dammers, J., Chen, Y.H., Norra, C., Mathiak, K., 2010. Early sensory encoding of affective prosody: neuromagnetic tomography of emotional category changes. NeuroImage 50, 250–259.

Tiitinen, H., May, P., Reinikainen, K., Näätänen, R., 1994. Attentive novelty detection in humans is governed by pre-attentive sensory memory. Nature 370, 90–92.

van Zuijen, T.L., Simoens, V.L., Paavilainen, P., Näätänen, R., Tervaniemi, M., 2006. Implicit, intuitive, and explicit knowledge of abstract regularities in a sound sequence: an event-related brain potential study. Journal of Cognitive Neuroscience 18, 1292–1303.

Vestergaard, M.D., Háden, G.P., Shtyrov, Y., Patterson, R.D., Pulvermüller, F., Denham, S.L., et al., 2009. Auditory size-deviant detection in adults and newborn infants. Biological Psychology 82, 169–175.

Vuust, P., Brattico, E., Glerean, E., Seppänen, M., Pakarinen, S., Tervaniemi, M., Näätänen, R., 2011. New fast mismatch negativity paradigm for determining the neural prerequisites for musical ability. Cortex 47, 1091–1098.

Wijnen, V.J., van Boxtel, G.J., Eilander, H.J., de Gelder, B., 2007. Mismatch negativity predicts recovery from the vegetative state. Clinical Neurophysiology 118, 597–605.

Winkler, I., Karmos, G., Näätänen, R., 1996. Adaptive modeling of the unattended acoustic environment reflected in the mismatch negativity event-related potential. Brain Research 742, 239–252.

Winkler, I., Kujala, T., Tiitinen, H., Sivonen, P., Alku, P., Lehtokoski, A., et al., 1999. Brain responses reveal the learning of foreign language phonemes. Psychophysiology 36, 638–642.

Winkler, I., Schröger, E., Cowan, N., 2001. The role of large-scale memory organization in the mismatch negativity event-related brain potential. Journal of Cognitive Neuroscience 13, 59–71.

Winkler, I., Denham, S.L., Nelken, I., 2009. Modeling the auditory scene: predictive regularity representations and perceptual objects. Trends in Cognitive Science 13, 532–540.

Woldorff, M.G., Hackley, S.A., Hillyard, S.A., 1991. The effects of channel-selective attention on the mismatch negativity wave elicited by deviant tones. Psychophysiology 28, 30–42.

Yabe, H., Tervaniemi, M., Reinikainen, K., Näätänen, R., 1997. Temporal window of integration revealed by MMN to sound omission. Neuroreport 8, 1971–1974.