

## AUDITORY HABITUATION IS PREVENTED IN THE BACKGROUND SOUND OF 4-KHZ PURE TONE -A MAGNETOENCEPHALOGRAPHY STUDY-

TOSHIZO KOIZUMI, TADASHI NISHIMURA, SEIJI NAKAGAWA\* and HIROSHI HOSOI

*Department of Otorhinolaryngology and Head & Neck Surgery, Nara Medical University*

*\*Living Informatics Group, National Institute of Advanced Industrial Science and Technology (AIST)*

Received November 18, 2013

*Abstract* : Auditory evoked magnetic field (AEF) is gradually attenuated as the number of presentation of auditory stimuli increases. The attenuation of AEF is auditory habituation, and is prevented in the condition where a noise exists in the background. In this study, we investigated whether the background sound of pure tone prevent the auditory habituation to repeating stimuli. Subjects were 17 normal hearing individuals. Auditory stimuli were 1-kHz tone bursts set at 30 dB SL with durations of 100 ms and inter-stimulus intervals of 1.9-2.1 s. The background sounds were silent, 4-kHz pure tone presented set at 5 and 20 dB SL which were presented with 1-kHz tone bursts. N1m component of AEF induced by auditory stimuli was measured using 122-channel neuromagnetometer. As a result, N1m amplitudes induced by repeating auditory stimuli were gradually attenuated in the condition of silent background due to the auditory habituation. Meanwhile, the attenuation of N1m amplitude was small in the conditions of background sounds of 4-kHz pure tones at 5 and 20 dB SL, compared to the conditions of silent background. Moreover, the time course of N1m amplitudes was not different between the condition of background sound at 5 and 20 dB SL. These results suggested that the background sound of pure tone, independent of its intensity, drove the subject to unconsciously pay attention to repeating auditory stimuli without disturbing signal-to-noise ratio of them, or the neural process of the background pure tone continuously activated the auditory pathway and resulted in the prevention of auditory habituation.

---

**Key words** : auditory attention, auditory evoked magnetic field, magnetoencephalography, N1m

### INTRODUCTION

Event related potential (ERP) reflects the Neural activity in the cerebral cortex associated with specific perception, cognition, and psychological processes<sup>1-3)</sup>, and is influenced by habituation and attention to the stimulus<sup>1-9)</sup>. As the ERP induced by auditory stimuli, auditory evoked magnetic field (AEF) is often measured. Previous studied reported that

N1m components of AEF induced by repeating auditory stimuli with a brief duration were gradually attenuated in amplitude and increased in latency as the number of presentation of stimuli increased; This attenuation and increase were auditory habituation to repeating stimuli<sup>1-7</sup>. The conditions to occur the auditory habituation were related to the type of auditory stimulus<sup>10</sup>, the inter-stimulus interval (ISI)<sup>1,2,4,6</sup>, and the existence of background sound<sup>5,7-9,11</sup>. Previously, The attenuation of N1m induced by auditory stimuli was not remarkable in the condition where a noise existed in the background<sup>5,7,9,12</sup>. That is, the background sound of noise prevented the auditory habituation to repeating stimuli. Thus, we have the question whether the auditory habituation to repeating stimuli also occurs in the condition where a pure tone exists in the background. To clarify the question about auditory habituation, the time courses of N1m induced by repeating tone bursts were measured for normal hearing subjects in three conditions of background sound of pure tones. Thus, this study investigated the influence of background sound of pure tone on the auditory habituation to repeating stimuli.

## MATERIALS AND METHODS

The subjects were 17 normal hearing volunteers (4 females and 13 males, mean age 25.1 years) participated in this study. All subjects were right-handed.

This study used two kinds of sounds; tone burst as the auditory stimulus and the background sound of pure tone. The tone burst was 1-kHz pure tone with durations of 100ms including rise and fall ramps of 5 ms. The background sound was air-conducted 4-kHz pure tone.

Subjects were seated in a magnetically-shielded room and their thresholds (0 dB SL) of both 1-kHz tone bursts and 4-kHz pure tone were measured. Furthermore, thresholds of 1-kHz tone burst with background sound of 4-kHz pure tone set at 5 and 20 dB SL were respectively measured, and then the difference in the threshold of 1-kHz tone burst with and without background sound was measured.

In this study, auditory evoked magnetic fields (AEFs) induced by 1-kHz tone bursts was measured using 122-channels whole head neuromagnetometer (Neuromag-122; Neuromag Ltd., Helsinki, Finland). Fig. 1 shows the outline of presentation of 1-kHz tone bursts and background sound of 4-kHz pure tone. The intensity of 1-kHz tone burst was set at 30 dB SL, and its ISI was randomly set at  $2.0 \pm 0.1$  s. More than 600 tone bursts were presented in each of three conditions of background sound which was silent, or whose intensities of 4-kHz pure tone were set at 5 or 20 dB SL. The order of the three condition of background sound was randomized: The background sounds were presented five minutes before the measurement of AEFs. All subjects were measured in all three conditions of background sound. The intervals of condition of background sound were set at more than five minutes. Total time of measurement in three condition of background sound was approximately 90 minutes. During the measurement, the subject watched a self-chosen movie in silent and was instructed to pay no attention to 1-kHz tone burst and background sound of 4-kHz pure tone. 1-kHz tone burst was generated by the software (0105, NF Co., Yokohama, Japan) and controlled to stimulate by the software on Macintosh PC (Psyscope, <http://psyscope.psy.cmu.edu/>). The background sound of 4-kHz pure tone was generated by a function generator (WF1946, NF Electronic Instruments Co.,

Yokohama, Japan). Both 1-kHz tone bursts and 4-kHz pure tone were controlled logarithmically in its intensity using the dB scale through an attenuator (PA5, Tucker Davis Technologies, Gainesville, FL, USA) and delivered to the left ear of subject by an earphone (E-A-R TONE 3A, Cabot Safety Co., Indianapolis, IN, USA) through a plastic tube. An earplug was inserted into the right ear.

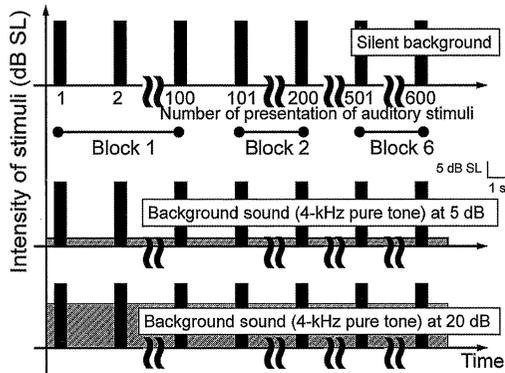


Fig. 1 : Outline of presentation of 1-kHz tone bursts and background sounds of 4-kHz pure tone  
 More than 600 tone bursts were presented in each of three conditions of background sound which was silent, 4-kHz pure tone set at the intensities of 5 and 20 dB SL. The intensity of 1-kHz tone burst was set at 30 dB SL, and its inter-stimulus intervals were randomly set at 1.9-2.1 s. The responses induced by 600 tone bursts were divided into 6 blocks of each 100 burst; Block 1, responses to tone burst 1-100, Block 2, responses to tone burst 101-200, ..., and Block 6, responses to tone burst 501-600.

The data of AEFs induced by 1-kHz tone bursts were recorded with sampling rates of 0.4-kHz after band-pass filtered between 0.03 and 100 Hz. The analysis time was 0.7 s from 0.2 s prior to the onset of 1-kHz tone burst. The average of 0.2 s pre-stimulus period served as the baseline. Any response coinciding with magnetic signal exceeding 3000 fT / cm was rejected from further analysis. In each condition of background sound, AEFs induced by 600 tone bursts were divided into 6 blocks according to the responses to every 100 tone bursts (Block 1, response to tone burst 1-100, Block 2, response to tone burst 101-200, ..., Block 6, response to tone burst 501-600) and averaged. The averaged AEFs were digitally band-pass filtered between 0.3 and 30 Hz. The neuromagnetometer has two pick-up coils in each position, which measure two tangential derivatives,  $\delta B_z / \delta x$  and  $\delta B_z / \delta y$ , of field component  $B_z$ .

$$\text{We determined; } B' = ((\delta B_z / \delta x)^2 + (\delta B_z / \delta y)^2)^{1/2}$$

The target of analysis was N1m component of AEF whose peak amplitude located at 80-130 ms after the onset of 1-kHz tone burst. We picked up the channel which showed the maximum N1m amplitude of  $B'$  in the right temporal area in each of three conditions of background sound and analyzed the peak N1m amplitude and its latency of  $B'$ . Fig. 2 shows the outline of procedures for analyzing N1m of  $B'$ .

To investigate the influence of background sound on initial response of N1m, the amplitudes and latencies of N1m at Block 1 were analyzed using one-way repeated-measure analysis of variance (ANOVA). Afterwards, the time course of N1m from Block 1 to Block 6 was analyzed. The data of N1m amplitude from Block 2 to Block 6 were normalized using the relative values to that at Block 1, because the data of N1m amplitude were distributed with large deviation among the subjects. In analysis of the N1m time course, two-way repeated-measure ANOVA was used with two factors of conditions of background sound (Silent vs. 5 dB SL vs. 20 dB

SL) and blocks (Block 1 vs. Block 2 vs. ... vs. Block 6). Moreover, Fisher's PLSD tests as post-hoc tests were used to measure the differences among the conditions of background sound (Silent vs. 5 dB SL, silent vs. 5 dB SL, or 5 dB SL vs. 20 dB SL). In all analyses,  $p < 0.05$  was considered statistically significant.

The procedure of this study was thoroughly explained to all subjects and written informed consent was obtained. This study was approved by the local ethics committee.

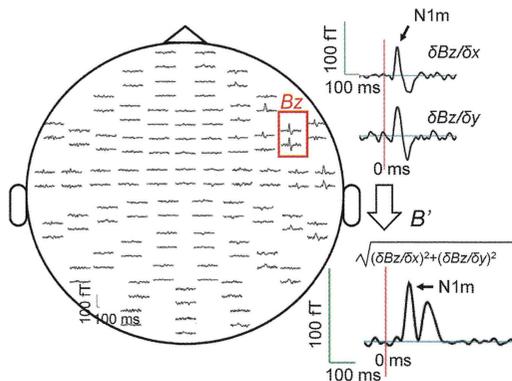


Fig. 2 : Outline of procedures for analyzing N1m  
Both 1-kHz tone bursts and background sound of 4-kHz pure tone were delivered to the left ear. The auditory evoked magnetic fields induced by 1-kHz tone bursts were measured using 122-channels neuromagnetometer. We picked up the channel of Bz which showed the maximum amplitude in the right temporal area in each of three conditions of background sound. The peak amplitude of N1m component and its latency of B' were analyzed. Vertical bars indicate the onset of 1-kHz tone bursts.

## RESULTS

In all subjects, the differences in the threshold of 1-kHz tone burst were within 3 dB among three conditions of background sound. In the analysis of N1m at Block 1, the amplitude (Silent,  $45.5 \pm 17.8$ , Background sound at 5 dB,  $40.0 \pm 19.1$ , Background sound at 20 dB,  $44.7 \pm 17.6$  fT) and the latencies (Silent,  $94.0 \pm 6.21$ , Background sound at 5 dB,  $94.1 \pm 6.29$ , Background sound at 20 dB,  $94.3 \pm 9.81$  ms) were not different among the three conditions of background sound. Thus, we confirmed that the background sound of 4-kHz pure tone had no influence on the perception of 1-kHz tone burst and initial response of N1m.

Figs. 3 show the result of N1m time course of the representative subject. In the condition of silent background, N1m amplitudes and latencies were gradually attenuated and extended as the number of presentation of auditory stimuli increased. The relative value of N1m amplitude at Block 6 was 0.261 (Fig. 3A). In the condition of background sound at 5 dB SL, the attenuation of N1m amplitude was small, and the relative value at Block 6 was 0.73 (Fig. 3B). In the condition of background sound at 20 dB SL, the relative value of N1m amplitude at Block 6 was 0.675 (Fig. 3C).

Figs. 3 : Time course of N1m of representative subject

(3A) The time course of N1m induced by repeating 1-kHz tone burst at Block 1–6 in the condition of silent background.

(3B) The time course of N1m in the condition of background sound of 4-kHz tone set at 5 dB SL

(3C) The time course of N1m in the condition of background sound of 4-kHz tone set at 20 dB SL

Vertically dotted lines indicate the onset of 1-kHz tone burst presentation.

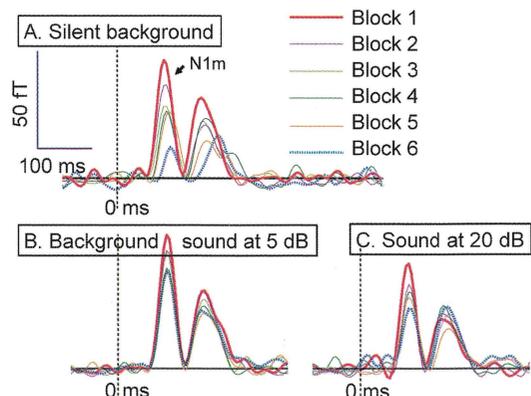


Fig. 4 shows the mean time courses of relative values of N1m amplitudes. No interaction was observed two factors of conditions of background sound  $\times$  blocks ( $F(10, 160) = 1.348$ , not significant). However, the factor of blocks involved a main effect ( $F(2, 32) = 29.932$ ,  $p < 0.001$ ); The N1m amplitudes were significantly attenuated as the number of presentation of auditory stimuli increased. Furthermore, the factor of conditions of background sound also involved a main effect ( $F(5, 80) = 3.800$ ,  $p < 0.05$ ); The time courses of N1m amplitude were significantly different among the conditions of background sound of 4-kHz pure tone. Post-hoc tests showed significant differences among the conditions of background sound (Silent vs. 5 dB SL,  $p < 0.05$ , silent vs. 20 dB SL,  $p < 0.05$ ). However, no difference was observed between the condition of background sound at 5 and 20 dB SL.

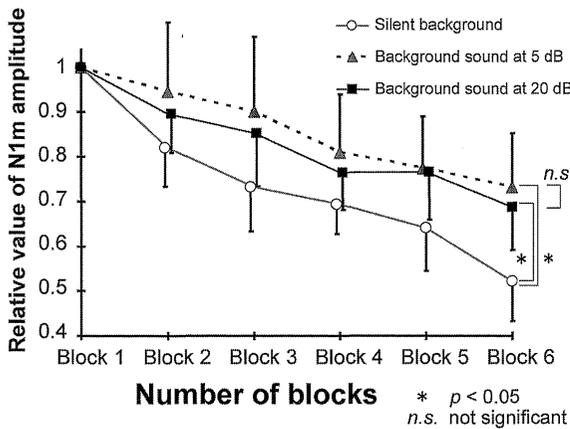


Fig. 4 : Time course of normalized N1m amplitude  
 The data of N1m amplitudes at Block 2-6 were normalized by using relative value to N1m amplitude at Block 1. Lines and error bars indicate mean and 95% confidence intervals, respectively.

Fig. 5 shows the mean time courses of N1m latencies. No interaction was observed between two factors of conditions of background sound  $\times$  blocks ( $F(10, 160) = 0.709$ , not significant). The factor of blocks involved a main effect ( $F(5, 80) = 5.308$ ,  $p < 0.05$ ); The N1m latencies were significantly extended as the number of presentation of auditory stimuli increased. However, the factor of conditions of background sound involved no main effect ( $F(5, 80) = 0.731$ , not significant); The time courses of N1m latency were not significantly different among the conditions of background sound.

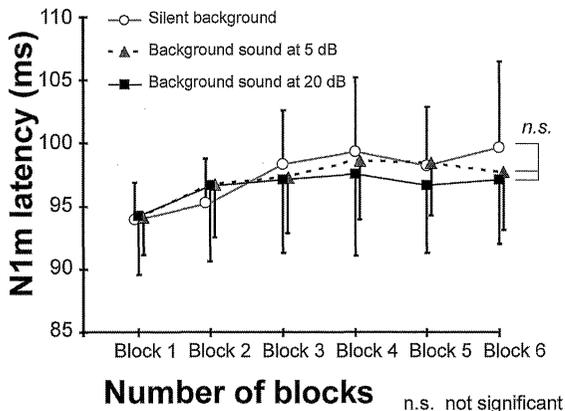


Fig. 5 : Time course of N1m latency  
 Lines and error bars indicate means and 95% confidence intervals, respectively.

## DISCUSSION

The amplitudes of N1m induced by repeating 1-kHz tone bursts were gradually attenuated as the number of presentation of auditory stimuli increased, especially in the condition of silent background. The latencies of N1m amplitude were also gradually extended. This time course of N1m might be the auditory habituation to repeating stimuli. The auditory habituation derives from the lateral inhibition of neural activity in the auditory pathway<sup>13,14</sup>, or refractoriness to the auditory stimulus<sup>2,4,6</sup>, or learning mechanism to ignore the auditory stimulus<sup>1</sup>. The conditions to occur the auditory habituation depend on that the type of auditory stimulus is monotonous<sup>10</sup>, that the ISI is sufficiently long<sup>1,2,4,6</sup>, and that background sound does not exist<sup>5,7,8,9,11</sup>. As for the type of auditory stimulus, the only 1-kHz tone bursts with 100 ms duration were monotonously presented in this study. Therefore, the type of auditory stimulus may facilitate to the auditory habituation. As for the ISI, the 1-kHz tone bursts were presented in the interval of about two seconds in this study. This ISI was shorter than 10 s enough to sufficiently occur the auditory habituation. However, it was considered that the auditory habituation observed in this study was not relevant to the refractoriness and lateral inhibition which were often observed in the ISI shorter than 1 s<sup>1,2,4,6</sup>. As for the background sound, remarkable attenuation of N1m amplitude was observed in the conditions of silent background, whereas the attenuation was small in the conditions of background sound of 4-kHz pure tone. These results suggested that the background sound of 4-kHz pure tone might prevent the auditory habituation to repeating 1-kHz tone bursts.

The time course of ERP such as N1m keeps high responses when the subject pays attention to the auditory stimulus<sup>5,7</sup>. If the subject continuously pays attentions to repeating auditory stimuli, the time course of N1m amplitude keeps high level without auditory habituation due to the bottom-up driven neural processing<sup>7,9</sup>. Therefore, the background sound of 4-kHz pure tone prevented auditory habituation to repeating 1-kHz tone bursts in this study because of the possibility that the background sound drove the subject to unconsciously pay attention to repeating auditory stimuli. That is, the simultaneous perception of the background sound of 4-kHz pure tone could increase involuntary attention of the subject to repeating auditory stimuli. Furthermore, it has been shown that in several psychophysical studies that cueing a tone with a tone of the same frequency facilitate the active detection of tone<sup>15,16</sup>. Therefore, the background sound of 4-kHz pure tone might facilitate to perceive 1-kHz tone bursts in this study.

The background sound of noise at large intensity decreases the signal-to-noise ratio (SNR) of auditory stimuli and result in the decline in the responses of AEF<sup>8,9,12,17</sup>. In this study, however, the raw data of N1m amplitude and latency at Block 1 were not different among the conditions of silent background and background 4-kHz pure tone at 5 and 20 dB. That is, the background sound of 4-kHz pure tone had no influence on initial response of N1m induced by 1-kHz tone bursts. The background sound of noise decreased the amplitude of N1m induced by repeating auditory stimuli compared to the silent background, while a habituation of N1m time course was not observed<sup>5,7,9</sup>. Although the background sound of noise decreases the SNR of auditory stimulus, the neural process of background sound of noise may activate the auditory pathway

and resulted in the prevention of auditory habituation<sup>57,11,18</sup>. In contrast, the background sound of 4-kHz pure tone did not disturb SNR of auditory stimuli in this study, because the frequency of background sound was sufficiently far from that of 1-kHz tone bursts. Actually, the background sound of 4-kHz pure tone did not influence on the initial responses of N1m at Block 1 to repeating auditory stimuli. These suggested that and the neural process of background sound of 4-kHz pure tone could continuously activated the auditory pathway and result in the prevention of auditory habituation.

No difference in the time course of N1m amplitude was observed between the conditions of background sounds at 5 and 20 dB SL. This suggested that background sound of 4-kHz pure tone could prevent the auditory habituation independent of its intensity.

## CONCLUSION

The amplitudes of N1m induced by repeating 1-kHz tone bursts were gradually attenuated in the condition of silent background. This attenuation seemed to be the auditory habituation to repeating stimuli. In contrast, the attenuation of N1m amplitude was small in the condition of background sound of 4-kHz pure tone, compared to the condition of silent background. This indicated that the background of 4-kHz pure tone sound prevent the auditory habituation. The background sound of 4-kHz pure tone probably drove the subject to unconsciously pay attention to repeating auditory stimuli without disturbing SNR of them. Furthermore, the neural process that the background sound of 4-kHz pure tone continuously activated the auditory pathway might result in the prevention of auditory habituation. In contrast, no difference in the time course of the N1m amplitude was observed between the conditions of background sounds at 5 and 20 dB SL. This suggested that background sound of 4-kHz pure tone might prevent the auditory habituation to repeating stimuli, independent of its intensity.

## REFERENCES

- 1) Thompson, R. F. and Spencer, W. A. : Habituation: a model phenomenon for the study of neuronal substrates of behavior. *Psychol. Rev.* **73** : 16-43, 1966.
- 2) Ritter, W., Vaughan, H. G. Jr. and Costa LD. : Orienting and habituation to auditory stimuli: a study of short term changes in average evoked responses. *Electroencephalogr. Clin. Neurophysiol.* **25** : 550-6, 1968.
- 3) Barry, R. J., Cocker, K. I., Anderson, J. W., Gordon, E. and Rennie, C. : Does the N100 evoked potential really habituate? Evidence from a paradigm appropriate to a clinical setting. *Int. J. Psychophysiol.* **13** : 9-16, 1992.
- 4) Budd, T. W., Barry, R. J., Gordon, E., Rennie, C. and Michie, P.T. : Decrement of the N1 auditory event-related potential with stimulus repetition: habituation vs. refractoriness. *Int. J. Psychophysiol.* **31** : 51-68, 1998.
- 5) Okamoto, H., Stracke, H., Wolters, C. H., Schmael, F. and Pantev, C. : Attention improves population-level frequency tuning in human auditory cortex. *J. Neurosci.* **27** : 10383-90, 2007.
- 6) Rosburg, T., Zimmerer, K. and Huonker, R. : Short-term habituation of auditory evoked potential and neuromagnetic field components in dependence of the interstimulus interval. *Exp. Brain Res.* **205** : 559-70, 2010.
- 7) Okamoto, H., Stracke, H., Lagemann, L. and Pantev, C. : Bottom-up driven involuntary auditory evoked field change: constant sound sequencing amplifies but does not sharpen neural activity. *J. Neurophysiol.* **103** : 244-9, 2010.

- 8) Lagemann, L., Okamoto, H., Teismann, H. and Pantev, C. : Bottom-up driven involuntary attention modulates auditory signal in noise processing. *BMC neurosci.* **11** : 156–62, 2010.
- 9) Lagemann, L., Okamoto, H., Teismann, H. and Pantev, C. : Involuntary monitoring of sound signals in noise is reflected in the human auditory evoked N1m response. *PLoS ONE* **7** : e31634, 2012.
- 10) Rosburg, T., Haueisen, J. and Sauer, H. : Habituation of the auditory evoked field component N100m and its dependence on stimulus duration. *Clin. Neurophysiol.* **113** : 421–8, 2002.
- 11) Okamoto, H., Stracke, H., Zwitterlood, P., Roberts, L.E. and Pantev, C. : Frequency specific modulation of population-level frequency tuning in human auditory cortex. *BMC Neurosci.* **10** : 1, 2009.
- 12) Hari, R. and Mäkelä, J. P. : Modification of neuromagnetic responses of the human auditory cortex by masking sounds. *Exp. Brain Res.* **71** : 87–92, 1988.
- 13) May, P., Tiitinen, H., Ilmoniemi, R. J., Nyman, G., Taylor, J. G. and Näätänen, R. : Frequency Change Detection in Human Auditory Cortex. *J. Comput. Neurosci.* **110** : 99–120, 1999.
- 14) Pantev, C., Okamoto, H., Ross, B., Stoll, W., Ciurlia-Guy, E., Kakigi, R. and Kubo, T. : Lateral inhibition and habituation of the human auditory cortex. *Eur. J. Neurosci.* **19** : 2337–44, 2004.
- 15) Hafter, E. R., Schlauch, R. S. and Tang, J. : Attending to auditory filters that were not stimulated directly. *J. Acoust. Soc. Am.* **94** : 743–7, 1993.
- 16) Hübner, R. and Hafter, E. R. : Cuing mechanisms in auditory signal detection. *Perception & psychophysics* **57** : 197–202, 1995.
- 17) Morita, T., Fujiki, N., Nagamine, T., Hiraumi, H., Naito, Y., Shibasaki, H. and Ito, J. : Effects of continuous masking noise on tone-evoked magnetic fields in humans. *Brain Res.* **1087** : 151–8, 2006.
- 18) Alain, C., Quan, J., McDonald, K. and Van, Roon, P. : Noise-induced increase in human auditory evoked neuromagnetic fields. *Eur. J. Neurosci.* **30** : 132–42, 2009.