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Running head: Attention effect in the brainstem

Attention-related modulation of auditory brainstem responses during contralateral noise exposure

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Abstract

As determinants facilitating attention-related modulation of the auditory brainstem response (ABR), two experimental factors (i) auditory discrimination and (ii) contralateral masking intensity were examined. Tone pips at 80 dB SPL were exposed to the left ear via either single-tone exposures or oddball exposures, while a white noise was continuously delivered to the right ear with variable intensities (none to 80 dB SPL). Participants each conducted two tasks during the stimulation: either reading books (ignoring task) or detecting target tones (attentive task). Task-related modulation within the ABR range was found only during oddball exposures at contralateral masking intensities ≥ 60 dB. Attention-related modulation of the ABR thus can be detected reliably during auditory discrimination under contralateral masking with sufficient intensity.

Keywords: auditory brainstem response, attention, contralateral masking, white noise, corticofugal system

INTRODUCTION

Since the demonstration of peripheral attention effects in cats [1], the auditory efferent pathway, which departs from the auditory cortex and, through the brainstem, achieves outer hair cells in the cochlea, has been the possible basis for top-down neural activities in human audition [2-4]. This notion has been proved in the cochlear level via attention-related modulation of otoacoustic emissions [2,5,6]. In the brainstem level, however, most studies recording human event-related potentials (ERPs) have failed to verify attention-related modulation, except for the frequency following response (FFR) [7,8]. Given the functional anatomy of the auditory efferent pathway, therefore, revealing research conditions that enable attention effects on the auditory brainstem response (ABR) remains to be solved in humans.

Most researches that failed to detect attention-related modulation of the human ABR contain one of the two next features [9-14]: (i) they permitted simultaneous activation of both lateral brainstem pathways giving rise to interfering with the ABR amplitudes [15], i.e. either binaural stimulation or monaural stimulation without masking the untested ear adequately was used in the studies; (ii) they employed only single-tone exposures, i.e. discrimination between two auditory stimuli was not tested. Although few studies conducting auditory discrimination in binaural exposures obtained positive outcomes, their modulations of the ABR were inconsistent [16,17].

Considering the previous conditions (i) and (ii), the introduction of adequate monaural masking into auditory discrimination tasks would be expected to replicate

attention-related modulation of the ABR reliably. Supporting this, Ikeda and Hayashi [18] found attention-related modulation of scalp potentials (negative shift) within the ABR latency of waves IV-VII in response to monaural targets (intensity at 80 dB SPL), when participants executed auditory oddball tasks under continuous and contralateral masking (intensity at 60 dB SPL). Contrary to previous studies [16,17], Ikeda and Hayashi [18] found difficulty to identify attention effects within the ABR range during binaural stimulation without masking.

Based on the outcomes by Ikeda and Hayashi [18], we examined two working hypotheses in the present study: (i) attention-related modulation within the ABR range would occur at the intensity of contralateral masking that was sufficient to prevent interaural crosstalk elicited by ipsilateral stimuli; (ii) auditory oddball but not single-tone procedures would establish attention-related modulation within the ABR range. The assumption (i) added to the replication of Ikeda and Hayashi [18] was tested in Experiments 1 and 2, and the assumption (ii) was scrutinized in Experiment 2.

METHODS

Participants

Participants were 24 healthy-hearing and right-handed adults. Twelve of them (6 males) participated in Experiment 1, and the other 12 (6 males) in Experiment 2. All participants signed informed consent for the research. Their mean age was 21.7 ±5.7 years in Experiment 1 and 19.2 ±1.5 years in Experiment 2. All participants exhibited behavioral thresholds of hearing at 15 dB HL or less for both ears at conventional audiometric frequencies of 0.5, 1, 2, 4 and 8 kHz. Participant's handedness was assessed by the Edinburgh

inventory [19]. In an electrically shielded room both the audiometry testing and electrophysiological recording were completed.

Auditory Stimuli

Tone pips of 10-ms duration (5-ms ramps without plateau), which were identical to the previous study [18], were delivered at a peak intensity of 80 dB SPL. Stimuli were produced by a stimulator (Nihon Kohden SMP-4100) and then presented through headphones (Elega DR-531) at a stimulation rate of 3 Hz. The polarity of stimuli was alternated across trials for preventing the emergence of cochlear microphonics or the FFR. The left ear was stimulated with tone pips while the right ear continuously received a white noise (20-8000 Hz) at variable intensities, i.e. without exposure, at 40, 60 or 80 dB SPL.

Procedure

Experiment 1: For maintaining participant's vigilance, all procedures were conducted in time slots of 9:00-13:00. Participants were given target (1 kHz and p = 0.3) and non-target (0.5 kHz) tones. Because target probability was set strictly, two targets sometimes emerged in succession. Relying on the white noise intensity, Experiment 1 had three conditions (i.e. without exposure, at 40 or 80 dB SPL). In each condition two experimental tasks, either reading books (ignoring task) or pressing a button with the right thumb if participants with eyes open identified targets (attentive task), were executed. A rest period of at least 3 minutes between tasks was taken for avoiding adaptation effects. Added to this, a rest interval for a few minutes was inserted at trisection points of the attentive task. The order of 3 conditions × 2 tasks

was distributed across participants by a Latin square design.

Experiment 2: All procedures in Experiment 2 were identical to those in Experiment 1 except for the followings. In one condition among three, only a single tone (1 kHz) was exposed as targets with the white noise intensity at 60 dB SPL. In the other two conditions, an oddball procedure equivalent to Experiment 1 (i.e. 1-kHz targets and 0.5-kHz non-targets) was employed with the white noise intensity at either 60 or 80 dB SPL. As attentive task in each condition, participants were required to mentally count the number of targets with eyes open.

Physiological Recordings

Electrodes (Ag/AgCl) for recording scalp potentials were placed at the vertex (Cz) with reference to the left or right earlobes (A1 or A2), and at the forehead assigned to the ground electrode (all impedance between electrodes < 5 kΩ). Amplification of potentials (gain = 20 k) was implemented via an amplifier (Dia Medical System DPA-2008) with band pass of 16-3000 Hz (-6 and -12 dB/octave for high- and low-pass filters, respectively). The high-pass frequency was adopted for measuring the ABR to low-frequency tones (e.g. 0.5 kHz) and the middle-latency potentials relevantly [20]. Using a personal computer with a 16-bit converter and commercially available software, the potentials were digitized at a sampling rate of 10 kHz and were averaged over 1000 epochs for targets and 2000 for non-targets. An exception was the single-tone condition in Experiment 2 for which 2000 epochs were averaged. The analysis windows were 22 ms and 52 ms including a 2-ms pre-stimulus baseline for Experiments 1 and 2, respectively. Trials with voltages exceeding ±15 μV were excluded from the averaging.

Data Analysis

Time intervals of potentials revealing task-related effects were assessed by a repeated two-way (ignoring and attentive tasks × Cz-A1 and Cz-A2 derivations) analysis of variance (ANOVA). The dependent variable for each participant comprised mean amplitudes in 0.5-ms time bins within the analysis windows starting at stimulus onset. Post-hoc multiple comparisons were performed using the Bonferroni method. A statistical significance was defined as a probability < 0.05. Added to this, task-related differences for peak amplitudes and latencies of a wave IV-V complex were analyzed by the same ANOVA. This component was specified as the highest positive peak within an interval of 6.5-9.5 ms.

RESULTS

Experiment 1

Grand-average waveforms elicited by targets (1 kHz) and non-targets (0.5 kHz) are shown in Figs. 1 and 2, respectively. For both stimuli mean amplitudes revealing significant task-related effects were restricted to the condition with masking at 80 dB. Main task effects (ignoring < attentive) for targets were found at intervals of 4.0-4.5 ms (within latency of wave II), 5.0-5.5 ms (wave III), 6.0-6.5 ms (wave IV), 7.0-7.5 ms (wave V) and 8.0-8.5 ms (wave VI) as shown in Fig. 1, bottom ($ps < 0.05$). Significant interactions for targets at an interval of 14.5-17.0 ms (within latency of Po) resulted in "ignoring < attentive" at Cz-A2 derivation ($ps < 0.05$).

Opposite to targets, the direction of main task effects for non-targets were "ignoring > attentive" at intervals of 7.5-8.0 ms (within latency of wave V) and 8.5-10.0 ms (waves VI-VII) as indicated in Fig. 2, bottom ($ps < 0.05$). Significant interactions

for non-targets at an interval of 8.0-10.5 ms (within latency of waves VI-VII) gave rise to "ignoring > attentive" at Cz-A2 derivation (*ps* < 0.04).

Any task-related effects for wave IV-V complex measures were insignificant although the peak amplitudes for both targets and non-targets at 80-dB masking approached to significance (Table 1).

Experiment 2

Figures 3 and 4 demonstrate grand-average waveforms in response to targets and non-targets, respectively. Significant task-related effects in mean amplitudes within the ABR latency were limited to oddball procedures with masking at 80 dB. Among outcomes provoked by targets, main task effects in the single-tone condition (ignoring < attentive) were detected for the latency corresponding to Pa component (at 27.5-28.0 and 28.5-36.0 ms, *ps* < 0.05) as shown in Fig. 3, top. In the oddball condition with 60-dB masking (Fig. 3, middle) the latency corresponding to Nb component (at 41.0-43.0 and 44.0-45.0 ms) revealed main task effects for targets (ignoring > attentive, *ps* < 0.05), although the main effects within the ABR range approached to significance (*ps* < 0.10) at 4.5-5.0 (wave II), 5.5-6.0 (wave III) and 9.5-11.0 ms (wave VII). Figure 3 bottom reveals the oddball condition with 80-dB masking in which main task effects for targets (ignoring < attentive) emerged at intervals corresponding to Pa component (at 31.0-34.0 and 35.0-36.0 ms, *ps* < 0.05). Significant interactions for targets in this condition were obtained at latencies of 7.0-8.5 (waves V-VI) and 10.5-11.0 ms (an interval following wave VII) leading to "ignoring < attentive" at Cz-A2 derivation (*ps* < 0.05).

In response to non-targets at 60-dB masking condition, none

of task-related significance was observed within the ABR range (Fig. 4, top). Main task effects in this condition were "ignoring < attentive" at latencies of Pa component (at 29.5-30.0 and 31.0-31.5 ms, *ps* < 0.05). Significant task effects within the ABR range for non-targets existed in 80-dB masking condition (Fig. 4, bottom). Significant intervals were 1.5-3.0 (an interval preceding wave I), 3.5-16.0 (wave I to Po component), 22.0-22.5 (Na component) and 27.5-28.0 ms (Pa component), all of which exhibited "ignoring > attentive" (*ps* < 0.05).

Task-related effects for wave IV-V complex measures were detected in peak amplitudes for non-targets at 80-dB masking and in peak latencies for targets at 60-dB masking (Table 1). Other task-related effects in peak measures were all *ps* > 0.10.

DISCUSSION

The present outcomes support the two working hypotheses raised in the Introduction. Consistent with the assumption (i), contralateral masking at the intensity of 60-80 dB revealed attention-related modulation in mean amplitudes within the ABR latency if recognizing statistics of *p* < 0.10 (Figs. 1-4). The assumption (ii) can be corroborated since the main task effects within the ABR range for targets approached to significance only when auditory discrimination was conducted (Fig. 3).

According to the assumption (i) the effects of contralateral masking intensity > 40 dB related to the ABR modulation can be explained by the next idea. Presuming interaural attenuation at 50 dB [21], ipsilateral tones delivered at 80 dB arrive the contralateral ear at the intensity of 30 dB. Since masking effects of white noise are 20-30 dB weaker than those of narrow band noise

[21], contralateral masking in the present case might be effective at the intensity of 50-60 dB or greater. In another explanation the effects of contralateral masking intensity are attributable to efferent effects by contralateral stimulation, i.e. stimulating the contralateral ear activates the olivocochlear pathway to the other ear [22,23]. This interprets the ABR modulation as arising from the interaction of corticofugal attention effects with the olivocochlear activity due to contralateral sounds.

The assumption (ii) might suggest some selective filter specific to auditory discrimination in the brainstem. Based on this view the 80-dB masking conditions in the present study are of interest since significant task effects within the ABR range in the conditions exhibited opposite directions between responses to targets and non-targets (Figs. 1-4, bottom). An evidence compatible with the present outcomes can be found in neurophysiological studies for bats, where cortical stimulation of neurons tuned to specific frequencies facilitates activities for subcortical neurons (at the inferior colliculus and medial geniculate body) having the same or near best frequencies, whereas the same procedure inhibits the subcortical neurons having best frequencies remote from the above [4].

If corticofugal mechanisms in humans possess analogous properties to those in bats, task-related differences in response to non-targets (ignoring > attentive) found in the 80-dB masking conditions might show subcortical inhibition to auditory signals. At the same time, the equivalent direction of the ABR differences in response to targets during the 60-dB masking condition was detected in the previous [18] and present (Fig. 3, middle) studies.

This suggests the possibility that negative potential shifts within the ABR latency during auditory discrimination might not be restricted to representing subcortical inhibition. Comparing task-related differences in the ABR modulation between the 60- and 80-dB masking conditions, the direction of those differences seems to be influenced by contralateral masking intensity.

In a model of human auditory processing [24] passive and active attention are managed by two independent functional modes, respectively. Among them, task-dependent sensory analysis establishing active attention well matches with the research procedures in this study. Concurrent with previous ERP studies using dichotic listening paradigms [8,25], attention-related modulation of the middle-latency components Pa or Nb was consistently seen in Experiment 2 (Figs. 3 and 4). A novel finding in the current research was that the task-related modulation of Pa component occurred in single-tone procedures while the ABR modulation was limited to oddball exposures (Fig. 3). Compared to mean amplitudes the sensitivity for task-related effects in peak measures seemed to be low (Table 1), supporting the inference that attention-related modulation in the ABR might be distinguished from the basic ABR components [18]. In Ikeda and Hayashi [18] significant task-related effects of the ABR during the 60-dB masking condition were identified from Cz-A1 derivation for targets. Since main task effects independent of derivations were frequently seen in the present two-way ANOVA, the attention-related ABR modulation is considered basically common to both Cz-A1 and Cz-A2 derivations.

CONCLUSION

The auditory efferent pathways in humans can be a foundation for

attention-related activities in the auditory brainstem, whereas most researches have failed to identify attention-related modulation of the ABR. The present study shows that fulfilling simultaneously two conditions, i.e. (i) auditory discrimination and (ii) contralateral masking with sufficient intensity, can facilitate to detect attention-related modulation of the human ABR.

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Table 1

Significant task-related effects for peak amplitude and latency of a wave IV-V complex assessed by a two-way ANOVA (task × derivation)

Measure	Stimulus	Mask (dB SPL)	Direction	$F(1,11)$	$p <$
Experiment 1					
Amplitude	Target	80	Ignore < Attend	4.55	0.06
	Non-target	80	Ignore > Attend	3.95	0.08
Experiment 2					
Amplitude	Non-target	80	Ignore > Attend	9.12	0.02
Latency	Target	60	Ignore > Attend	5.08	0.05

Note. None of interactions in the ANOVA was significant.

Figure Captions

Fig. 1. Grand-average waveforms for targets (1-kHz tone) in an oddball procedure without masking (top), with contralateral masking at 40 dB SPL (middle) and at 80 dB SPL (bottom). From left to right, the vertex-left earlobe (Cz-A1) and vertex-right earlobe (Cz-A2) derivations. Broken lines, ignoring task; solid lines, attentive task. Upper rectangles, main task effects in ANOVA; lower rectangles, interactions of task × derivation in ANOVA. Filled rectangles, intervals representing task-differences of $ps < 0.05$ within one condition; open rectangles, those of $ps < 0.10$.

Fig. 2. Grand-average waveforms for non-targets (0.5-kHz tone) in an oddball procedure without masking (top), with contralateral masking at 40 dB SPL (middle) and at 80 dB SPL (bottom). Other details are the same as in Fig. 1.

Fig. 3. Grand-average waveforms for targets in single-tone exposures with contralateral masking at 60 dB SPL (top), in oddball exposures with the same masking at 60 dB SPL (middle) and at 80 dB SPL (bottom). Other details are the same as in Fig. 1.

Fig. 4. Grand-average waveforms for non-targets in an oddball procedure with contralateral masking at 60 dB SPL (top) and at 80 dB SPL (bottom). Other details are the same as in Fig. 2.

Fig. 1.

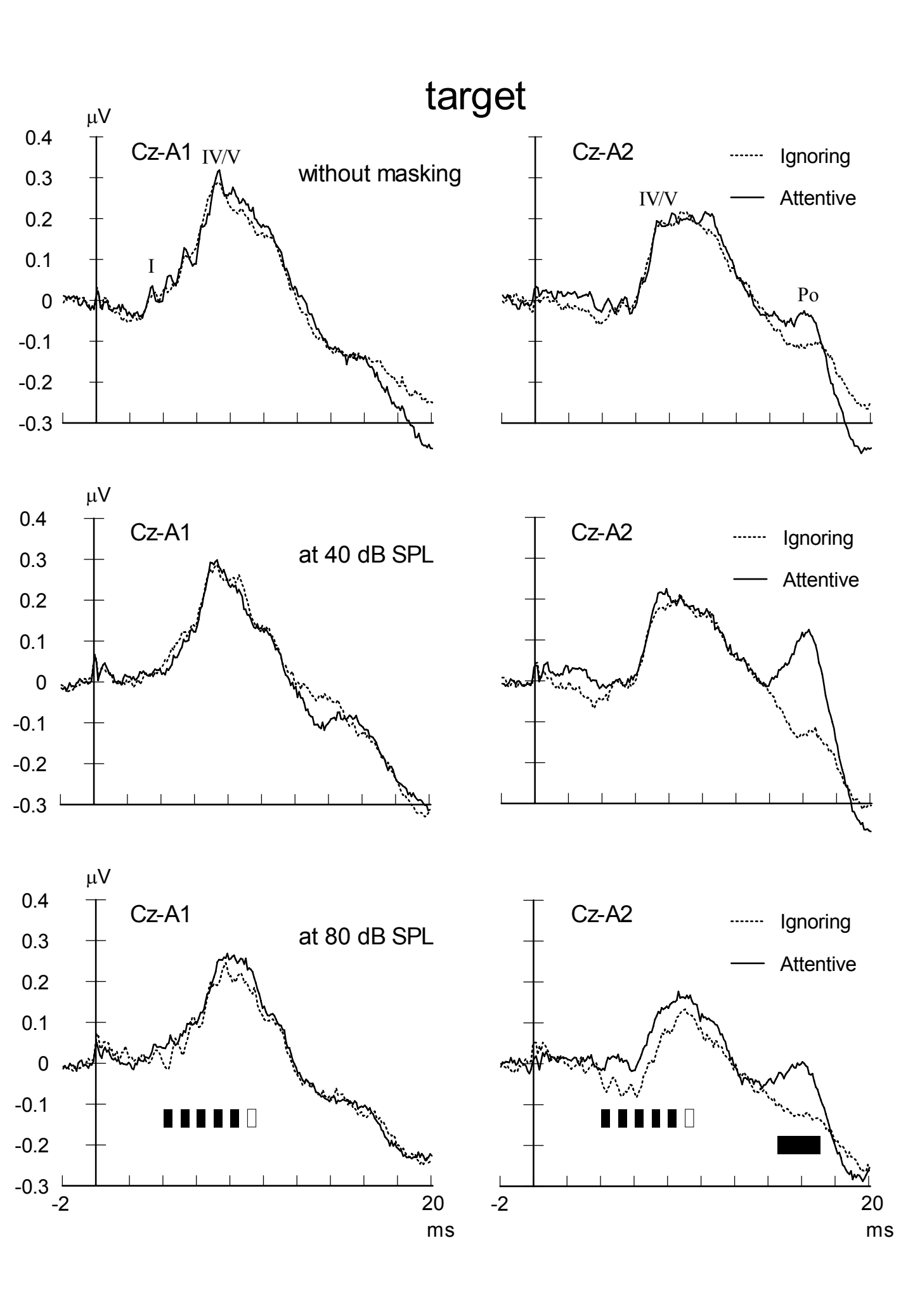
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Fig. 2.

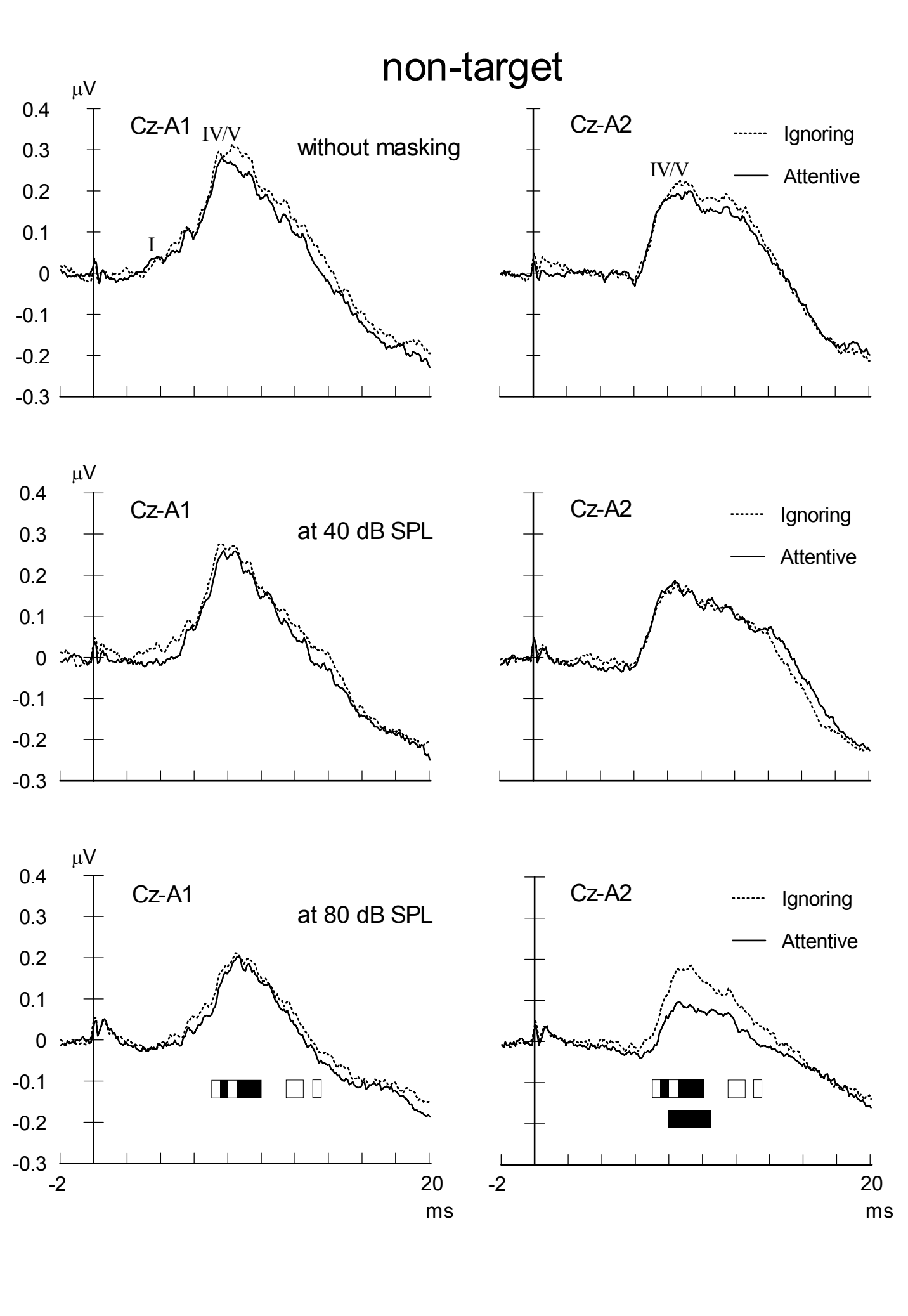
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Fig. 3.

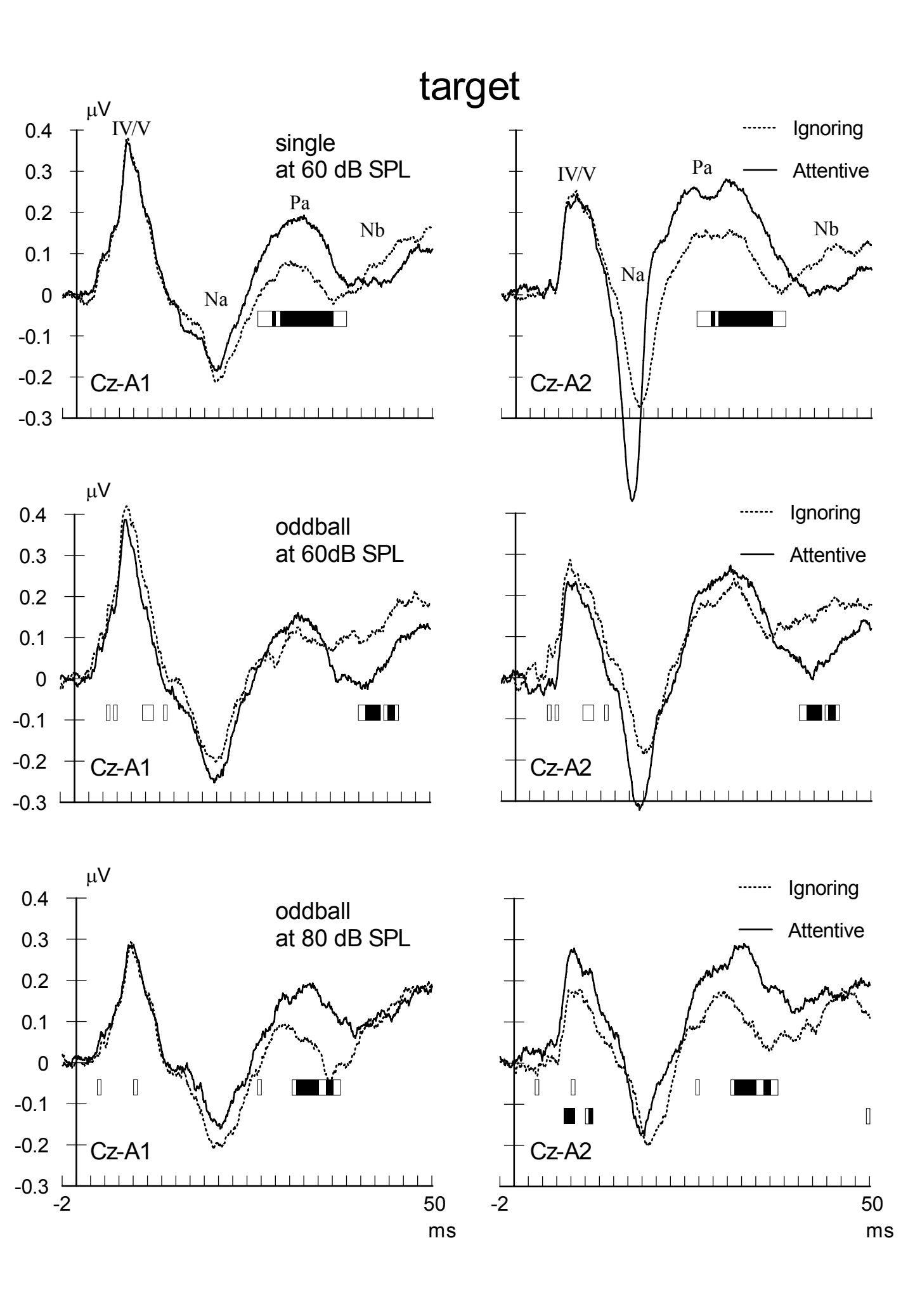
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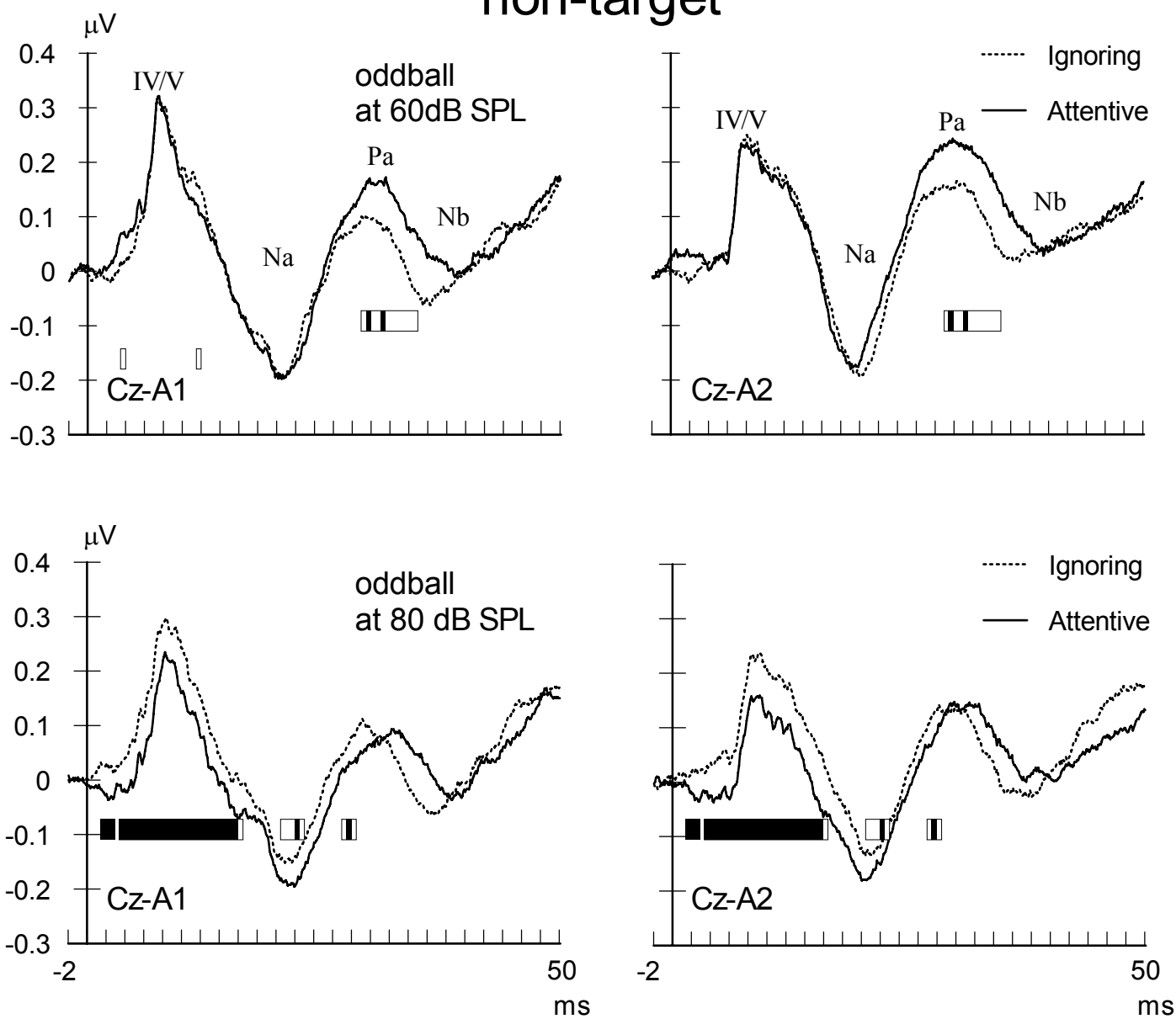
Fig. 4.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