Stimulus Context Affects Auditory Cortical Responses to Changes in Interaural Correlation

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Chait M, Poeppel D, Simon JZ. Stimulus context affects auditory cortical responses to changes in interaural correlation. *J Neurophysiol* 98: 224–231, 2007. First published May 9, 2007; doi:10.1152/jn.00359.2007. We use magnetoencephalography to study human auditory cortical processing of changes in interaural correlation (IAC). We studied transitions from correlated (identical signals at the 2 ears) to uncorrelated (different signals at the 2 ears) or vice versa for two types of wide-band noise stimuli: CHANGE signals contained a single IAC change (or none) and ALT signals alternated between correlated and uncorrelated at a constant rate. The relevant transitions, from correlated to uncorrelated or vice versa, are physically identical in both stimulus conditions, but auditory cortical response patterns differed substantially. CHANGE stimuli exhibited a response asymmetry in their temporal dynamics and magnetic field morphology according to the direction of change. Distinct field patterns indicate the involvement of separate neural substrates for processing, and distinct latencies are suggestive of different temporal integration windows. In contrast, the temporal dynamics of responses to change in the ALT stimuli did not differ substantially according to the direction of change. Notably, the uncorrelated-to-correlated transition in the ALT stimuli showed a first deflection ~90 ms earlier than for the same transition in the CHANGE stimuli and with an opposite magnetic field distribution. This finding suggests that as early as 50 ms after the onset of an IAC transition, a given physical change is processed differentially depending on stimulus context. Consequently, even early cortical activation cannot be interpreted independently of the specific long-term stimulus context used in the experiment.

INTRODUCTION

Interaural correlation (IAC) is a measure of the similarity of the sound waveforms at the two ears. The estimation of interaural similarity is considered to be a fundamental computation in the ascending binaural system and a basic cue for a variety of binaural phenomena (Stern and Trahiotis 1995). Auditory scene analysis, such as detection and localization of auditory objects in noisy environments, involves comparison of acoustic signals across ears. The appearance or disappearance of sound sources in the environment may introduce changes in the interaural correlation of the inputs to a listener's ears and sensitivity to IAC and specifically to change in IAC has been suggested to be an important factor underlying listeners' ability to detect temporal edges in ongoing sounds, corresponding to onsets and offsets of auditory objects (Durlach et al. 1986; Palmer et al. 1999). In humans, the processing of IAC has mostly been studied through psycho-

physics (Boehnke et al. 2002; Culling et al. 2001; Gabriel and Colburn 1981; Pollack and Trittipoe 1959a,b), using paradigms that are similar to those used in vision with dynamic random dot stereograms (Julesz and Tyler 1976). Recently, several functional MRI (fMRI) (Budd et al. 2003; Hall et al. 2005) and electrophysiological (Chait et al. 2005; Dajanai and Picton 2006; Soeta et al. 2004) studies have sought to identify a noninvasive brain activation correlate of auditory cortical IAC sensitivity that has the potential of elucidating the underlying neuronal mechanisms beyond behavioral data alone.

The assumption behind these studies, and many other low-level auditory magnetoencephalography (MEG)/EEG studies, is that early auditory cortical responses largely reflect bottom-up driven neural activations that depend on short-term physical properties of the stimulus, and therefore the comparison of input (the relevant aspect of the stimulus) and the recorded brain responses should be a good and objective means to measure the computational parameters underlying IAC processing. It is thus quite surprising that two recent studies of auditory cortical processing of changes in IAC (Chait et al. 2005; Dajani and Picton 2006) reported quite different patterns of auditory evoked responses to what appeared to be the same stimulus event. In an MEG study, Chait et al. (2005) used a series of wide band noise stimuli that either did or did not contain a change in IAC (Fig. 1, *top*). Dajani and Picton (2006), in an EEG study, used ongoing dichotic noise signals that alternated between two levels of IAC at a constant repetition rate (Fig. 1, *bottom*). The relevant transitions: from correlated (identical signals at the 2 ears) to uncorrelated (statistically independent signals at the 2 ears) or vice versa (1→0 and 0→1, respectively), for which brain responses were reported, are physically identical in both studies; however, the recorded temporal response patterns were quite different, resulting in competing conclusions about IAC change processing mechanisms in human auditory cortex.

In this study, we sought to investigate the source of this discrepancy by measuring brain responses to the two kinds of stimuli (CHANGE and ALT; see Fig. 1) in the same experimental session, within the same subject group, and using a single measurement technique (MEG), all of which could have been factors contributing to the aforementioned divergence in previous experimental results. The data reveal that even when all of the above factors are controlled for, CHANGE and ALT stimuli still evoke fundamentally different activation proper-

CHANGE stimuli

(in random order:)

800 ms   300 ms

```
1  0    0  1    1    0  . . .
1→0     0→1    1→1   0→0   time →
```

ALT stimuli

800 ms   800 ms

```
1  0  1  0  1  0  1  . . .
        1→0
          0→1          time →
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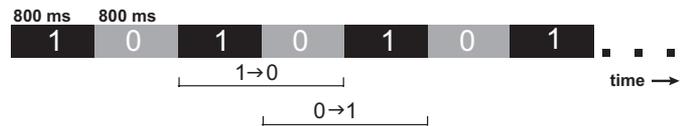
FIG. 1. Schema of stimuli. All signals consisted of a concatenation of wide-band noise bursts that were either interaurally correlated (interaural correlation (IAC) = 1) or interaurally uncorrelated (IAC = 0). CHANGE stimuli (*top*) were 1,100 ms long and either did ($1\rightarrow0$, $0\rightarrow1$) or did not ($1\rightarrow1$, $0\rightarrow0$) contain a change in IAC at 800 ms after stimulus onset. ALT stimuli (*bottom*) alternated between IAC = 0 and IAC = 1 at a constant rate (every 800 ms). IAC transitions ($1\rightarrow0$ and $0\rightarrow1$) are physically identical in both kinds of stimulus conditions; however, the longer-scale stimulus context is different.

ties. Indeed, our analysis shows that, in auditory cortex, physically similar stimulus events can result in very different brain responses: As early as 50 ms after the onset of an IAC transition, the same physical change is processed differently depending on the longer-term stimulus context (in this case, we hypothesize that a key consideration is whether or not a transition is predictable), suggesting that early cortical responses cannot be related directly to stimuli without taking into account the particular stimulus environment and context used in the experiment.

METHODS

Subjects

Seven subjects (mean age, 23.1 years; 4 women) took part in the MEG experiment. All were right handed (Oldfield 1971), reported normal hearing, and had no history of neurological disorder. The experimental procedures were approved by the University of Maryland institutional review board, and written informed consent was obtained from each participant. Subjects were paid for their participation.

Stimuli

Figure 1 presents a schematic description of the stimuli used in this study. All signals consisted of a concatenation of wide-band (8 kHz) noise bursts that were either interaurally correlated (IAC = 1) or interaurally uncorrelated (IAC = 0). The uncorrelated noise stimuli were constructed by generating two independent noise signals, played to each ear. Random samples of noise are not exactly orthogonal. For this reason, only signal pairs with an interaural correlation coefficient value (measured over segments of 800 ms) <0.005 were used for the generation of the experimental stimuli. The bandwidth and spectral power were equal at each ear and constant across conditions. The IAC changes occurred without any detectable change in either monaural signal. Thus any differences in brain responses can be interpreted as specifically resulting from binaural interaction.

In both experimental conditions, participants were required to respond to "deviant" stimuli. These stimuli, which were not included in the analysis, served to assure the subjects' vigilance and attention to the auditory signals during the recording but did not require any processing of changes in interaural correlation.

The stimuli were created off-line, gated on and off using 15-ms raised-cosine ramps (with no gating between IAC transitions), and saved in 16-bit stereo wave format at a sampling rate of 16 kHz. The signals were delivered to the subjects' ears with a tubephone (E-A-RTONE 3A 50 ohm, Etymotic Research) attached to E-A-RLINK foam plugs inserted into the ear canal and presented at a comfortable listening level.

CHANGE STIMULI (CHANGE; FIG. 1, *TOP*). The stimuli are a subset of those used in Chait et al. (2005). The signals were 1,100 ms long, consisting of an initial 800-ms-long segment (reference correlation IAC = 0 or 1), followed by a 300-ms "test segment" (IAC = 0 or 1) resulting in four experimental conditions. To reduce response dependency on a particular sample of frozen noise, 10 different instances were generated for each of the four conditions. The purpose of the relatively long initial segment was to ensure that responses to change in IAC do not overlap with those associated with stimulus onset. The length of the test segment was chosen based on the fact that human listeners' performance on detecting changes in IAC remains approximately constant for signal durations >300 ms (Pollack and Trittipoe 1959b).

In addition to the four experimental conditions, the stimulus set included a proportion (17%) of deviant stimuli, which consisted of 800 ms of either interaurally correlated (IAC = 1) or interaurally uncorrelated (IAC = 0) wide-band noise, followed by 300-ms-long interaurally correlated (IAC = 1) or interaurally uncorrelated (IAC = 0) noise amplitude modulated at a rate of 10 Hz and a depth of 50%. Subjects were instructed to respond as fast as they could to each onset of the modulation. These stimuli were not included in the analysis. They served to assure the subjects' alertness and to focus attention on the time of change (800 ms after onset) but did not require any processing of interaural correlation.

In total, each listener heard 160 repetitions of each of the four experimental conditions ($0\rightarrow0$, $0\rightarrow1$, $1\rightarrow0$, $1\rightarrow1$) and 32 repetitions of each of the four devient conditions ($0\rightarrow$ 0-modulated, $0\rightarrow1$-modulated, $1\rightarrow0$-modulated, $1\rightarrow1$-modulated). The order of presentation was randomized, with the interstimulus interval (ISI; the interval between the offset of one stimulus to the onset of the next) randomized between 1,000 and 1,700 ms.

ALTERNATING STIMULI (ALT; FIG. 1, *BOTTOM*). The signals were designed to be similar to those used by Dajani and Picton (2006). The signals were 64,000 ms long (1.06 min), consisting of 80 different 800-ms-long segments with IAC = 0 or IAC = 1 in alternating order. Two different "frozen" instances (beginning with IAC = 0 or 1, respectively) were used in the experiment. The stimulus set also contained deviant stimuli that were 300-ms-long interaurally correlated noise bursts, amplitude modulated at a rate of 10 Hz and a depth of 50%. Subjects were instructed to respond as fast as they could to these modulated segments. These stimuli served to assure the subjects' alertness and general attention to the auditory modality.

In total, each listener heard ∼25 repetitions of the alternating IAC sequences and 25 repetitions of the modulated noise bursts. The order of presentation was randomized, with the ISI randomized between 1,100 and 2,300 ms.

Subjectively, correlated noise (IAC = 1) sounds like a single focused source in the center of the head. At IAC = 0, the percept is that of a diffuse source, or two independent sources, one at each ear. Thus $0\rightarrow1$ CHANGE stimuli evoke a percept of focusing of the sound image, whereas $1\rightarrow0$ CHANGE signals are perceived as broadening of the source. The ALT stimuli, perhaps because of the fact that change is regularly occurring, evoke a different perceptual experience. Listeners often report a percept similar to the "continuity illusion" effect, with one of the segments (IAC = 1 or IAC = 0) being constantly present and the other appearing and disappearing.

Procedure

The subjects lay supine inside a magnetically shielded room. The experimental session included two phases: a preliminary "source localizer" recording, followed by the main experiment. In the source localizer recording, subjects listened to 200 repetitions of a 1-kHz, 50-ms sinusoidal tone (ISI randomized between 750 and 1,550 ms). These responses were used to verify that the subject was positioned properly in the machine, that signals from auditory cortex had a satisfactory signal to noise ratio (SNR), and to determine which MEG channels best respond to activity within auditory cortex. In the main experiment, subjects listened to stimuli while performing the modulation detection tasks by pressing a button, held in the right hand. The instructions encouraged speed and accuracy. The order of the two stimulus conditions (CHANGE and ALT; 30 min each) was counterbalanced across listeners. The experiment was divided into blocks of ~7 min (4 consecutive blocks for each stimulus condition). Between blocks, subjects were allowed a short rest but were required to stay still.

Neuromagnetic recording and data analysis

The magnetic signals were recorded using a 160-channel, whole-head axial gradiometer system (KIT, Kanazawa, Japan). Data for the localizer recording were acquired with a sampling rate of 1 kHz, filtered on-line between 1 Hz (hardware filter) and 58.8 Hz (17-ms moving average filter), and stored in 500-ms stimulus-related epochs starting 100 ms before onset. Data for the main experiment were acquired continuously with a sampling rate of 0.5 kHz, filtered in hardware between 1 and 200 Hz with a notch at 60 Hz (to remove line noise), and stored for later analysis. The data were noise-reduced using the time-shift principle component analysis algorithm (TSPCA) (de Cheveigné et al. 2007; de Cheveigné and Simon 2007). This algorithm removes the projection of brain responses on a basis of time-shifted signals from reference sensors sensitive to environmental fields.

In the localizer run, auditory evoked responses to the onset of the pure tones were examined, and the M100 response (Hari 1990) was identified for each subject as a dipole-like pattern (i.e., a source/sink pair) in the magnetic field contour plots distributed over the temporal region of each hemisphere. The M100 current source is quite robustly localized to the upper banks of the superior temporal gyrus in both hemispheres (Hari 1990; Lütkenhöner and Steinsträter 1998; Pantev et al. 1995). For each subject, the 20 strongest channels at the peak of the M100 (5 in each sink and source, yielding 10 in each hemisphere) were considered to best reflect activity in the auditory cortex and thus chosen for the analysis of the experimental data. This procedure serves the dual purpose of enhancing the auditory response components over other response components, and compensating for potential channel-misalignment between subjects.

For the CHANGE stimuli, 1,400-ms epochs (including 200 ms before onset) were created for each of the four stimulus conditions. These were averaged and low-pass filtered at 30 Hz (67-point-wide Hanning window). The root mean square (RMS) of the field strength across the 10 channels, selected in the pre-experiment, was calculated for each sample point. Eight RMS time series, one for each condition in each hemisphere, were thus created for each subject. This RMS-based channel space approach is an appropriate method to summarize the combined activity of multiple underlying sources and is model free (to the extent that it does not depend on any of the different assumptions required by different source localization methods).

For each subject, the analysis of the ALT stimuli was performed by averaging over all but the first four 1,600-ms epochs centered around an IAC transition. About 1,500 transitions, in each direction (correlated-to-uncorrelated and uncorrelated-to-correlated), were averaged in this way and low-pass filtered at 30 Hz (67-point-wide Hanning window). In each hemisphere, the RMS of the field strength across the 10 channels, selected in the localizer experiment, was calculated for each sample point. Four RMS time series, one for each condition in each hemisphere, were thus created for each subject.

To show the main effects across the entire subject population, we plot the RMS computed over all 156 channels of the grand-averaged data (averaged across subjects). However, statistical analysis is always performed on a subject-by-subject basis, using the RMS values of the channels chosen for each subject in each hemisphere. The congruity of activation time-course and magnetic field distributions across subjects were evaluated using the bootstrap method (Efron and Tibshirani 1993; 500 iterations; balanced) based on the individual RMS time series as described in Chait et al. (2005).

To compare the activation between conditions, we used a repeated-measures analysis in which, for each subject, the squared RMS value of one condition is subtracted from the squared RMS value of the other condition and the individual difference time series are subjected to a bootstrap analysis (500 iterations; balanced; Efron and Tibshirani 1993). At each time-point, the proportion of iterations below the zero line is counted. If that proportion is <5%, or >95% ($\alpha = 0.05$) for five adjacent samples (10 ms) and if the average absolute difference at that time exceeded a threshold of 200 fT^2, the difference is judged to be significant.

RESULTS

CHANGE stimuli

Figure 2 presents the grand-average (over subjects) of the response to 1→0 and 0→1 stimuli. Plotted in gray are the responses recorded from each of the 156 channels, averaged over subjects. The RMS over all channels is plotted in black. In both stimulus conditions, onset responses are dominated by two peaks (M50 and M150; considered to be the MEG counterparts of the P1 and P2 EEG deflections) at ~78 and 190 ms after stimulus onset, both with a characteristic M50-like magnetic field distribution. Similarly to Chait et al. (2005, 2006), an M100 peak which usually dominates auditory onset responses is greatly attenuated here.

Consistent with previous reports (Chait et al. 2005; Soeta et al. 2004), onset amplitudes are significantly higher for uncorrelated (IAC = 0) than correlated (IAC = 1) noise: a repeated-measures ANOVA on peak amplitudes with condition, time-window (M50, M150), and hemisphere as factors revealed only a main effect of stimulus condition [$F(1,6) = 26.73$ $P = 0.002$]. Similar findings, showing the fact that auditory cortex seems to be more strongly activated by uncorrelated than correlated noise-signals have been reported in an fMRI study by Hall et al. (2005).

Unlike onset responses that are qualitatively similar across conditions, transition responses differ greatly between 0→1 and 1→0 in both temporal dynamics and field distribution (Fig. 4). Figure 3 presents the post-transition RMS activation time course in the right and left hemispheres for 0→1 (Fig. 3, A and B) and 1→0 (Fig. 3, C and D) CHANGE conditions compared with their respective control (no change; 0→0 and 1→1, respectively) conditions. Gray shading marks temporal intervals where a repeated-measures bootstrap (see METHODS) indicated a significant difference between change (black) and control (gray) conditions. Indeed, in the case of 1→0 stimuli, the first difference from the control condition emerges at 58 ms after change in the right hemisphere (Fig. 3D) and 70 ms after change in the left hemisphere (Fig. 3C). For 0→1 stimuli, the first difference from the control condition emerges much later,
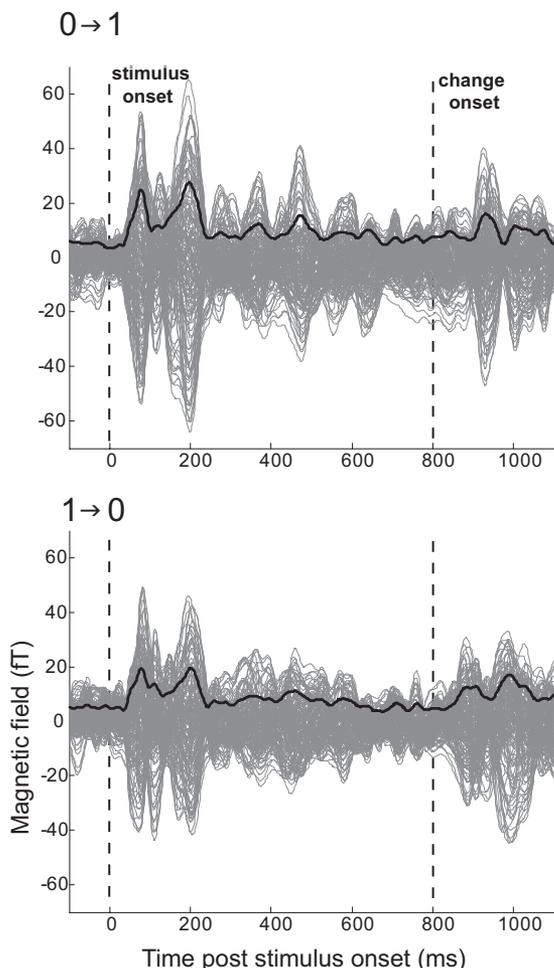
FIG. 2. Grand-average (average over all subjects for each of the 156 channels; in gray) of evoked auditory cortical responses to 0→1 (*top*) and 1→0 (*bottom*) transitions in CHANGE stimuli. Root mean square (RMS) over all channels is plotted in black. Onsets of both stimuli are characterized by a 2-peaked noise onset response at ~70 (M50) and 170 ms (M150) after onset. A response to the IAC transition is seen after 800 ms post-stimulus onset.

at 108 ms after change in the right hemisphere (Fig. 3*B*) and 124 ms after change in the left hemisphere (Fig. 3*A*).

To facilitate the comparison between the responses to the two kinds of transitions, Fig. 4*A* presents an overlay of the postchange RMS amplitude time-course of 1→0 (in black) and 0→1 (in gray) conditions (collapsed over hemispheres). A clear difference in both temporal dynamics and field distribution is visible in the response dynamics: the 1→0 transition evokes an activation pattern dominated by deflections at ~80 and 180 ms after transition. The opposite, 0→1, transition evokes peaks at ~140 and 200 ms after transition (this last peak was not prominent in a previous experiment with the same stimuli, which suggests that it is not consistent across subjects; Chait et al. 2005).

Magnetic field distributions also differ between conditions: the dipolar distribution of the first peak in the 1→0 transition is of opposite polarity from that of the first peak in 0→1 (Fig. 4*A*, cf. *a* and *b**), indicating that the underlying currents flow in opposite directions. The sources underlying the two dipolar patterns are too close to be adequately differentiated with the spatial resolution of our recording technique. However, given how measurable magnetic fields are produced by dendritic

currents in pyramidal neurons (Nunez and Silberstein 2000), distributions of opposite polarity most likely reflect the activation of distinct neural substrates (Lutkenhoner 2003; see also Jones 2002). Therefore the first peak in the response to the 0→1 transition is not only delayed with respect to that of the 1→0 transition but also involves different neural populations (see also Chait et al. 2005, 2007) and is interpreted as indicating that different neural mechanisms are involved in processing the two transitions.

ALT stimuli

Figure 5 presents the grand-average (over subjects) of the response to 0→1 and 1→0 transitions in the ALT stimuli. Plotted in gray are the responses recorded from each of the 156 channels, averaged over subjects. The RMS over all channels is plotted in black. The higher response amplitudes evoked by the transition to uncorrelated noise (1→0) in this case seem to mirror the higher onset response amplitudes recorded for uncorrelated noise relative to correlated noise stimuli. Both transition directions exhibit a first deflection at ~80 ms after transition with a characteristic M50-like magnetic field distribution (the MEG counterpart of the P1 EEG deflection; see Fig. 4*B*), followed by another deflection at ~200 ms after transition (M150 or P2 in EEG; see Fig. 4*B*). Thereafter, correlated noise activity shows a return to baseline, whereas uncorrelated noise exhibits a slowly attenuating sustained re-
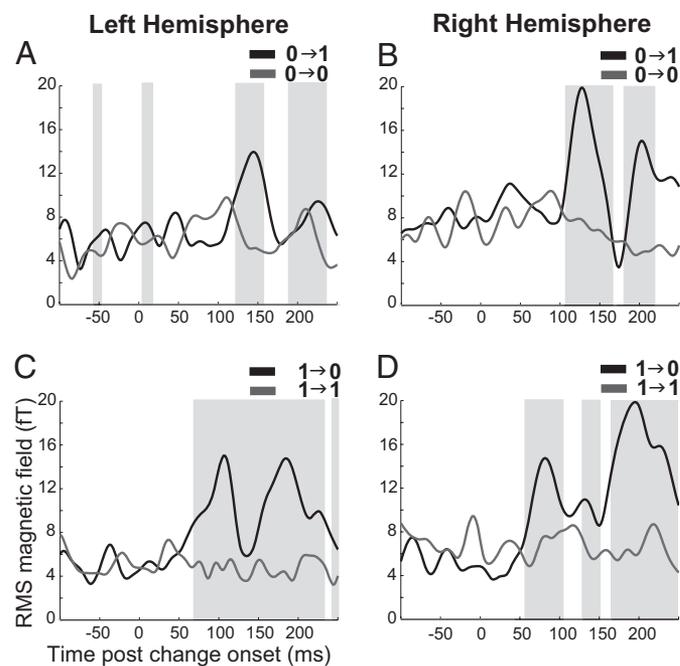

FIG. 3. Transition responses in CHANGE stimuli. *A*: grand-average RMS magnetic field of the 0→1 transition (black) and its control (no change; 0→0) in the left hemisphere. *B*: grand-average RMS magnetic field of the 0→1 transition (black) and its control (no change; 0→0) in the right hemisphere. *C*: grand-average RMS magnetic field of the 1→0 transition (black) and its control (no change; 1→1) in the left hemisphere. *D*: grand-average RMS magnetic field of the 1→0 transition (black) and its control (no change; 1→1) in the right hemisphere. Shaded areas mark time intervals where a significant difference is found between transition and control. Note that differences are computed in a repeated measures analysis and therefore may be marked as significant even when grand-average RMS plot shows no difference between conditions.
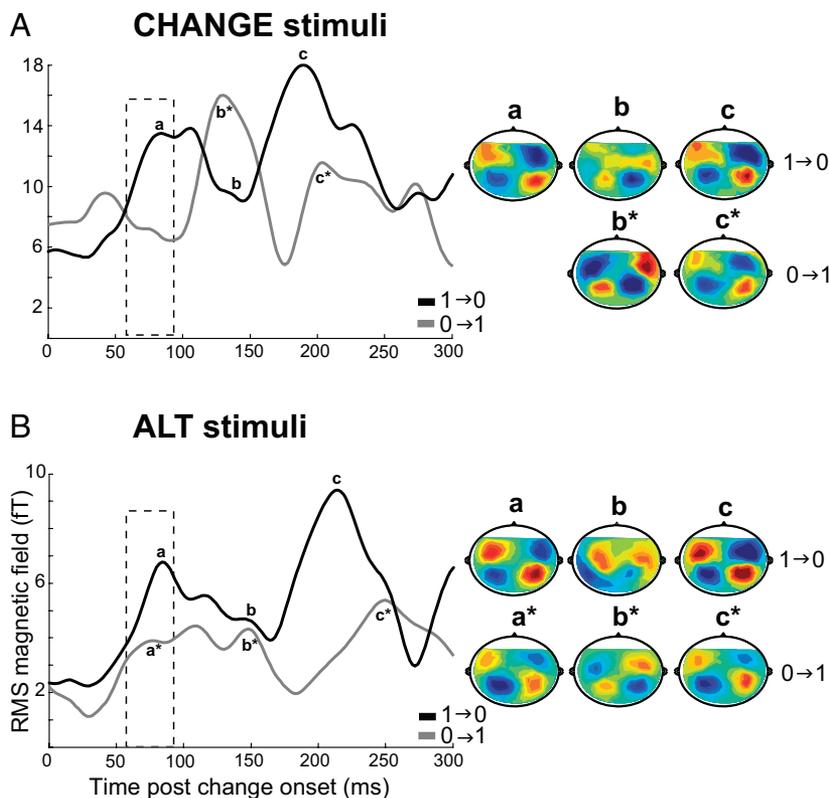
FIG. 4. Comparison of response dynamics for 1→0 (black) and 0→1 (gray) transitions in CHANGE and ALT contexts. Note the *y*-axis scale difference between *A* and *B*. Contour plots indicate the topography of the magnetic field at the peaks. Source, red; sink, blue. *A*: responses in the CHANGE context. 1→0 and 0→1 responses exhibit a difference in temporal dynamics and magnetic field morphology depending on the direction of change. The first observed peak for 1→0 condition occurs ~80 ms earlier than the 1st observed peak in 0→1 condition (at ~140 ms) and with an opposite polarity (compare *a* and *b**, 1st peaks in 1→0 and 0→1 conditions, respectively). The *a*, *c*, and *c** patterns correspond to an upward directed current (generating a vertex positive electrical field, denoted M50 and M150 in the MEG literature and P1 and P2, respectively, in the EEG literature). The *b** pattern corresponds to a downward directed current (generating a vertex negative electrical field, denoted M100 in MEG literature and N1 in EEG literature). The noisy *b* contour plot, which is the magnetic field pattern in the 1→0 condition that is temporally corresponding to the *b** peak in the 0→1 condition is provided for reference. *B*: responses in the ALT context. Aside from a global amplitude difference, dynamics of responses to both change directions do not differ substantially from each other. Both transitions are processed with the same latency and exhibit the same temporal dynamics and similar magnetic field morphology. The *a*, *a**, *c*, and *c** patterns correspond to an upward directed current (generating a vertex positive electrical field, denoted M50 and M150 in MEG literature and P1 and P2, respectively, in EEG literature). The *b* pattern in the 1→0 transition is noisy, whereas the temporally corresponding *b** pattern in the 0→1 transition reflects a downward directed current (generating a vertex negative electrical field, denoted M100 in the MEG literature and N1 in the EEG literature). Dashed squares mark time interval where ALT 0→1 transitions (gray lines) exhibit a 1st onset peak. CHANGE 0→1 transitions are still flat (not significantly different from control; see Fig. 3*A*) at that time.

sponse (visible in Fig. 5 ~250 ms after the onset of the 1→0 transition), which is also reported in Dajani and Picton (2006).

To facilitate the comparison between the responses to the two kinds of transitions, Fig. 4*B* present the change-related auditory evoked responses for the ALT stimuli: the 1→0 transition in black and 0→1 transition in gray. A repeated-measures bootstrap analysis (see METHODS) revealed significant amplitude differences between the two transition directions at 66–100, 178–248 and 298–424 ms after change onset in the right hemisphere and at 126–176 and 298–432 ms after change onset in the left hemisphere. This latter time interval (298 ms after onset), which is not shown in Fig. 4*B*, corresponds to the sustained response, mentioned above, exhibited by uncorrelated noise but not correlated noise (Fig. 5).

Aside from this overall amplitude difference between ALT 1→0 and 0→1 transitions, it is clearly visible that the temporal/morphological difference observed for CHANGE stimuli is not apparent. ALT transitions, in both directions, evoke similar response dynamics. The repeated-measures bootstrap analysis above revealed no significant rise-time differences between conditions. An additional repeated-measures ANOVA on peak

latencies (defined as the time with maximum amplitudes in the 0–100, 100–150, and 150–300 ms time intervals) with time-window, condition, and hemisphere as factors revealed no significant effects.

Both transition directions exhibit a first deflection, with an M50-like magnetic field distribution at ~80 ms after transition (Fig. 4*B*, *a* and *a**). This is followed by a series of noisy peaks, without a clear auditory dipolar pattern. However, in the 0→1 condition, a peak with a clear M100 distribution that is consistent across listeners, appears at ~140 ms after transition (Fig. 4*B*, *b**). A third deflection, with a M150-like magnetic field pattern, dominates the response in both conditions (Fig. 4*B*, *c* and *c**). Although there appears to be a latency difference between the *c* and *c** peaks in the average plot, this was found to not be statistically significant across participants (repeated-measures ANOVA on peak latencies with hemisphere and transition direction as factors). Overall, although we did not see clear magnetic M50-M100-M150/P1-N1-P2 patterns for these deflections as reported by Dajani and Picton (2006), the general similarity between dynamics of responses to the two transition directions is
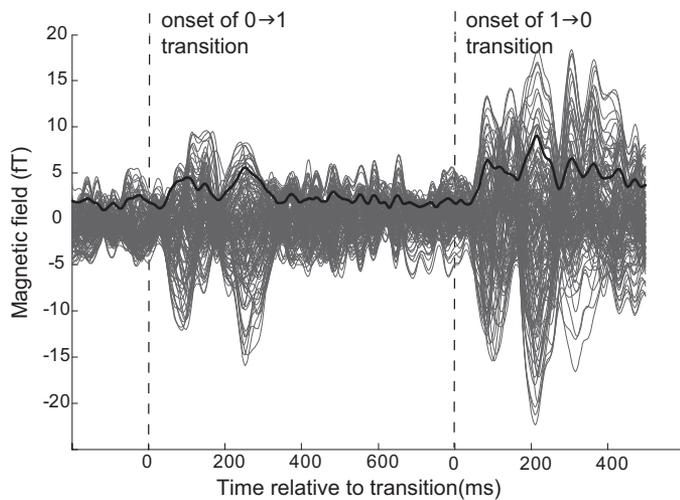
FIG. 5. Grand-average (average over all subjects for each of 156 channels; in gray) of evoked auditory cortical responses to the 2 transition directions in the ALT context. RMS over all channels is plotted in black. Transitions to uncorrelated noise (1→0) evoke higher response amplitudes. Both transition directions exhibit a 1st deflection at ~80 ms after transition, with a characteristic M50-like magnetic field distribution (Fig. 4B, a and a*), followed by another deflection at ~200 ms after transition (Fig. 4B, c and c*). Subsequently, correlated noise activity shows a return to baseline, whereas uncorrelated noise exhibits a slowly attenuating sustained response.

consistent with their findings, and subtle differences can be attributed to the complementary blind-spots of the EEG and MEG techniques and differences in analysis.

Comparison between CHANGE and ALT responses

A comparison of first peak latency in the 0→1 and 1→0 ALT transitions (Fig. 4B, a and a*) and the 1→0 CHANGE transition (Fig. 4A, a) revealed no differences between conditions. We also found no difference between peak latencies between 100 and 180 ms after change (corresponding to the M100 deflection) in the 0→1 and 1→0 ALT transitions (Fig. 4B, b and b*) and the 0→1 CHANGE transition (Fig. 4A, b*); however, a +30-ms latency difference was found between the third peaks in the ALT transitions (Fig. 4B, c and c*) and the third peaks in the CHANGE transitions (Fig. 4A, c and c*). A repeated-measures ANOVA on third peak latency, with hemisphere, stimulus context, and transition direction as factors, revealed only a main effect of stimulus context [$F(1,6) = 14.84$ $P = 0.008$].

The comparison of Fig. 4, *A* and *B,* shows that the dynamics of responses to the 1→0 transition in both ALT and CHANGE are fairly similar; however, the opposite transition, 0→1, evokes quite different activation patterns in the two stimulus contexts. Whereas the first response peak observed in the CHANGE context (M100-like response; Fig. 4A, b*) occurs at ~140 ms after onset, the same transition in the context of ALT stimuli (Fig. 4B, a*) shows a first deflection peak ~90 ms earlier (with an M50-like magnetic field distribution; Fig. 4, *A* and *B*, dashed squares).

A possible explanation for such a pattern is that the enhanced amplitude of the M100 in some conditions is a side effect of the lack of an M50 peak in those same conditions. These data sets do not allow us to address this interpretation: We cannot distinguish whether the amplitude of the M100-like

response in the 1→0 CHANGE transition (as well as in both transition directions in the ALT context) reflects mutual cancellation between the source of the M50, and the opposite polarity source that causes the M100, or whether it reflects a genuine modulation of the M100 generator. We note, however, that related studies (Chait et al. 2007; unpublished data), in which we manipulated the statistical properties of stimulus transitions, revealed that transition-related M50 and M100 responses are independently modulated by different properties of the transition, suggesting a functional dissociation between their generators.

DISCUSSION

Responses to CHANGE stimuli exhibited an asymmetry in temporal dynamics and magnetic field morphology depending on the direction of change (Fig. 4A). The first observed peak for the 1→0 condition occurs ~90 ms earlier than the first observed peak in the 0→1 condition (at ~940 ms) and with an opposite polarity, suggesting the involvement of different neural substrates. This electrophysiological latency difference mirrors behavioral response time differences to the same stimuli (Chait et al. 2005). On the other hand, responses to both change directions (1→0 and 0→1) in the ALT stimuli, while exhibiting a general amplitude difference between transition directions, did not differ significantly in their temporal dynamics and magnetic field morphology (Fig. 4B; see also Dajani and Picton 2006). The consequence of this difference between CHANGE and ALT is that the response to the 0→1 transition in the ALT context starts much earlier (~90 ms) than in the CHANGE context and with an opposite magnetic field distribution.

The IAC transitions within the ALT and CHANGE stimuli are physically identical. What is different is the broader stimulus context (>800 ms) within which these transitions are presented. The different cortical response patterns observed in this study for ALT and CHANGE stimuli, and specifically for the 0→1 transition, indicate that as early as 50 ms after onset, the same physical transition is processed differently, depending on the longer-term stimulus environment (see also Dyson et al. 2005; Ulanovsky et al. 2003, 2004).

One obvious difference is related to the fact that CHANGE stimuli were short and presented amid silent intervals, whereas ALT stimuli contained few onsets and offsets. Consequently, there are large stimulus onset/offset responses in the CHANGE condition that do not occur in the ALT condition. Seither-Preisler et al. (2004) used signals similar in structure to our 0→1 CHANGE stimuli to study the effect of onset responses on transition-related responses. Their stimuli, containing transitions between noise and iterated rippled noise (IRN) segments, evoked transition responses that are identical to those evoked by our 0→1 CHANGE stimuli (no early M50 response, 1st deflection consisting of a late M100 peak; see also Chait et al. 2007 for a discussion of this similarity). They reported that shortening the interval between stimulus onset and the transition affected the amplitude of the transition-related M100 response; however, there was no evidence of an associated emergence of an earlier transition-related M50 response, as we see in the 0→1 ALT stimuli here. It is therefore unlikely that the presently observed differences between the 0→1 transition

in the ALT and CHANGE contexts were caused by an interaction with stimulus onset generators.

We hypothesize that the relevant stimulus context difference that may have contributed to the divergence of responses to ALT and CHANGE transitions in this study is the fact that ALT transitions were regular and predictable, whereas CHANGE transitions were not. We interpret the processing asymmetry observed for CHANGE stimuli as reflecting different temporal integration requirements in the process of change detection (see also Chait et al. 2005, 2007). Binaural disparity is hypothesized to be revealed centrally by a process akin to subtraction of the signals at the two ears (Durlach 1963). For interaurally correlated noise, the result of this subtraction would be a constant value of zero, whereas interaurally uncorrelated noise results in a randomly fluctuating value. Detection of a transition from the former to the latter can occur rapidly, by detecting the first waveform sample for which interaural difference differs from zero. Detection of the opposite (0→1) transition necessarily involves some form of temporal integration to distinguish the onset of the series of "zeros" evoked by interaurally correlated noise from a spurious zero caused by random fluctuations in uncorrelated noise. The early deflections observed at ~70 ms after transition in the 1→0 condition may reflect the output of a minimal integration window, representing the integration that occurs at subcortical and early cortical processing stages. In contrast, the 0→1 transition requires longer integration, which seems to be provided by a distinct neuronal population, giving rise to a later response. Supporting evidence for this interpretation comes from closely parallel response characteristics observed in another study that measured MEG responses evoked by transitions between constant tones and random sequences of tone pips (Chait et al. 2007). Those stimuli were specifically designed to mimic the abstract properties of the CHANGE stimuli used here—a transition between disorder (or random fluctuation) and order (or constancy)—while changing the acoustic properties completely (narrowband vs. broadband, monaural vs. binaural, stationary vs. fluctuating). The similarity indeed suggests that we may be tapping, in both cases, the same "acoustic edge detection" computation.

Given the above interpretation, the fact that ALT stimuli evoke different response patterns suggests that they involve a different kind of processing—not change detection per se. In the case of CHANGE stimuli, the occurrences of IAC edges are unpredictable and need to be derived from the input—the system is performing a change detection task. The fact that 0→1 transitions in the ALT case were processed ~90 ms faster than in the CHANGE case suggests that, when change is predictable, the system learns to use this knowledge and expect the occurrence of the next transition, resulting in faster responses. Note that predictability does not necessarily imply the involvement of top down conscious processing. Rather, the build-up of predictions expected from a specific auditory scene can also characterize relatively low-level mechanisms that preattentively acquire models of the environment (Dean et al. 2005; Ulanovsky et al. 2003, 2004).

This design cannot identify whether these effects are caused by listeners' conscious perception of the stimuli (as noted in METHODS above, the transitions in the 2 contexts have quite different perceptual qualities) or whether the effects of adjustment to stimulus environment are bottom-up driven (we note,

however, that in all cases, the task performed by the listeners was unrelated to change in IAC). Nevertheless, the results indicate that this affects relatively early auditory cortical responses (as early as the M50 response) that are hypothesized to originate from inside or near primary auditory cortex (Yvert et al. 2001).

We do not yet understand the specific computations these different responses reflect, nor how the transition-related responses that are the focus of this study are related to the more commonly studied MEG/EEG auditory onset responses. However, these data suggest that the generators of responses as early as 50 ms after transition cannot be explained as operating exclusively on the physical aspects of stimuli (Rupp et al. 2002) and are already affected by the long-term stimulus context (our stimuli repeated at a rate of 800 ms, which is probably too long for explanations in terms of simple adaptation).

Beyond the specific issue of interaural correlation, these results show that methodological choices (and constraints) regarding which stimuli to use and the manner in which they are presented to the listeners can have severe effects on the resulting brain activity, and by extension, on the conclusions one ends up drawing from the data. Unexpectedly, this is so even for acoustically simple stimuli (white noise) and at latencies associated with low-level cortical processing.

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