

Differential Post-Stimulus Inhibition of N1 Activity Underlies Mismatch Response Generation at the Human Auditory Cortex

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Previous MEG studies, utilizing single equivalent current dipole modeling approaches, have suggested that the mismatch and N1 responses are generated by independent auditory-cortex sources. Our combined fMRI/MEG results suggest, however, that differences in the source loci of the mismatch and N1 responses result from differential post-standard inhibition of anterior and posterior N1 sources contributing to the deviant-stimulus response. Further, these inhibitory effects became weaker as a function of increasing stimulus difference. These findings suggest that post-stimulus inhibition of N1 activity may explain elicitation of the mismatch response.

Ignoring irrelevant auditory stimuli while letting novel ones enter consciousness is essential for intact human selective attention and goal-directed behavior¹. Two distinct auditory-cortex processes have been thought to underlie this phenomenon: (1) adaptation of stimulus-detection related N1 with repeated stimulus presentation, and (2) elicitation of a mismatch response by stimulus changes². This view was largely based on previous MEG studies suggesting that source loci of mismatch and N1 responses are different, as estimated using single equivalent current dipole (ECD) fits³. Recently, it was proposed that mismatch response arises through post-stimulus inhibition of N1 activity, whereby N1 responses to auditory stimuli are automatically suppressed in amplitude and delayed in latency as a function of their similarity to preceding auditory events⁴. However, this model *per se* fails to explain the noted differences in mismatch and N1 source loci. Here, we hypothesized that differential post-standard inhibition of auditory-cortex N1 activity explains the mismatch response.

We studied 7 healthy right-handed male volunteers (ages: 21–42 years) using whole-head 306-channel magnetoencephalography (MEG). Additionally, 3-Tesla functional magnetic resonance imaging (fMRI) data was utilized to bias the cortically constrained continuous electromagnetic source estimates (fMEG)⁵. The subjects were presented infrequent ($P = 0.1$) deviant sounds that were, in separate blocks, either by 1, 2, or 4 octaves higher in sound center frequency than intervening homogeneous standard stimuli (i.e., ‘oddball’ conditions). The standard stimuli were 1/5-octave wide noise bursts with a center frequency of 251 Hz and a presentation rate of 2 Hz. In separate control conditions, we presented the deviant stimuli without the intervening standard stimuli (i.e., ‘deviants alone’ conditions).

Our MEG data shows that differential post-standard inhibition of anterior and posterior auditory-cortex N1 sources (here termed as N1m(A) and N1m(P)⁶) may explain the noted differences in the ECD-estimated source loci of mismatch and N1 responses. Confirming the previous findings³, we observed more anterior single-ECD loci for responses to deviant sounds in the oddball than in the deviants-alone conditions. However, this effect seemed to vanish with larger differences between the deviant and standard stimuli (6.2 ± 3.1 mm, 1.1 ± 2.8 mm, and -0.6 ± 2.9 mm for the 1, 2, and 4 octave differences, respectively). Correspondingly, N1m(P) amplitude was suppressed with decreasing standard-deviant stimulus difference in the oddball conditions ($p < 0.01$ for the interaction term of the ANOVA), while that of the N1m(A) was little affected. Notably, this differential post-standard inhibition of the N1m(P) and N1m(A) could well explain the observed differences in the source loci of the mismatch and N1 responses, since ECD fits tend to approximate the center-of-gravity of underlying neural activity⁷. The latencies of the N1m(A) and N1m(P) were also increased with smaller deviant-standard sound differences in the oddball conditions. Further illustrating this, **Figure 1** shows the fMEG-estimated source configurations giving rise to the N1m(P) and N1m(A) in a single subject. In conclusion, our findings tentatively suggest that post-standard inhibition of deviant-sound N1 activity at the human auditory cortex underlie the mismatch response.

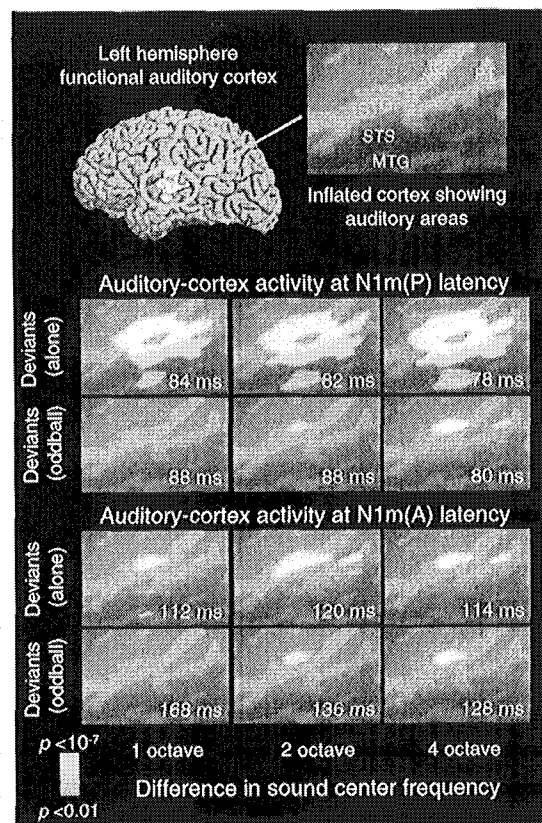


Figure 1: Single-subject fMEG maps of estimated cortical activity to deviant sounds at N1m(P) and N1m(A) latencies. (TOP LEFT) Reconstructed cortical surface of the left hemisphere is shown, with fMEG activity to low-frequency deviants encircled. (TOP RIGHT) Inflated cortex showing the temporal-lobe anatomical structures disclosing significant fMEG activity. HG=Heschl’s gyrus, PT=planum temporale, STG=superior temporal gyrus, STS=superior temporal sulcus, MTG=middle temporal gyrus. (BOTTOM) Auditory-cortex fMEG activity at the N1m(P) and N1m(A) latencies. The center of gravity of activity seemed to be more posterior at the N1m(P) latency than at the N1m(A) latency. Whereas activity originating from the anterior/lateral aspects of Heschl’s gyrus dominated at the N1m(A) latency, more widespread activity patterns were observed at the N1m(P) latency, extending into PT, STS, MTG, and posterior aspects of STG. In the oddball conditions, the activity at the anterior/lateral aspects of HG seemed to be less robustly suppressed than activity in other areas, thus supporting the hypothesis that differential inhibition of auditory-cortex areas by preceding standard stimuli underlies the mismatch response.

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