The Development of Memory Trace Depending on the Number of the Standard Stimuli

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Key Words
Auditory Event-Related Potentials
Memory Trace Development
Mismatch Negativity

ABSTRACT

The mismatch negativity (MMN) component of the event-related potentials reflects the automatic detection mechanism of sound change. MMN is elicited by a neuronal mismatch process between deviant (infrequent) auditory input and the sensory memory trace of the standard (frequent) stimuli. Although many previous studies have investigated MMN to reveal the sensory memory mechanism, the development of memory representation still remains unclear, in particular, the topographical aspect of the trace-development in sensory memory has not been clarified.

We measured the frontal and the temporal MMN components, respectively, when the sound trace was developed as the number of standard stimuli was changed to 1, 3, 5 or 7. In this experiment, the inter-train interval was 15 sec. The stimulus train with the different frequency of 800Hz, 900Hz, or 1000Hz was repeatedly presented. Thus, we reduced the influence of the previous train. For the first time, we found not only the enhanced amplitude but also the shortened latency for both MMN components when the number of standard stimuli was increased. These findings indicate that both frontal and temporal MMN components reflect the development of memory trace depending on the number of standard stimuli.

INTRODUCTION

The mismatch negativity (MMN), an event-related potential (ERP) component, is elicited when an auditory deviant stimulus interrupts a regular sequence of standard stimuli, even in the absence of attention.[1] Näätänen et al[1,2] proposed the memory trace hypothesis that MMN reflects a neuronal mismatch process between deviant auditory input and the sensory memory trace representation of the standard stimulus. Many findings in previous research support this hypothesis.[1-3] MMN is very sensitive to the subtle deviation of sounds. Even for near-threshold change, the MMN amplitude is correlated with the accuracy of sound discrimination.[4,5] Therefore, MMN has been used as a probe for evaluating the discriminative ability in sensory memory.

In the ordinary MMN paradigm, the subject is presented with a train of frequent, "standard" stimuli, which are infrequently and randomly replaced by "deviant" stimuli. Although the memory trace as reflected by the MMN is formed by a series of standard stimuli, Winkler et al.[6] proposed that the previous MMN studies could address the question of whether the sensory memory representation was accurately formed on the basis of an automatic feature analysis of incoming sensory stimuli or information from long-term memory was also incorporated. Therefore, we need to exclude the effect of the preceding train in the case of making an investigation into the memory trace depending on the number of the standard stimuli. Cowan et al.[7] employed a paradigm for the exclusion of the effect of the preceding train. They presented subjects with trains of 9 tone bursts separated by 11-15 sec of silence. These trains consisted of one deviant and eight standard stimuli. The deviant stimulus could occur in the position 1, 2, 4, 6, or 8 of each stimulus train. Standard and deviant stimuli changed from train to train, while the relative pitch change of the deviant was the same regardless of the standard-stimulus frequency. Cowan et al. termed this condition "roving-standard." These findings were that MMN was elicited from position 4 onward and MMN was not elicited at position 2. When the order of the deviant sound was 2nd, that is, when the meaning of the "frequent" stimulus is equivalent to that of the "infrequent" stimulus, the deviant stimuli did not elicit MMN. These findings confirmed that the memory information of the previous standard train was not represented. Several researchers have investigated the memory trace formed in this condition.[6-13]

Although another feature of MMN is that the topographies of the scalp current density allowed dissociating the temporal and frontal generators of MMN,[14-16] there is little agreement as to the difference of MMN among the temporal and frontal generators. Sato et al.[17] reported that as the

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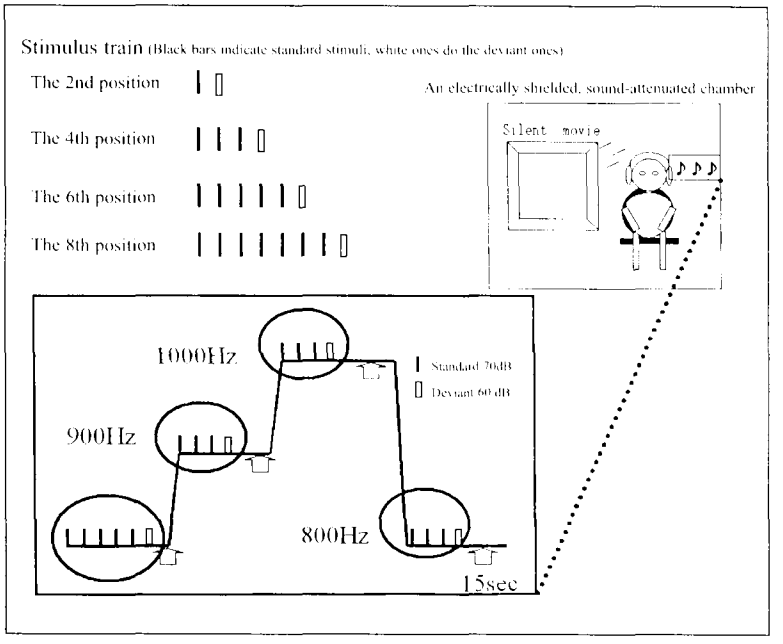


Figure 1.
This schema is the sample of experimental paradigm. Subjects were studied in an electrically shielded, sound-attenuated chamber, instructed to concentrate on watching a self-selected silent movie and to disregard the auditory stimulation. Stimuli were delivered to the subject's left ear through earphones. A stimulus train consisted of a fixed number of standard stimuli and a deviant stimulus followed by a deviant stimulus of different intensity. Four types of stimulus trains were used in which the deviant occurred as the 2nd, 4th, 6th or 8th stimulus after the initial standard stimulus. The stimulus train with the different frequency of 800Hz, 900Hz, or 1000Hz was repeatedly presented. Bars represent the auditory stimuli (black bar stand for standards, white ones for deviants).

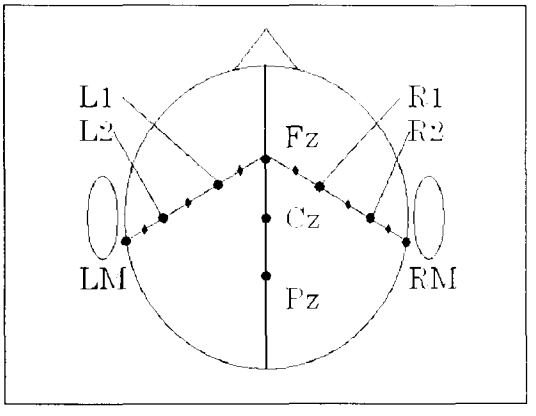


Figure 2.
The schema indicates the montage of the experiment. The electrode locations at the midline were Fpz, Fz, Cz and Pz (according to the International 10-20 System). Six lateral electrodes were placed equidistantly on the coronal line connecting the mastoids through Fz. The electrodes over the left hemisphere were designated L1, L2 and LM (left mastoid) and those over the right hemisphere as R1, R2 and RM (right mastoid).

probability of standard stimuli was increased, the frontal MMN component was significantly increased in amplitude, while the temporal one was not changed. Furthermore, they also reported that schizophrenic patients might fail to cause involuntary attention switch to stimulus change as reflected in the lowered amplitude of frontal MMN due to the effect of the probability of standard stimuli.[18] The deviation between standard and deviant stimulus was not investigated by employing the condition of the increase of the preceding standard stimuli in the roving-standard and the condition of the increase of the standard-stimulus probability. The development of memory trace depending on the number of standard stimuli was investigated by employing their conditions. Therefore, there may be the difference between the response to the temporal MMN and the response to the frontal MMN under the roving-standard condition, too. Nevertheless, the previous studies have not focused on the topographical aspect of the development of memory trace. Although these studies investigated the frontal MMN component in the roving-standard condition,[6-8] they did not investigate the temporal one. Moreover, the previous studies measured only the amplitude of the MMN on the roving-standard condition.[9-12] Also few studies have paid attention to the latency of frontal MMN.[13]

The aim of this study was to research the development of memory trace depending on the number of the standard stimuli using MMN. Furthermore, we investigated topographically the amplitude and the latency of MMN components depending on the number of standard stimuli under the condition of reducing the influence of the previous train.

MATERIALS AND METHODS

Nine healthy adult subjects (5 males and 4 females, mean age 30.6 ± 6.2 years) were studied in an electrically shielded, sound-attenuated chamber. Informed consent was obtained from all subjects prior to the experiment. During the experiment, subjects were instructed to concentrate on watching a self-selected silent movie and to disregard the auditory stimulation.

Standard and deviant tone bursts (duration 50 ms including 5 ms rise and fall times) were delivered to the subject's left ear through earphones with stimulus onset asynchronies (SOA) of 400 ms. Two types of stimuli used were different in intensity: the standard stimuli were 70 dB and the deviant ones were 60 dB. A stimulus train consisted of a fixed number of standard stimuli and a deviant stimulus followed by a deviant stimulus of different intensity. Four types of stimulus trains were used in which the deviant occurred as the 2nd, 4th, 6th or 8th stimulus after the initial standard stimulus. Each subject performed two kinds of stimulus sessions that consisted of the "2nd (1 standard and 1 deviant)" trains and "8th (7 standards and 1 deviant)" trains, or the "4th (3 standards and 1 deviant)" trains and "6th (5 standards and 1 deviant)" trains. Two types of trains in one session were presented to the subject randomly. The inter-train interval was 15 sec. The stimulus train with the different frequency of 800Hz, 900Hz, or 1000Hz was repeatedly presented, as shown in Figure 1. Thus, we reduced the influence of the previous train.

The electroencephalogram (EEG) was recorded from 10 scalp locations. The electrode locations at the midline were Fpz, Fz, Cz and Pz. Six lateral electrodes were placed equidistantly on the coronal line connecting the mastoids through Fz. The electrodes over the left hemisphere were designated L1, L2 and LM (left mastoid) and those over the right hemisphere as R1, R2 and RM (right mastoid), as shown in Figure 2. The electro-oculogram was recorded from electrodes placed at the canthus of the right eye and below the left eye. The reference electrode was attached to the nose. The EEG was amplified with frequency limits of 0.1-120 Hz. The analysis period was 450 ms (sampling rate 450Hz), including a 50 ms pre-stimulus baseline. The EEG epochs contaminated by extracerebral artifacts (amplitude change exceeding ±120 μV) were automatically rejected.

ERPs were separately averaged for standard and deviant stimuli in each type of train. The average number of trials was 480 for the standard stimuli and 120 for the deviant stimuli. One session consisted of the 2nd position trains and 8th position trains, and another session consisted of the 4th position trains and 6th position trains. The responses to standard stimuli were calculated in each session. Difference waveforms were obtained by subtracting the ERPs to the standards from those to the deviants. The peak latencies and peak amplitudes of the difference waves were determined with reference to the prestimulus baseline of 50 ms by finding the most deflective negative peak at Fz (or positive peak at RM) during the time window 100-200 ms from stimulus onset for each subject. The Scherg's analysis program[19] including these procedures was used for the present data.

The statistical analysis was conducted using the paired t-tests, the Geisser-Greenhouse (ε) corrected analysis of variance (ANOVA) with repeated measures, and Tukey multiple comparison test.

RESULTS

Figure 3 shows the grand-averaged difference waveform (Fz, R1 and RM) in the 2nd, 4th, 6th and 8th positions at which a deviant stimulus occurred. A positivity at Fz (and negative wave at RM) with nearly 100 ms in latency was calculated in all responses. This wave is identified as N1 component after the subtraction from the responses to small deviant sounds (i.e., the intensity of 60 dB) minus the responses to large standard ones (i.e., the intensity of 70 dB). The negative wave at Fz shows the polarity reversal toward the positive wave at RM wave in the 4th, 6th and 8th position. These negative waves at Fz (the positivity at RM) were identified as MMN component. Furthermore, Figure 4 shows the Grand-averaged ERP waveforms to deviant (red lines) and standard (black lines) stimuli at the Fz and RM in each (the 2nd, 4th, 6th and 8th) position at which a deviant stimulus occurred. Shaded area represents MMN component in the 100-200 msec poststimulus interval.

The results of the peak amplitude in each position are shown in Figure 5. (One way) ANOVAs showed a main effect of deviant position on the peak amplitudes of the MMNs [frontal: $F(3,24) = 4.614$, $p = 0.09$, $\varepsilon = 0.869$; temporal: $F(3, 24) = 2.581$, $p = 0.071$, $\varepsilon = 0.808$]. A subsequent multiple comparison test on each position showed significant MMN peak amplitude differences between the 6th position and 8th position ($p < 0.05$) at Fz, and between the 4th position and 8th position ($p < 0.05$) at RM.

The results of the peak latencies in each position are shown in Figure 6. (One way) ANOVAs showed a main effect of deviant position on the peak latencies of the MMNs [frontal: $F(3,24) = 3.824$, $p = 0.019$, $\varepsilon = 0.637$; temporal: $F(3, 24) = 5.453$, $p = 0.004$, $\varepsilon = 0.529$]. A subsequent multiple comparison test on each position showed significant differences in the MMN peak latency between the 2nd position and 4th position ($p < 0.05$) at Fz, between the 2nd position and 6th position ($p < 0.05$) at Fz, and between the 2nd position and 8th position ($p < 0.05$) at Fz, between the 2nd position and 4th position ($p < 0.01$) at RM and between the 4th position and 8th position ($p < 0.05$) at RM.

Table 1 shows with the results of the two-tailed t-test for peak amplitudes vs. zero in each position. The results (one-tailed t-test) at Fz and RM were statistically significant with the 6th position ($p<0.05$) and the 8th position ($p<0.01$). No significant negativity at Fz (or positivity at RM) was observed with the 2nd position ($p>0.1$) and the 4th position ($p>0.1$).

DISCUSSION

MMN, one of the indices of memory trace, reflects an automatic process discriminating the deviation of the incoming stimulus from the trace of the previous regular stimulus.[1] The development of the memory trace remains unclear. The evaluation of the memory trace would be required when we

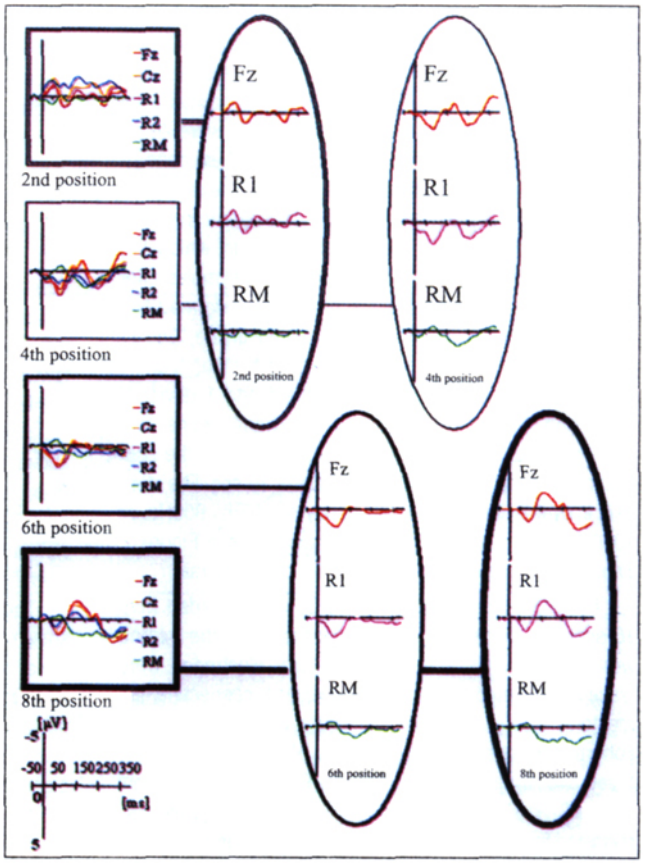
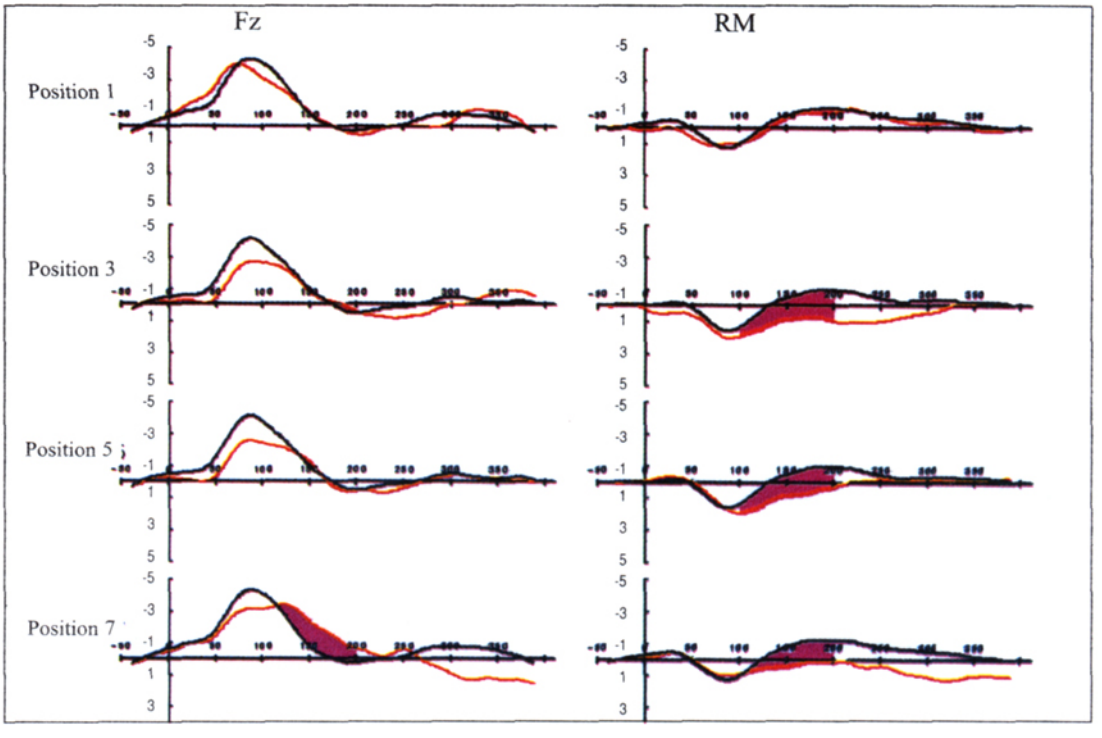


Figure 3.
Grand-averaged difference waves of deviant-standard at the right hemisphere (Fz, Cz, R1, R2 and RM) in each (the 2nd, 4th, 6th and 8th) position.

Figure 4.
Grand-averaged ERP waveforms to deviant (red lines) and standard (black lines) stimuli at the Fz and RM in each (the 2nd, 4th, 6th and 8th) position at which a deviant stimulus occurred. Shaded area represents MMN component in the 100-200 ms post-stimulus interval.



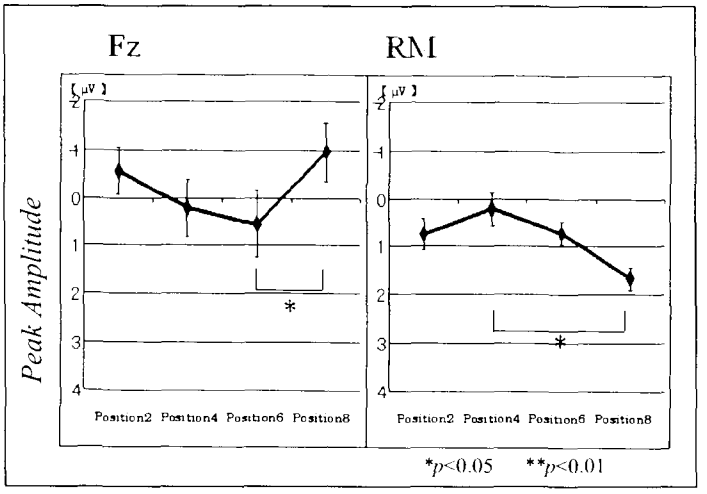


Figure 5.
The peak amplitudes of MMN at Fz and RM across conditions for each position at which a deviant occurs. The vertical error bar indicates the standard error of mean (S.E.M.) (Tukey multiple comparison test: *p<0.05, **p<0.01).

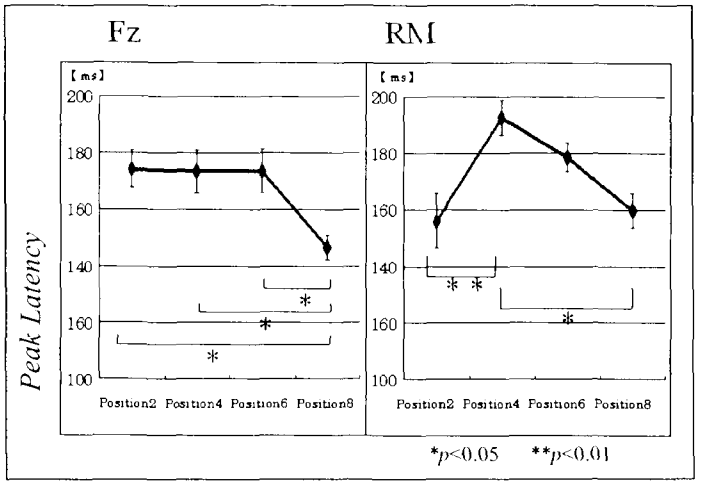


Figure 6.
The peak latencies of MMN at Fz and RM across conditions for each position at which a deviant occurs. The vertical error bar indicates the standard error of mean (S.E.M.) (Tukey multiple comparison test: *p<0.05).

use the MMN as an index of psychotic disease and memory disturbance disease. Therefore, it is important that the memory trace could be strictly evaluated by using the MMN. We paid attention to the accuracy of the measurement. That is to say, we delivered the stimuli to the subject's left ear only, because the stimulation for one ear might elicit MMN in both hemispheres of the brain in the individual. At that time, the brain responses evoked by the stimulation to both ears might overlap, resulting in the inaccurate measurement.

The present study investigated the memory trace as reflected by the MMN depending on the number of the standard stimuli. MMN usually peaks at about 100-200 ms after deviant-stimulus onset, and a part of MMN overlaps the N1 and P2 components in the general MMN condition. The N1 component depends on the stimulus intensity. In this experiment, standard stimuli were different in intensity from deviant stimuli. The standard stimuli were 70 dB and the deviant stimuli were 60 dB. Therefore, we obtained a positive wave at Fz (and negative wave at RM) with nearly 100 ms in latency, as shown in Figures 3 and 4. The scalp distribution of MMN usually shows a frontal-central scalp maximum and a polarity reversal in mastoid recordings when nose is used as a reference. The P2 component does not show a polarity reversal. Therefore, the wave peaked at about 100-200ms and showed a polarity reversal that dissociated the MMN from N2b which was reflected in the attentive component. The wave showed a polarity reversal in each 4th, 6th and 8th position for each subject. We measured the peak latencies and amplitudes of the difference waves with 100-200 ms in latency for each subject. The peak amplitude in the 4th position and 6th position at Fz was positive, as shown in Figure 3. The MMN amplitude was decreased as the result of the biased subtraction, which was induced by the difference of N1 amplitude for each subject, as shown in Figure 4. However, the waveform showed clear negativity and a polarity reversal. Therefore, this wave was identified as MMN component.

The present study is based on the concept of Cowan

Table 1

Statistical significance of peak amplitudes tested with two-tailed *t*-test for peak amplitude vs. zero

	Peak Amplitude (μV)	t(9) to Peak Amplitude vs. Zero	
Fz position 2	-0.562	1.335	($p > 0.1$)
Fz position 4	0.206	0.552	($p > 0.1$)
Fz position 6	0.538	2.538	($p > 0.05$)
Fz position 8	-0.955	6.503	($p > 0.01$)
RM position 2	0.734	-1.559	($p > 0.1$)
RM position 4	0.2	0.552	($p > 0.1$)
RM position 6	0.706	1.937	($p > 0.05$)
RM position 8	1.66	-3.698	($p > 0.01$)

et al[7] that is concerned with the development of memory trace. The Cowan's paradigm is suitable for investigating only the development of memory trace depending on the number of the standard stimuli, because the effect of the preceding train can be excluded. However, the design of this study is not the same as theirs. Cowan et al.[7] also found that no MMN was elicited when the repetitive standard stimuli were separated from the deviant by 11-15 sec. Böttcher-Gandor and Ullsperger[20] found that MMN was elicited even when the interstimulus interval was 10 sec. Winkler et al.[8] suggested that some kinds of acoustic stimuli induced reactivation of a memory trace even if the interstimulus interval was longer than 30 sec. In this experiment, there was time for over 45 sec until the same frequency stimulus was presented. In the result, no significant negativity at Fz (or positivity at RM) was observed with the 2nd position and the 4th position, as shown Table.1. In other words, MMN was not elicited when the deviant stimulus occurred as the 2nd stimulus after the standard stimuli, in accordance with the previous studies. Therefore, the experiment design seems to be appropriate for the strict investigation into the formation of memory trace.

The previous study has not paid attention to the latency of MMN. Moreover, no study has investigated in detail the latency of MMN in the roving-standard condition. Sams et al.[4] suggested an effect of the magnitude of stimulus deviance on the latency but not the amplitude of MMN. According to Novak,[21] when the task was difficult, the MMN latency increased. Näätänen et al.[1] concluded that the MMN latency is a more reliable correlate of the magnitude of frequency difference than the MMN amplitude, which may saturate at a moderate magnitude of stimulus deviation. However, the relation between the development of memory trace and the latency of MMN was not clarified in the previous studies. In this study, the latencies of both frontal and temporal MMN components were significantly shortened when the number of the standard stimuli preceding the deviant stimuli was increased. This result suggests that the MMN latency was shortened when the memory trace was developed.

MMN has both the temporal and the frontal generator. Rinne et al.[22] found in their MMN source current analysis that the frontal MMN generator was activated later than the temporal one. Furthermore, Sato et al.[17] reported that when the probability of standard stimuli was increased, the amplitude of frontal MMN was increased, while the temporal one was not changed. The difference between the frontal and the temporal MMN was found in the present study, in which the amplitude of the temporal MMN was enhanced and its latency was gradually shortened as the number of standard stimuli increased, while the amplitude of the frontal MMN was slightly larger and its latency was shorter only for the 8th position as the number of standard stimuli increased. These findings were different from Sato's finding. The development of memory trace was investigated by employing the condition of the increase of the preceding standard stimuli without the effect of the preceding train (that is, the present paradigm) and the condition of the increase of the standard-stimulus probability (that is, Sato's paradigm). However, Sato's paradigm had similarly investigated whether the sensory memory representation was accurately formed of incoming stimuli or the memory information was reactivated by the memory trace of the preceding stimulus train. We studied the development of memory trace without the effect of the preceding train. However, the frontal and temporal MMN component was significantly increased in amplitude in the present study. Therefore, we can speculate that the findings of the "Sato's" probability effect were affected by the preceding stimulus trains.

In this study, the amplitude of the frontal MMN was significantly enlarged when the number of the standard stimuli preceding the deviant stimuli was increased, in accordance with the finding of the previous studies. Then the amplitude in the temporal MMN was also significantly enlarged when the number of the standard stimuli preceding the deviant stimuli was increased. Moreover, the latencies of both MMN components were significantly shortened.

Consequently, the present study suggested that the transient memory trace was developed by the increase in the number of standard stimuli. These developments were reflected by the amplitudes and latencies of the frontal and temporal MMN components.

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