



Auditory M50 and M100 responses to broadband noise: functional implications

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The functional significance of the M50 and M100 auditory evoked fields remains unclear. Here we report auditory evoked field data from three different studies employing wide-band noise stimuli. We find that, for the same stimuli, the strength of the M100, as well as its lateralization, are task-modulated. The M50, in contrast, shows three properties: It is dramatically more pronounced for noise

stimuli than for pure tones, does not seem to be task dependent, and, is significantly stronger in the left hemisphere in all task conditions. These contrasting patterns of activation shed light on the properties of the response-generating mechanisms and suggest roles in the process of auditory figure-ground segregation. *NeuroReport* 15:000–000 © 2004 Lippincott Williams & Wilkins.

Key words: Auditory evoked response; Lateralization; M50; M100; MEG; NIm; Primary auditory cortex

INTRODUCTION

Electrophysiological tools such as MEG and EEG expose the sequence and relative timing of the cortical systems processing a stimulus, and their relationship to perception. The earliest auditory evoked responses in auditory cortex (AC) peak near 20, 30 and 50 ms. These responses are followed by a deflection at about 100 ms (M100/N1m) which, because of its prominence and robustness across listeners and stimuli has been the most investigated auditory response [1,2]. The source of the M100 response is localized to planum temporale [4]. A growing body of research reveals that its amplitude and latency vary with certain physical and temporal aspects of stimuli [1,2]. Investigations of the M100 typically employ clicks, tones, or speech stimuli, which almost always elicit the response, leading to a commonly held hypothesis that the M100 reflects the process of detecting changes in sensory input, although the underlying mechanisms remain ambiguous. Specifically, it is not clear why an onset detector would operate so late (100 ms post-onset) in the processing stream.

The functional significance of the earlier and smaller M50 peak, believed to originate in or near the primary auditory cortex (PAC) [5,6], is even more obscure. A recent study found it to activate the antero-lateral portion of Heschl's gyri and Heschl's sulcus [3]. This might reflect activity in the human counterpart of the anterior areas in the core line region or in the antero-lateral belt region described in monkey [7]. The M50 response plays an important role in the investigation of the PAC [8] and early auditory system maturation [9] in humans, and is implicated in neurological disorders such as schizophrenia [10,11]. Apart from their differing cortical locations, there is evidence that M100 and M50 are parts of different systems: the M50 does not exhibit

ear-of-stimulation effects [5], dependence on interaural time differences [6] or contralateral masking effects [12].

Here we report on the auditory evoked responses to wide-band noise stimuli (more natural than pure tones since most natural sounds are wide-band), in three experimental settings. We characterize new noise response types and discuss their significance to the functional role of the M50 and M100 auditory evoked fields.

MATERIALS AND METHODS

Subjects: Twenty, 16 and 7 paid subjects participated in Experiments 1, 2 and 3, respectively. All were right handed [13], reported normal hearing and no history of neurological disorder. The procedures were approved by the University of Maryland institutional review board and written informed consent was obtained from each participant.

Stimuli: Experiments 1 and 2 were part of a study investigating the detection of tonal objects in noise [14]. The stimuli were 1500 ms long: 1000 ms of interaurally correlated white noise (N_1 ; diotic stimuli) followed by a 500 ms tonal object embedded in noise or by 500 ms of the same correlated noise (control condition). The stimuli of Experiment 2 were identical to those of Experiment 1 except that the initial noise was interaurally uncorrelated (N_0 ; statistically independent signals). The stimuli in Experiment 3 were 400 ms long white noise. In order to create a perceptually diverse stimulus set, five different interaural correlations were used: correlated (correlation value $r=1$; N_1), uncorrelated ($r=0$; N_0), partially correlated ($r=0.5$; $N_{0.5}$), anti-correlated ($r=-1$; N_{-1}) and partially anti-correlated ($r=-0.5$; $N_{-0.5}$) noise. A target stimulus (not

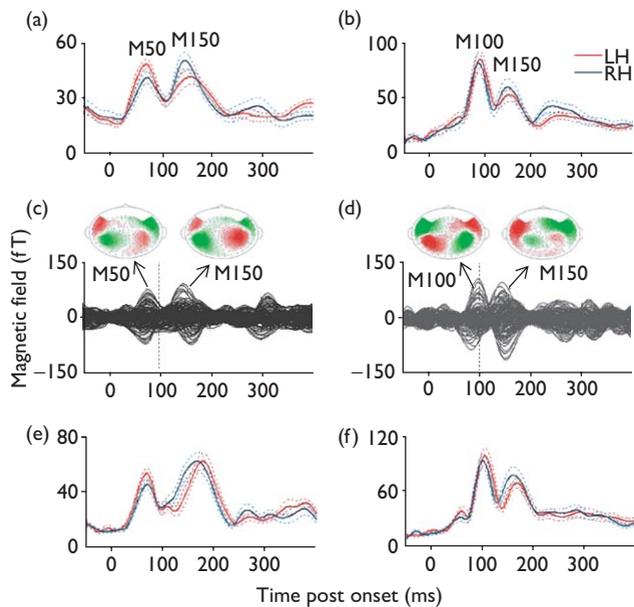


Fig. 1. Summary of the data from Experiments 1 and 2 (dotted lines are 1 standard error, derived by bootstrap). (a) Experiment 1: Auditory evoked response to N_1 in the left and right hemispheres (red and blue respectively). (b) Responses to 1 kHz tones for the same subjects as in (a). (c) Contour maps for a representative subject at the critical times for N_1 in Experiment 1 (10 fT/iso-contour; source=red, sink=green). Plotted is an overlay of the peristimulus waveforms of all 156 channels. (d) Contour maps from the same subject as in (c) at the critical times for pure tone stimuli in Experiment 1. (e) Experiment 2: Responses to N_0 in the left and right hemispheres. (f) Responses to 1 kHz tones for the same subjects as in (e). The higher amplitudes of the M50 and M150 in Experiment 2 over Experiment 1 are due to the overall stronger responses in Experiment 2, as evident from the amplitudes of the responses to tones in Experiment 1 vs 2. Note the scale differences in the plots.

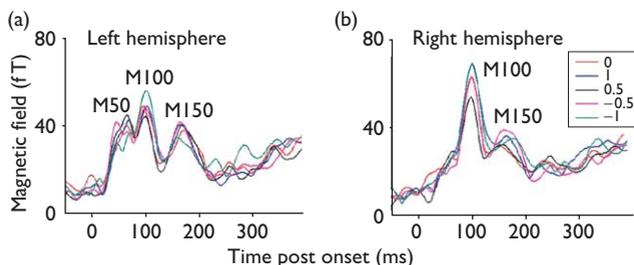


Fig. 2. Summary of the data from Experiment 3. Responses for all tested noise conditions in the LH (a) and RH (b). The response is characterized by a three-peaked (M50, M100 and M150) noise onset response. The M50 response is attenuated in the right hemisphere.

analyzed), which was one of the same stimuli modulated sinusoidally, appeared in 25% of the trials. The signals were created by choosing Gaussian distributed numbers (sampling frequency 16 kHz, bandwidth 8 kHz). The partial interaural correlations used the method described earlier [15]. To reduce dependency on a specific instance of the noise signal, four different instantiations were used in Experiments 1 and 2, and 10 in Experiment 3. The stimuli were gated on and off with 15 ms cosine-squared ramps. The signals (~75 dB SPL) were delivered via 50 Ω sound tubing (E-A-RTONE 3A, Etymotic Research, Inc), attached

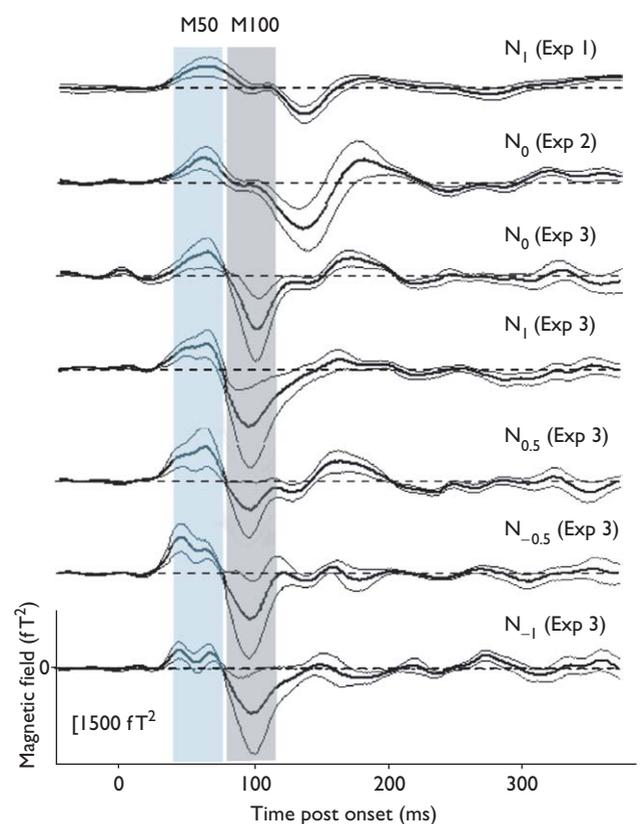


Fig. 3. Comparison of hemispheric activation. For each subject, in each experiment, the squared RMS value of the right hemisphere was subtracted from the squared RMS value of the left hemisphere. The resulting difference vectors for each subject were averaged together (thin lines are 1 standard error, derived by bootstrap). Positive values=left hemisphere dominant, negative values=right hemisphere dominant. Blue and Grey shading marks the M50 and M100 time windows, respectively. M50 showed significant left hemisphere lateralization in all task and experimental conditions tested. M100 lateralization and amplitude are task dependent (compare Experiments 1 and 2 to Experiment 3).

to E-A-RLINK plugs inserted into the ear-canal. Presentation order was randomized with an inter-stimulus interval (ISI) between 500 and 2000 ms in Experiments 1 and 2 and 900–1600 ms in Experiment 3.

Procedure: The recordings (~1.5h) were in two parts. First, subjects heard 200 repetitions of a 1 kHz (50 ms) sinusoidal tone (ISI randomized between 750 and 1550 ms) as a pre-experiment. Then subjects listened to the noise stimuli and either performed a pitch detection task (50% of trials in Experiments 1 and 2) by pressing a button held in the right hand, as soon as they heard a tonal object pop out of the noise (at 1000 ms post-onset), or a modulation detection task (25% of the trials in Experiment 3). Subjects were encouraged to respond as quickly and as accurately as possible.

Neuromagnetic recording and analysis: Magnetic signals were recorded using a 160-channel, whole-head axial gradiometer system (KIT, Kanazawa, Japan). Raw data were noise-reduced using CALM [16]. The pre-experiment data were filtered from 1 Hz and 58.8 Hz, baseline corrected to the 100 ms pre-onset interval and stored in 500 ms (100 ms

pre-onset) stimulus-related epochs. The M100 response was identified as a dipole-like pattern distributed over the temporal region. The 20 strongest channels at the peak (5 sinks and 5 sources in each hemisphere) were considered to best reflect auditory activity and chosen for further analysis.

The data for all three experiments were filtered between 1 and 200 Hz with a notch at 60 Hz. In Experiments 1 and 2, 1500 ms long epochs (50 ms pre-onset) were extracted (we report here only results from the first 1000 ms that were identical in all conditions) and averaged over 800 trials (though as few as 100 gives similar results). In Experiment 3, 500 ms long epochs (100 ms pre-onset) were extracted and averaged over 200 trials. Epochs with amplitudes > 3 pT ($\sim 5\%$) were considered artifactual and discarded. The averages were band-pass filtered at 1–20 Hz and base-line corrected to the full range of the epoch. In each hemisphere, the root mean square (RMS) of the field strength across the 10 channels (selected from the pre-experiment), was calculated for each sample point.

Confidence intervals are computed using Bootstrap (1000 iterations; balanced) [17], a computationally intensive resampling method useful when the sampling distribution of the statistic of interest is unknown.

RESULTS

Figure 1 shows the group RMS (RMS of the individual subject RMSs) of the auditory evoked responses to the noise stimuli and the responses to pure tones (in the pre-experiment) for Experiments 1 and 2. The pure tone responses (Fig. 1b,f) reveal the classic pattern of activation: a prominent M100 response and much smaller M50 and M150 peaks. The contrast to the responses to the noise stimuli (Fig. 1a,e) is dramatic. The responses contain a two-peaked 'noise onset response' at ~ 70 ms and ~ 150 ms post-noise-onset, both with a characteristic M50 spatial distribution (all participants had comparable response trajectories). The strong M50 response, lack of an M100 peak roughly 100 ms after noise-onset, and a second, later vigorous response at ~ 150 ms (with an M50 distribution) characterize the responses to both correlated and uncorrelated noise stimuli. The waveforms and dipolar patterns observed in the iso-contour maps for a representative subject in Experiment 1 are displayed in Fig. 1c,d.

Figure 2 shows the group RMS for the stimuli in Experiment 3 for all experimental conditions. The responses to all stimuli contained a three-peaked noise onset response at ~ 65 ms, ~ 100 ms and ~ 150 ms post-noise-onset. Although perceptually quite different, no statistically significant response differences were observed between the different conditions in Experiment 3.

The N_1 and N_0 stimuli in Experiment 3, although shorter, are physically identical to the stimuli in Experiments 1 and 2, but the respective responses are strikingly different. Our results show that a reduced M100 is not a general property of white noise stimuli (as implied in [18]). Instead, we propose that the lack of an M100 response in Experiments 1 and 2, and the appearance of an M100 response in Experiment 3 are related to the task the subjects were performing and specifically the differing attentional-focus requirements (discussion below). The M50 response is quite pronounced across all experiments, especially in the left hemisphere (LH), and is much stronger than the M50 response for the tone stimuli in the pre-experiment.

Strikingly, the noise onset responses show significant hemispheric differences. In Experiment 1, the M50 was larger on the left, and M150 was larger on the right (paired t -tests at the peak for each subject, $df=19$: for M50 $t=2.14$, $p=0.046$; for M150: $t=-3.56$, $p=0.02$). The results of Experiment 2 showed the same effect: the differences between left and right hemispheres approached significance for the M50 ($t=1.97$, $df=15$, $p=0.067$) and were significant for the M150 ($t=-2.31$, $df=15$, $p=0.035$). The same effect for the M50 was also noted in Experiment 3 (Fig. 2). For pure tones, no such hemispheric differences were found for the M100 in any experiment (see also [19]), but the M50 exhibited a weak (non-significant) LH dominance trend in all three pre-experiments. Figure 3 illustrates these hemispheric differences. There is also an indication of interplay in hemispheric dominance between the M100 and M150 responses. Although of opposite orientation (Fig. 1, Fig. 2), M150 shows right lateralization only in the absence of and M100.

DISCUSSION

In Experiments 1 and 2 subjects detected tonal objects in background noise that appeared after (1000 ms post-onset) the initial noise-only stimuli. Thus task demands allowed them to treat the initial noise as background. In Experiment 3, however, each stimulus was potentially a target, not a background. An additional difference between the experiments is that in Experiments 1 and 2 subjects heard only one kind of noise, whereas in Experiment 3 five different noise kinds were used. If the M100 indicates the onset of a new auditory 'object of attention', these findings would explain the significant attenuation of an M100 response in Experiments 1 and 2, and the prominent M100 response in Experiment 3. The M100 response is known to be modulated by attention [20] but reported effects are not as extreme as seen here. The lateralization of the M100 response also seems task related such that, although no lateralization is observed in the pure tone (pre-experiment) condition, a right-lateralization is observed in Experiment 3. This is attributable to the detection of slow-modulations hypothesized to be sub-served by the right hemisphere [21,22], although, crucially, the modulations were only physically present in the target (task inducing) stimuli, which are not analyzed. Similar (but opposite) task-related modulation in M100 lateralization is reported in [23] for speech discrimination.

In contrast to the M100, the prominence of the M50 peak seems to be a general attribute of wide-band noise stimuli (see also [18]), and not related to task demands: a prominent peak was observed in all experimental conditions in all experiments. Similarly, the M50 lateralization is not task dependent. The finding that the M50 is stronger in the LH is robust across subjects, stimuli and task demands. This effect is not related to the loudness or length of the stimuli; a similar trend was observed when 100 ms wide-band noise stimuli were presented near threshold loudness (unpublished data). The trend of stronger responses in the left hemisphere is even visible for pure tones (Fig. 1). Higher amplitudes for white noise signals might result from the fact that, relative to pure tones, white noise activates many more neurons in the ascending auditory system in general and PAC in particular.

The left-lateralization of the M50 might be related to surprising fMRI results [24] reporting left hemisphere dominance for processing tones in core AC. Thus, early left hemisphere dominance may be a general property of PAC in humans. This effect may be due to the greater volume of white matter underlying the left Heschl's gyrus compared to the right and other anatomical asymmetries (reviewed in [22]). Because of the stronger responses and clearer lateralization patterns, though, our findings indicate that wide-band stationary stimuli are more suitable to study early responses in AC.

The evidence described here indicates that the M100 does not result from a process of detecting changes in sensory input, but reflects later, more specialized, stages in processing, possibly related to auditory attention and figure ground segregation. The M50, because of its earlier location in the processing stream and relative independence of task demands or perturbation [12], is a more suitable candidate for the role of auditory input change detector. Together, the M50 and M100 might reflect the processes of 'background analysis' in A1 (M50) and the assignment of identity, such as pitch, phonemic quality, or location to these objects in higher auditory centers (M100) [25]. The functional significance of the left-lateralization of the M50 is unclear. Devlin *et al.* [24] relate it to the specialization of human AC for speech, another explanation is that the greater myelination in the left PAC [24] results in greater sensitivity to acoustic changes such as those present at the onset of auditory stimuli. Further study is needed in order to determine what functional role this hemispheric difference plays in the processing of auditory stimuli in the environment.

CONCLUSION

Experiments with wide-band noise stimuli show that, for the same stimuli, the strength and lateralization of the M100 response are task modulated. The M50 is consistently lateralized to the LH and its amplitude appears to be task independent, as long as wide-band noise stimuli are used. These differences are hypothesized to reflect their differing roles in the process of figure/ground segregation and construction of auditory objects.

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