Effects of Duration and Number of Onset/offsets in a Sound on Auditory Evoked Brain Magnetic Field

Seiji Nakagawa[1], Toshiaki Imada[2] and Shoogo Ueno[3]

[1]Life Electronics Laboratory, National Institute of Industrial Science and Technology (AIST), Midorigaoka, Ikeda, Osaka 563-8577, Japan

[2]Language Neuroimaging Laboratory, Center for Mind, Brain & Learning (CMBL), University of Washington, Seattle, WA 98195-7988, U.S.A.

[3]Department of Biomedical Engineering, Graduate School of Medicine, University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

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The effects of stimulus duration and numbers of onset/offsets in a stimulus on auditory-evoked brain magnetic fields (N1m) were examined. Trains of 0.2-ms clicks were used as auditory stimuli by changing the number of clicks and the click interval. Auditory brain magnetic fields evoked by the click-trains were recorded in 10 normal-hearing adult subjects with a whole-head neuromagnetometer. Equivalent current dipoles were estimated in both hemispheres at N1m peak latencies. Moments of equivalent current dipoles, i.e. N1m magnitudes, significantly increased with the stimulus duration, and leveled when the stimulus duration reached 32 ms. N1m latencies significantly decreased as the stimulus duration increased, and leveled at 16 ms. N1m magnitudes produced by the trains with the same number of clicks were larger in magnitude for 4-ms-interval than that for 1- and 8-ms-interval trains, and shorter in latency for 1-ms-interval than that for 4- and 8-ms-interval trains. These results indicate that all clicks received within 16-32 ms are integrated, and that this integration is affected by the click interval.

Keywords: stimulus duration, magnetoencephalography, auditory cortex

1. INTRODUCTION

Any abrupt sounds evoke electric and magnetic cortical responses with the most prominent deflection peaking at approximate 100 ms after the sound onset, i.e., electric N1 and magnetic N1m, respectively [1]. N1 and N1m are also elicited by sound offset or a change in the sound in a continuous auditory stimulus [1].

Many previous studies have shown various features of N1 and N1m. The source, the equivalent current dipole (ECD), of the N1m is perpendicular to the course of the Sylvian fissure and points toward the neck, thereby reflecting activation of the auditory cortex in the superior region of the temporal lobe [2, 3]. The generation site of the N1m is specific to the stimulus: it depends, for example, on the tone frequency, thereby indicating the tonotopic organization of the human auditory cortex [4]. The N1m source shifts from posterior to anterior and from superior to inferior in a latency window from 80 to 110 ms [5]. N1m evoked by contralateral stimuli is larger in amplitude and earlier in latency than that evoked by ipsilateral stimuli [6-8].

N1 and N1m also vary as functions of the stimulus parameters; intensity, rise time, interstimlus interval (ISI), and the stimuli sequence [1]. Stimulus duration also affected N1 and N1m. Rosburg et al. reported the stimulus duration affected the degree of dipole shift in anterior-posterior direction; the shift was found to be longer the longer the stimulus [9], while the degree of habituation of N1m were not affected [10]. Although N1 and N1m amplitudes increase as stimulus duration increase, they saturate at a certain duration. Onishi et al. investigated the effect of stimulus duration on N1-P2 amplitude [11], and reported that a longer plateau of 1 kHz sinusoids up to 30 ms can give a larger N1-P2 amplitude, and that stimulus intensity has no effect on the saturation point. Also, Gage et al. reported N1m amplitude increased with stimulus duration up to 40 ms irrespective of stimulus intensity [12]. Joutsiniemi et al. reported that the saturation point of N1m amplitude for noise bursts, 1 kHz sinusoids, and 1 kHz square-waves were identically 20 - 40 ms [13]. However, it is not clear whether these mechanisms depend on the stimulus duration or number of the onset/offsets in the stimulus. To

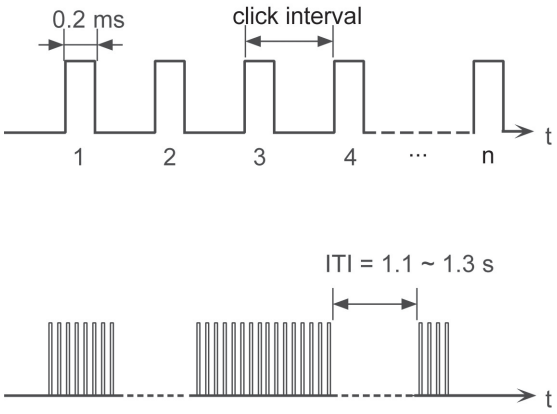

Fig. 1. Click-trains presented to subjects. (a) Individual click-train. The click interval and number of clicks were changed. (b) Stimuli sequence. Each kind of click-train was presented randomly and with equal presentation probability. ITI: Inter-train interval.

clarify the dependency of N1m increase and saturation mechanisms on stimulus parameters, we examined the effects of duration and the numbers of onset/offset in a stimulus on N1m magnitude (ECD moment) and latency.

2. MATERIALS AND METHODS

A. Stimuli

Trains of 0.2-ms clicks were used for auditory stimuli by changing the number of clicks and the click interval in a train (Fig. 1). The click interval was set to be constant at 1, 4 and 8 ms in sessions-1, -2 and -3 respectively, while the number of clicks in a train was selected randomly and with equal presentation probabilities. The number of clicks in the trains in each session are shown in Table 1. The three values; duration, click interval, and number of clicks in a train were connected by the following expression:

$$\text{Duration} = \text{Click interval} \times \text{Number of clicks} \qquad (1)$$

Table 1. The click intervals, numbers of clicks, and durations in click-trains in each session. 14 kinds of click-train were used in this experiment.

Session	Click interval (ms)	Number of clicks	Duration (ms)
1	1	2, 4, 8, 16, 32, 64	2, 4, 8, 16, 32, 64
2	4	2, 4, 8, 16, 24	8, 16, 32, 64, 96
3	8	2, 4, 8	16, 32, 64

The order of sessions was counterbalanced over subjects. Inter-train interval (ITI) was varied randomly between 1.1 and 1.3 s. With this setup, we obtained magnetic responses to all stimuli at the same measurement locations and during identical states of the subjects.

Stimuli were led to the subjects' left ear through a plastic tube and earpiece. The intensity of stimuli was 74 dB SPL at the earpiece, with a frequency spectrum quite evenly distributed from 50 to 6,000 Hz by a digital sound equalizer (DEQ5, YAMAHA Corp., Hamamatsu, Japan).

B. Subjects

Ten adult subjects (5 laboratory staffs and 5 volunteers, 22-34 years old, 7 male, right-handed) with normal hearing were enrolled in the study. During recording, the subjects sat in a chair with their bodies fixed in a vacuum-cast. The subjects were instructed to read a self-selected book and to pay no attention to the stimuli during recordings.

C. Measurements

Recordings of auditory evoked brain magnetic responses were carried out in a magnetically shielded room using a 122 channel whole-head DC superconducting quantum interference device (DC-SQUID) magnetometer (Neuromag-122™; Neuromag Ltd., Helsinki, Finland) [14]. The vertical electrooculogram (EOG) was recorded with infra- and supraorbital electrodes to monitor artifacts from eye blinks and movements.

D. Data Analyses

Magnetic data were sampled at 497 Hz after being band-pass-filtered between 0.03 and 100 Hz, and then averaged more than 100 times for each kind of click-train. Any responses coinciding with magnetic signals exceeding 3,000 fT/cm and/or a vertical EOG deflection beyond 150 μV were rejected from further analysis. The averaged responses were digitally low-pass-filtered at 40 Hz. The analysis time was 1.0 s from 0.2 s prior to the stimulus onset. An average 0.2 s pre-stimulus period served as the baseline.

Neuromag-122™ has two pick-up coils in each position, which measure two tangential derivatives, $\partial B_z/\partial x$ and $\partial B_z/\partial y$, of field component B_z [14]. We determined:

$$B' = \sqrt{(\partial B_z / \partial x)^2 + (\partial B_z / \partial y)^2} \qquad (2)$$

as the amplitude of the responses. In each subject, we

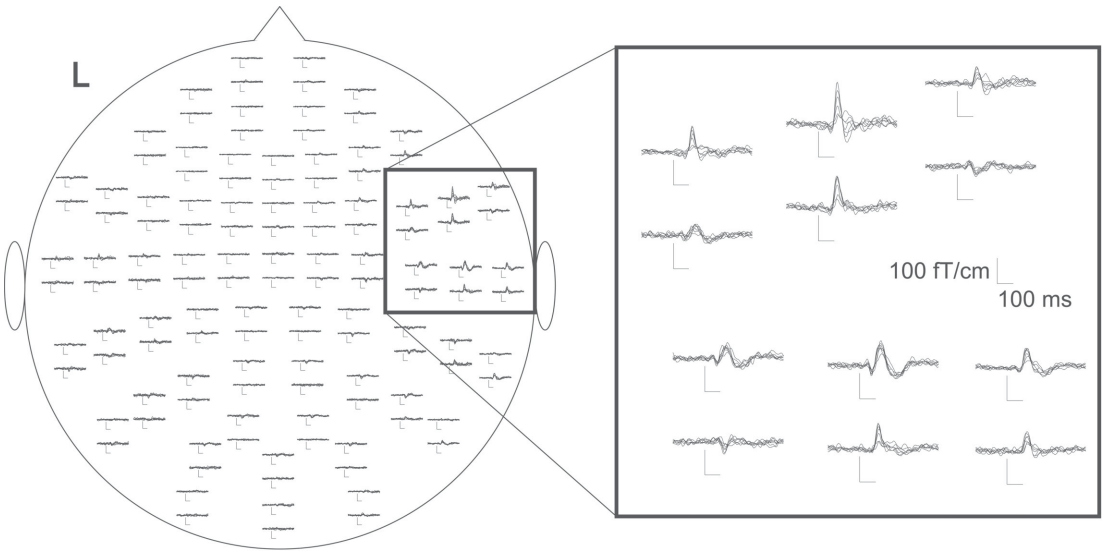

Fig. 2. Typical wave forms of brain magnetic fields from 122 channels (Subject S2, all waves recorded in session-1. N1m responses are clearly observed in both temporal regions. L: Left.

employed the N1m peak latency with a channel that showed the maximum amplitude placed over the right temporal area.

ECDs of N1m were estimated using a single-dipole model in each hemisphere at the N1m peak latencies. Calculations were based on the spherical conductor model, which takes into account the volume current within the sphere. The radius and the center of the sphere were determined by fitting a sphere onto the surface points on the cortex. N1m magnitudes, i.e. moments of ECDs were normalized within each subject with respect to the maximum value.

The total experimental noise, estimated from the standard errors of the means of the average responses, was 10 – 15 fT/cm. The 95 % confidence volumes for dipole locations were calculated according to the method described by Kaukoranta et al. [15].

3. RESULTS

Clear N1m responses were observed in both temporal regions in all subjects (Fig. 2). Figure 3 shows the response wave forms (B´) in a subject for all kinds of click-trains in each session, observed at the channel where the maximum N1m amplitude was observed. Basically, longer duration provided larger N1m amplitude.

Figure 4 shows a typical isocontour map and an estimated ECD overlaid on the subject's magnetic resonance image (MRI). All ECDs were localized in the superior temporal gyrus with a goodness-of-fit > 80 % and a 95 %-confidence volume < 2000 mm^3 [15]. Analysis of variance (ANOVA) showed no significant differences in ECD location among click-trains.

Figure 5 depicts the normalized mean N1m magnitudes (across 10 subjects) as a function of the number of clicks. ANOVA showed that the effect of the number of clicks was significant when the click interval was 1 ms ($P < 0.0001$), 4 ms ($P < 0.04$), and 8 ms ($P < 0.01$). The N1m magnitudes produced by the trains with the same number of clicks were significantly larger for the 4 ms click interval than the 1 ms and 8 ms click intervals ($P < 0.0003$). N1m magnitudes significantly increased as the number of clicks increased, but leveled at 32 clicks when the click interval was 1 ms, at 8 clicks when the click interval was 4 ms, and at 4 clicks when the click interval was 8 ms (by Wilcoxon signed-ranks test). The N1m magnitudes above the saturation point was smaller for the 8 ms-click interval than the 1 ms- and 4 ms-click intervals ($P < 0.01$), whereas no significant differences were observed between the 1 ms- and 4 ms-click intervals. Regression analysis applied to the data below saturation point obtained the following expressions:

$$\text{N1m magnitude} = 0.353 + 0.427 \times \log(\text{number of clicks}) \quad (3)$$
(click interval = 1 ms, $P < 0.0001$)

$$\text{N1m magnitude} = 0.356 + 0.588 \times \log(\text{number of clicks}) \quad (4)$$
(click interval = 4 ms, $P < 0.0001$)

$$\text{N1m magnitude} = 0.347 + 0.470 \times \log(\text{number of clicks}) \quad (5)$$
(click interval = 4 ms, $P < 0.0001$)

Figure 6 displays the mean N1m peak latency (across 10 subjects), as a function of the number of clicks. ANOVA showed that the effect of number of clicks was significant when the click interval was 1 ms ($P < 0.01$), and 4 ms ($P < 0.01$). The

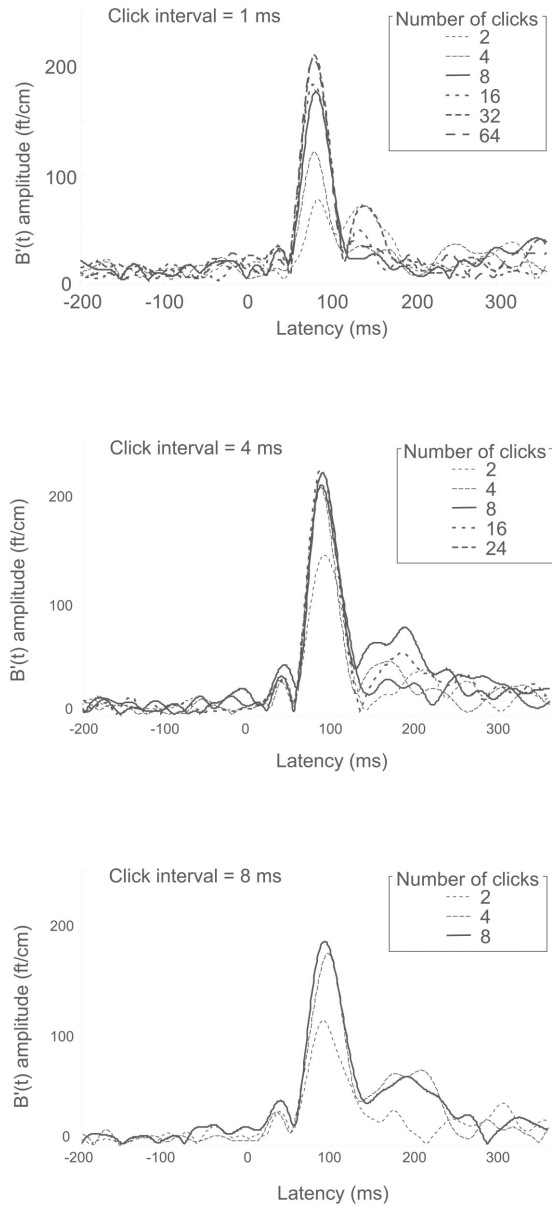

Fig. 3 Waveforms of brain magnetic fields (B´) observed in the right temporal region, evoked by each click-train in (a) session-1 (b) session-2, and (c) session-3.

number of clicks had no effect when the click interval was 8 ms. The N1m peak latencies produced by the trains with the same number of clicks were significantly larger for the 1 ms click interval than the 4 ms- and 8 ms-click intervals ($P < 0.001$). The N1m peak latency significantly decreased as the number of clicks increased, but leveled at 16 clicks when the click interval was 1 ms, and at 4 clicks when the click interval was 4 ms (by Wilcoxon signed-ranks test). The N1m latencies above the saturation point showed no significant differences among the 1 ms-, 4 ms-, and 8 ms-click intervals (1 ms-click interval: 94.5 ± 6.8 ms, 4 ms-click interval: 93.2 ± 4.0 ms, and 8 ms-click interval: 94.0 ± 5.1 ms). The following expressions were obtained by regression analyses applied to the data below saturation point:

$$\text{N1m peak latency} = 109.1 - 13.3 \times \log(\text{number of clicks}) \quad (6)$$
(click interval = 1 ms, $P < 0.01$)

$$\text{N1m peak latency} = 108.8 - 19.5 \times \log(\text{number of clicks}) \quad (7)$$
(click interval = 4 ms, $P < 0.01$)

4. DISCUSSION

The results of our experiments showed that N1m magnitude significantly increased as the number of clicks increased. N1m magnitude leveled at 32 clicks in session-1 (click interval = 1 ms), at 8 clicks in session-2 (click interval = 4 ms), and at 4 clicks in session-3 (click interval = 8 ms), i.e. N1m magnitude leveled off when the stimulus duration reached 32 ms.

N1m peak latency significantly decreased as the number of clicks increased, and leveled at 16 clicks in session-1, and at 4 clicks in session-2. In session-3, no significant difference was observed among 2-, 4-, and 8 clicks. These results suggest that N1m peak latency leveled at 16 ms stimulus duration.

These results agree with previous studies [11-13] and indicate that the increase/decrease and saturation mechanisms

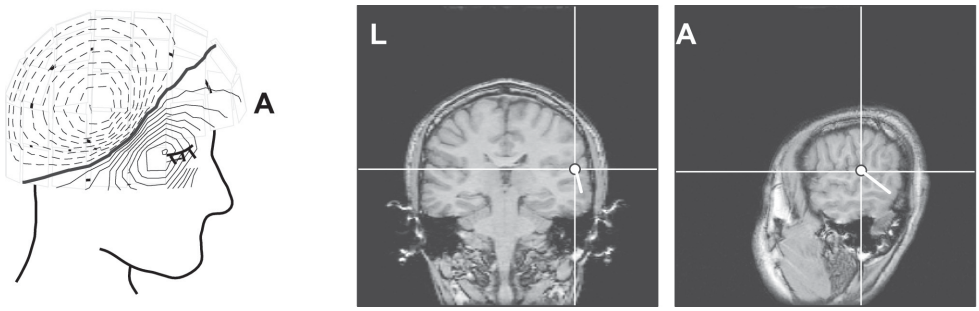

Fig 4. An isocontour map and a source location in subject S2, for session-1, number of clicks = 64. (a) A typical isocontour map. The dashed lines indicate flux into and the solid lines indicate flux out of the head. Contour step = 50 fT/cm. (b) An ECD overlaid on the subject's magnetic resonance image (MRI). L: Left, A: Anterior.

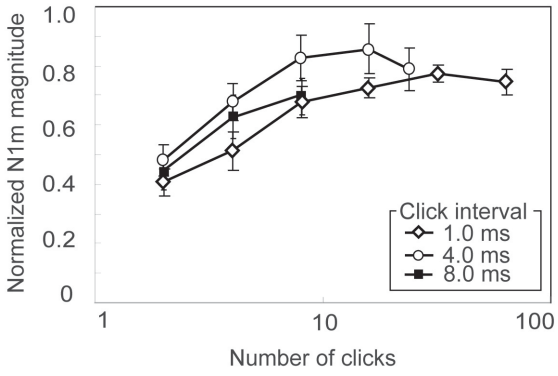

Fig. 5. Normalized mean N1m magnitude as a function of the number of clicks. The bars indicate the standard error of mean (SEM) used in this experiment.

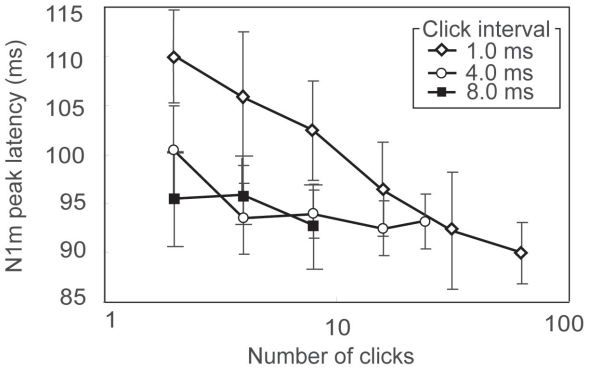

Fig. 6. Mean N1m peak latency as a function of the number of clicks. The bars indicate the standard error of the mean (SEM).

of the N1m magnitude/latency were dependent on stimulus duration, but not on number of onset/offsets in a stimulus. However, N1m magnitudes produced by the trains with the same number of clicks were larger in magnitude for 4-ms-interval than that for 1- and 8-ms-interval trains, and shorter in latency for 1-ms-interval than that for 4- and 8-ms-interval trains. Above the saturation point, the N1m magnitudes was smaller for the 8 ms-click interval than the 1 ms- and 4 ms-click intervals ($P < 0.01$), whereas no significant differences were observed between the 1 ms- and 4 ms-click intervals. It can be considered that all clicks received within 16-32 ms are integrated, and that this integration is affected by the click interval.

According to an earlier report, increases in stimulus duration up to about 60 ms can enhance loudness [16], and those up to about 200 ms can improve the threshold [17]. Evans considered that the auditory system was able to integrate energy up to about 200 ms [18]. Since Hecox et al. reported that the auditory brainstem responses were not affected by stimulus duration [19], it has been considered that some sort of temporal integration occurs in the central auditory system above the brainstem. Further, the importance of the cortical mechanisms in coding of stimulus durations is also emphasized by a report that lesions of the auditory cortex result in impaired detection of short (< 14 ms) sounds [20]. The current results, that the magnitude increases and latency decreases up to saturations at 16 - 32 ms, may roughly reflect the output of such an energy integrator. Whether duration specific cells, which were found in the frog thalamus [21], might also contributed to the recorded responses cannot be determined. Whatever the reason for it, this integration mechanism can be explained by increased synchrony of cells at the cortical level.

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