Clinical Neurophysiology 115 (2004) 140–144

www.elsevier.com/locate/clinph

The mismatch negativity (MMN): towards the optimal paradigm

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Accepted 9 April 2003

Abstract

Objective: Recent studies have shown that the mismatch negativity (MMN), a change-specific component of the event-related potential (ERP), for particular auditory features is degraded in different clinical populations. This suggests that the MMN could, in principle, reflect the whole profile and extent of the central auditory deficit. In the present article, we tested a new MMN paradigm allowing one to obtain MMNs for several auditory attributes in a short time.

Methods: MMN responses to changes in frequency, intensity, duration, location, and to a silent gap occasionally inserted in the middle of a tone were compared between the traditional 'oddball' paradigm (a single type of auditory change in each sequence) and the new paradigm (two versions) in which all the 5 types of changes appeared within the same sequence.

Results: The MMNs obtained in the new paradigm were equal in amplitude to those in the traditional MMN paradigm.

Conclusions: We propose a new paradigm that can provide 5 different MMNs in the same time in which usually only one MMN is obtained. The new paradigm enables one to objectively determine the profile of different auditory discrimination abilities within a very short recording time.

Keywords: Mismatch negativity; Event related potential; Central auditory processing; Sound discrimination

1. Introduction

The mismatch negativity (MMN), a change-specific component of the auditory event-related potential (ERP), is elicited by any discriminable change in auditory stimulation irrespective of the subject or patient's attention or behavioural task (Näätänen et al., 1978; for a review, see Näätänen and Winkler, 1999). Therefore it provides an objective index for sound-discrimination accuracy (for a review, see Näätänen and Alho, 1997), and thus represents a completely new phase in objective audiometry, which until now was able to measure only detection but not discrimination. This is one of the reasons of why the MMN has recently received considerable interest as a tool of clinical research, too, and a number of highly promising results have already been obtained. For instance, Baldeweg et al. (1999) found that the MMN to frequency change (but not to duration change) was attenuated in amplitude in dyslexic adults and, further, that this amplitude attenuation correlated with the severity of their reading problem. In addition, Kujala et al. (2001) observed that the attenuated MMN to the order reversal of two paired tones in 9-year-old dyslexic children was considerably enhanced after audio-visual training using non-linguistic stimuli (Karma, 1999). Furthermore, the magnitude of this amplitude enhancement correlated with the magnitude of improvement in reading skills (both in terms of reading speed and accuracy).

In contrast, in persons with schizophrenia, the MMN to duration change is more affected than that to frequency change (Michie et al., 2000; for a review, see Michie, 2001). Some of the most interesting results of these studies are that the magnitude of the MMN-amplitude attenuation (for duration change) above the left temporal lobe correlates with the magnitude of the grey-matter loss in this lobe, as indexed by magnetic resonance imaging (MRI) measurements (Ward et al., 1995). Furthermore, the MMN amplitude (both for frequency and duration changes) provides an index for the functional state of the NMDA-receptor system (Umbricht et al., 2002). Consistent with this, it has been shown that the functioning of the NMDA

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doi:10.1016/j.clinph.2003.04.001

system, which is essential for the formation of sensory-memory traces (Javitt et al., 1996), is deficient in schizophrenia (Javitt, 2000).

One practical problem in these MMN studies is, however, their relatively long duration when more than just one type of MMN is to be obtained. Each type of MMN is usually recorded in a separate block in order to rule out any contamination that might occur when several types of deviants are presented in the same stimulus block (see, however, Gomes et al., 1997). In the present article, we report a new paradigm (with two versions) in which 5 different MMNs can be recorded within one short recording session. We show that the MMNs recorded with the new paradigm very well correspond to the respective MMNs obtained in the traditional one-deviant paradigm.

2. Methods

2.1. Subjects

Fourteen subjects gave their informed consent and participated in the experiment. The data of 3 subjects were discarded because of excessive artifacts or technical problems. The mean age of the remaining 11 subjects (7 females) was 25 years (range 20–39 years).

2.2. Stimuli and procedure

The standard stimuli were harmonic tones composed of 3 sinusoidal partials of 500, 1000, and 1500 Hz, and were 75 ms in duration (including 5 ms rise and fall times). The intensity of the second and third partials was lower than that of the first partial by 3 and 6 dB, respectively. The stimuli were presented via headphones at 60 dB above the individual subject's hearing threshold with equal phase and intensity at both ears.

The deviant tones differed from the standards either in frequency, duration, intensity, perceived sound-source location, or by having a gap in the middle of the tone. Otherwise the deviants were identical to the standards. There were two types of stimuli for each of the frequency, intensity, and location deviants. A half of the frequency deviants were 10% higher (partials: 550, 1100, 1650 Hz) and the other half 10% lower (450, 900, 1350 Hz) than the standard. A half of the intensity deviants were -10 dB and the other half $+10$ dB compared with the standard. A change in the perceived sound-source location was in turn created by introducing an interaural time difference of 800 μs, for a half of the deviants to the right channel and for the other half to the left channel. The perceived difference between the standard stimulus and the location deviant was ~90°. The duration deviant, in turn, was 25 ms in duration. Further, the gap deviant was constructed by cutting out 7 ms (1 ms fall and rise times included) from the middle of the standard stimulus, leaving there a silent gap.

There were 3 different conditions in the present study (Fig. 1): one employing the traditional oddball paradigm (a single type of deviant in a sequence) and two other conditions (denoted as 'Optimum-1' and 'Optimum-2'), in which all 5 types of deviants occurred within the same sequence.

2.2.1. Optimum-1 condition

All the 5 deviants ($P = 0.1$, each) were presented in the same sequence so that every other tone was a standard ($P = 0.5$) and every other was one of the 5 deviants. The rationale of this paradigm was that the other deviants would strengthen the memory trace of the standard with respect to those levels of stimulus attributes they had in common. In each sequence, the first 15 tones were standards. The deviants were presented so that in an array of 5 deviants, each deviant category was presented once, and 2 deviants of the same category never followed each other (Fig. 1). The stimuli were presented at a stimulus-onset-asynchrony (SOA) of 500 ms in three 5 min sequences (1845 stimuli in total), with the total recording time for the 5 types of deviants thus being 15 min.

2.2.2. Oddball condition

The stimulus sequences of the traditional oddball condition were created using those of Optimum-1 condition by replacing with standards all deviants except for those of one category. In this way, the times of the occurrence of a certain type of deviant stimulus in the sequence were identical to those of Optimum-1 condition. Stimuli were presented in three consecutive 5 min sequences for each deviant type, resulting in a total recording time of 75 min.

2.2.3. Optimum-2 condition

This was a compromise between the two previously introduced conditions; all 5 types of deviants were presented in the same sequence but with 3 standards between each successive 2 deviants. In addition, the SOA was shortened to 300 ms in order to decrease the measurement time from 30 min with the normal 500 ms SOA to 18 min (three 6 min sequences).

In sum, Optimum-1 and -2 conditions were both composed of 3 stimulus sequences, whereas in Oddball condition, there were 15 sequences, 3 sequences for each deviant type. The order of the presentation of the stimulus sequences was pseudo-random so that 3 similar sequences were always delivered consecutively. Subjects were instructed to watch a self-selected subtitled video film (silenced) and not to pay attention to stimuli.

2.3. EEG recording and data analysis

The EEG was recorded (DC 40 Hz, sampling rate 500 Hz) from 31 channels using Ag/AgCl electrodes with an electrode placed at the nose as a common reference. The horizontal electro-oculogram (EOG) was recorded using

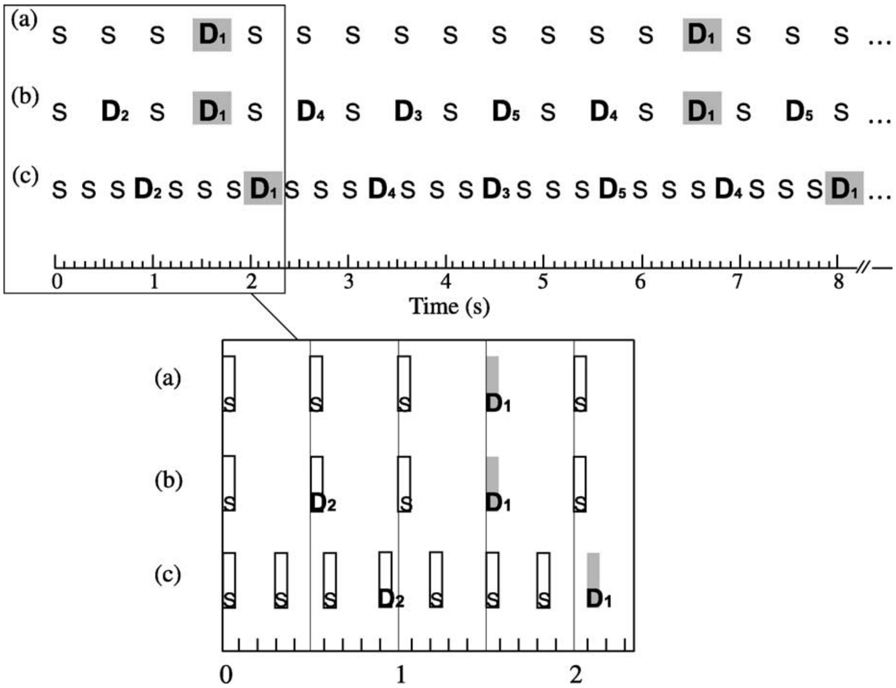

Fig. 1. Schematic illustration of the 3 stimulus conditions used: traditional Oddball (a), Optimum-1 (b), and Optimum-2 conditions (c). S denotes standard tone and Dx tones of different deviant types. Note how D1 (grey area) is positioned in these sequences. Stimulus-onset-asynchrony (SOA) was 500 ms in (a) and (b), and 300 ms in (c).

electrodes placed at the outer canthi of the left and right eyes.

The EEG was filtered (bandpass 1–30 Hz) offline and epochs of 100 ms pre-stimulus and 600 ms post-stimulus periods were separately averaged for the standard and for the 5 types of deviant stimuli in each condition. The mean voltage of the 100 ms pre-stimulus period served as a baseline for amplitude measurement. Epochs including an EEG or EOG change exceeding ± 75 μV and those for the first 15 standards of a sequence were omitted from the averaging.

To delineate the MMN, the standard stimulus ERPs were subtracted from the corresponding deviant-stimulus ERPs (of the same sequence), resulting in 15 difference waveforms, 5 for each condition. The MMN amplitude and latency were measured from the responses referenced to the mean of the two mastoids. Since the largest response was obtained for most deviants and conditions at a fronto-central electrode approximating the FCz in the 10–20 system, this channel was chosen for the statistical analysis. The MMN peak latencies were measured from the most negative peak occurring at the 90–250 ms post-stimulus period. The MMN amplitudes were calculated as a mean voltage at the 40 ms period centered at the peak latency in the grand-average waveform. One-tailed t tests were conducted to determine whether the MMN mean amplitudes significantly differed from zero. Two-way analyses of variance (ANOVA) with repeated measures were conducted to test the effects of condition (3 levels: Optimum-1, Optimum-2, Oddball) and deviant type (5 levels: location, intensity, gap, frequency, duration). Greenhouse-Geisser corrections were made when appropriate. Newman-Keuls tests were carried out as post hoc analyses.

3. Results

In all 3 conditions, deviants elicited MMNs that peaked around 150 ms from stimulus onset (Fig. 2). As shown in Table 1, the MMN mean amplitudes for the 5 types of deviants significantly differed from zero in all 3 conditions ($t_{10} = 3.7\text{–}14.6$, $P < 0.005$), except for the gap deviant in Optimum-2 condition ($t_{10} = 0.5$, not significant).

The MMN amplitude differed between the conditions (main effect of condition; $F_{2,20} = 12.78$, $P < 0.005$). A post hoc Newman-Keuls test showed that the MMN was largest in Optimum-1 condition and smallest in Optimum-2 condition ($P < 0.05$ for all combinations). The MMN amplitude also varied between the deviant types (main effect of deviant; $F_{4,40} = 27.04$, $P < 0.001$): the MMNs for the gap ($P < 0.01$) and duration ($P < 0.001$) deviants significantly differed from those for all other deviants. Although the interaction of the condition and deviant also was significant ($F_{8,80} = 5.5$, $P < 0.001$), this was mainly due to the diminished MMN amplitude for the gap deviant in Optimum-2 condition.

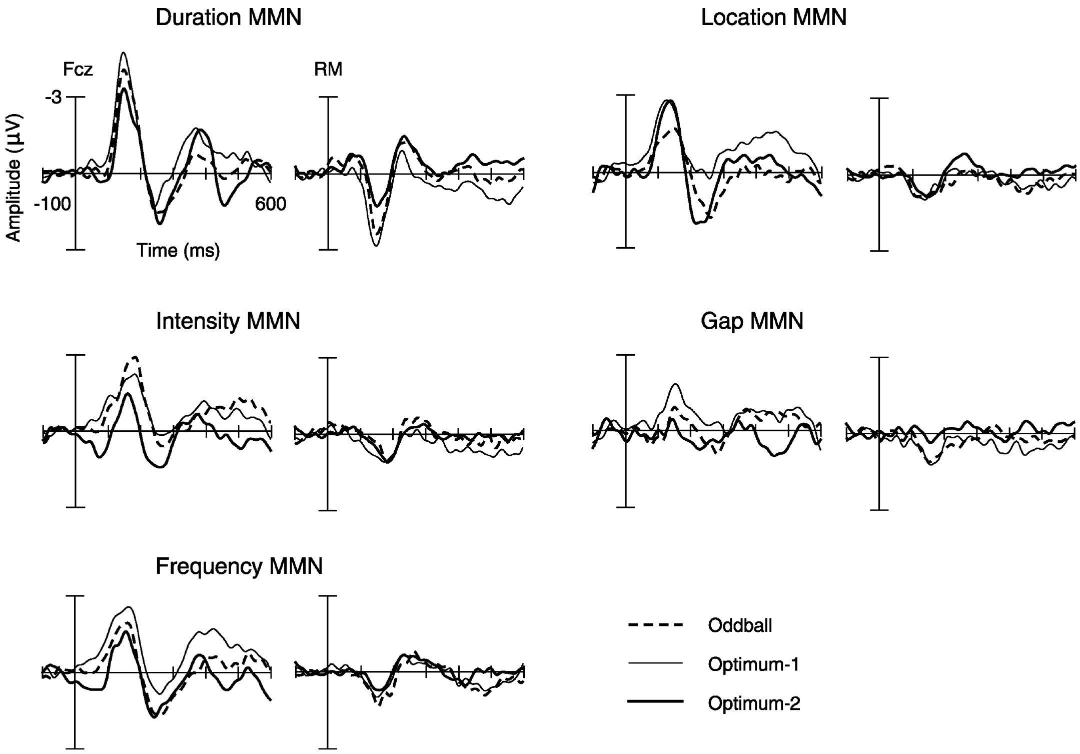

Fig. 2. Grand average difference waves (11 subjects) for 5 types of deviations recorded at a frontocentral (approximately FCz) and a right-mastoid electrode. Overlaid are the MMNs for the same type of deviation in the different conditions. The dotted line indicates the MMN in the traditional Oddball condition, the thin line that in Optimum-1 condition, and the thick line that in Optimum-2 condition. The data were referenced against the nose electrode.

4. Discussion

As is clear from Fig. 2 and Table 1, the 5 different sound changes presented in one short sequence (Optimum-1) resulted in MMN amplitudes that were at least as large as those obtained in the traditional one-deviant oddball paradigm. Optimum-2 condition produced decreased MMN amplitudes compared with the other two conditions probably because of its relatively short SOA (Schröger, 1996). The SOA was shortened from 500 to 300 ms to compensate for the prolonged measurement time caused by the two additional standards. It is likely that with a longer SOA, substantial MMN amplitudes could have been measured, but with the cost of an increased measurement time. However, the Optimum-1 condition allowed an even shorter measurement time and without compromising the MMN amplitude. On these grounds, we propose a new paradigm (Optimum-1) in which every other tone is a standard and every other a deviant, that can be used to obtain 5 different MMNs in the same time in which usually only one MMN is obtained (the traditional one-deviant oddball paradigm). This is of interest, in particular, in view of clinical research work and praxis, where time effectiveness is of primary importance. The proposed paradigm might, for instance, enable one to form multi-attribute ‘profiles’ of a subject or patient’s sound-discrimination abilities and their abnormalities in a time short enough to avoid vigilance, motivational, and other problems associated with too long recording conditions.

Table 1
Mean MMN amplitude for 5 types of deviants in different conditions

Deviant	Oddball		Optimum-1		Optimum-2	
	Mean	t	Mean	t	Mean	t
Duration	−5.69 (0.44)	12.80***	−6.75 (0.46)	14.63***	−3.98 (0.39)	10.09***
Location	−2.44 (0.45)	5.46***	−3.73 (0.45)	8.38***	−3.40 (0.63)	5.44***
Intensity	−3.59 (0.33)	10.75***	−3.25 (0.50)	6.51***	−2.07 (0.56)	3.71**
Gap	−1.60 (0.20)	8.00***	−2.80 (0.26)	10.82***	−0.17 (0.35)	0.47 −
Frequency	−3.29 (0.43)	7.61***	−3.65 (0.54)	6.79***	−2.19 (0.41)	5.31***

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

Acknowledgements

The useful discussions with Professor E. Schröger and Dr M. Tervaniemi are gratefully acknowledged. This study was supported by the Academy of Finland Grants 77322 and 80819.

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