Middle Latency Auditory-Evoked Fields Reflect Psychoacoustic Gap Detection Thresholds in Human Listeners

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1Section of Biomagnetism, Department of Neurology, University of Heidelberg, 69120 Heidelberg; 2Institut für Physik, Medizinische Physik, Universität Oldenburg, 26111 Oldenburg; and 3MEGIS Software GmbH, 82166 Gräfelfing, Germany

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Rupp, André, Alexander Gutschalk, Stefan Uppenkamp, and Michael Scherg. Middle latency auditory-evoked fields reflect psychoacoustic gap detection thresholds in human listeners. J Neurophysiol 92: 2239–2247, 2004; 10.1152/jn.00163.2004. The resolution of the temporal processing in the primary auditory cortex (PAC) was studied in human listeners by using temporal gaps of 3, 6, 10, and 30 ms inserted in 100-ms noise bursts. Middle latency auditory-evoked fields (MAEFs) were recorded and evaluated by spatio-temporal source analysis. The dependency of the neurophysiological activation at about 37 ms (P37m) on the temporal position of the gap was investigated by inserting silent periods 5, 20, and 50 ms after noise burst onset. The morphology of the waveforms evoked by the gap showed that the MAEFs were largely determined by the on-response to the noise burst following the gap. The comparison of the source waveforms revealed two major effects: 1) the amplitudes of the MAEFs increased with longer gap durations and 2) the amplitudes increased with the length of the leading noise burst. When the gap was inserted after 50 ms, a significant deflection of the collapsed left and right hemisphere data was observed for all gap durations. The P37m amplitude failed to reach significance for the shortest gap duration of 3 ms when the gap occurred after 20 and 5 ms. These neumagnetically derived minimum detectable gap responses closely resembled psychoacoustic thresholds obtained from the same subjects (leading hemisphere data was observed for all gap durations). The P37m amplitude increased with longer gap durations and showed that the MAEFs were largely determined by the ON-response to the noise burst following the gap. The comparison of the source waveforms revealed two major effects: 1) the amplitudes of the MAEFs increased with longer gap durations and 2) the amplitudes increased with the length of the leading noise burst. When the gap was inserted after 50 ms, a significant deflection of the collapsed left and right hemisphere data was observed for all gap durations. The P37m amplitude failed to reach significance for the shortest gap duration of 3 ms when the gap occurred after 20 and 5 ms. These neumagnetically derived minimum detectable gap responses closely resembled psychoacoustic thresholds obtained from the same subjects (leading noise burst, 50 ms: 2.4 ms; 20 ms: 3.2; and 5 ms: 5.3 ms). The correspondence between psychoacoustic thresholds and the cortical activation indicates that the recording of MAEFs provides an objective and noninvasive tool to assess cortical temporal acuity.

INTRODUCTION

A prerequisite for the reliable perception of speech and music is the ability of the auditory cortex to process rapid amplitude fluctuations of acoustic signals. An efficient and commonly used psychoacoustic measure to assess the temporal acuity of the auditory system is the gap detection paradigm. In this task, two relatively long broadband noise bursts are presented, one of which contains a brief silent period in the middle of the burst (late-gap detection). The listener has to indicate which burst was interrupted by a gap. In such a discrimination task, typical thresholds around 2 ms are reported (Eddins and Green 1995). When the leading and trailing noise burst share the same spectral content, this task is referred to as a “within-channel” discrimination task.

It is known from several studies that the temporal position of the gap has a significant influence on detection thresholds (Penner 1977; Phillips et al., 1998; Schneider and Hamstra 1999; Snell and Hu 1999). When the position of the temporal gap is moved toward the onset of the noise burst (early-gap detection), psychoacoustic thresholds increase significantly compared with late-gap detection tasks, where the silent period occurs after several hundred milliseconds. However, Forrest and Green (1987) observed just a slight increase in performance when the temporal position of the gap was moved from about 10 to 30 ms after stimulus onset.

Compared with the large number of psychoacoustic investigations on gap detection, only a few electrophysiological studies have been carried out. Walton et al. (1997) investigated the relationship of behavioral late-gap thresholds and neural correlates in the inferior colliculus (IC) in mice using broadband noise. They were able to show a close correspondence between the minimum gap detection threshold of 1–2 ms derived from single-unit poststimulus time histograms (PSTHs) of phasic-type (ON, ON-OFF) and primary-like cells with behavioral thresholds of the same animals of about 2 ms. In an experimental setting with comparable stimuli, Guo and Burkard (2001) observed neural gap detection thresholds in the IC of anesthetized chinchillas derived from auditory evoked potentials (AEPs) of about 0.75 ms and slightly higher cortical thresholds of about 1.8 ms. Furthermore, they showed that silent periods of <8 ms did not evoke an off-response to the leading noise burst.

Evidence that mainly cortical processes play a crucial role as the limiting factor of temporal acuity is given by Poth et al. (2001). They observed reduced brain stem wave V magnitudes and longer latencies evoked by the trailing noise burst in older compared with younger adults, although both groups exhibited comparable responses to the onset of the leading noise burst. These observations parallel earlier findings of Boettcher et al. (1996), where auditory brain stem responses (ABR) responses in older Mongolian gerbils differed from the responses of younger animals. In contrast, recordings of compound action potentials of the auditory nerve did not reveal any differences between younger and older animals. Further experimental evidence that support the importance of auditory cortex (AC) in gap detection tasks is given by the observation that the selective damage of inner hair cells after the administration of carboplatin resulted only in a minor elevation of neural gap thresholds in IC and AC (Guo and Burkard 2001), whereas lesions in auditory cortex significantly deteriorated gap thresholds (Ison et al. 1991; Kelly et al. 1996).

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Recently, Eggermont (1995, 1999, 2000) addressed the question of different processes evoked in late- and early-gap detection conditions in a series of single-unit (SU) and multi-unit (MU) recordings and local field potentials (LFPs) in the primary auditory cortex, the anterior auditory field (AAF), and the secondary auditory cortex (AII) of cats. Neural gap thresholds observed in the auditory cortex depended strongly on the duration of the leading noise burst. When the pause was placed 500 ms after stimulus onset (late-gap condition), thresholds in AI and AII were around 11 ms. When the silent period occurred 5 ms after stimulus onset (early-gap condition), an on-response by the trailing noise burst was evoked if the gap duration exceeded 40 ms. However, the analysis of the distributions of the MU recordings exhibited a large range of individual MU gap thresholds from 10 to 60 ms (Fig. 7).

Based on the relation of the neural minimum gap detection values that reflect behavioral data from human listeners, Eggermont assumed that AI and the AAF play a dominant role in early-gap detection tasks. Since, in these neurophysiological studies, the responses from AI and the AAF did not differ for within-channel gap detection tasks and LFPs reflected the findings of MU and SU recordings, we hypothesized that neuromagnetic recordings in human listeners provide a reliable method to assess the temporal resolution of the human primary auditory cortex noninvasively.

Previous neuromagnetic investigations of the middle latency auditory evoked components revealed that the magnitude of the P37m closely resembled psychoacoustic thresholds in a late-gap detection task (Rupp et al. 2002). Silent periods of 3 ms in the middle of a 600-ms broadband noise burst evoked a significant P37m deflection. This observation corresponds to the psychoacoustic thresholds observed for the same subjects of about 2 ms. Thus it was concluded that the P37-response provides an objective measure to assess gap detection thresholds.

The objective of this study was to investigate the middle latency auditory-evoked field (MAEF) responses in an early-gap detection task with different durations of the leading noise burst. We investigated whether the magnitude of the specific middle latency complex evoked by the gap would reflect behavioral data, especially if the placement of the silent period toward the onset of the noise bursts results in diminished responses of the auditory cortex.

To provide a comparable experimental setting according to the investigations of Eggermont, silent periods of 3, 6, 10, and 30 ms were inserted after 5, 20, and 50 ms of the noise burst onset. Furthermore, psychoacoustic thresholds were obtained in the same subjects to investigate the relationship between neurophysiological and perceptual thresholds and to allow for a comparison with thresholds published in the psychoacoustic literature.

METHODS

Subjects

Twelve subjects (3 females, 9 males; age, 22–40 yr) participated in this study. Eleven subjects had normal hearing (audiometric thresholds better than 20 dB HL for frequencies of 250–8,000 Hz in octave steps), and they had no history of peripheral or central hearing disorders or neurological deficits. One subject showed thresholds of 20 dB HL or better for frequencies up to 2 kHz and a high frequency hearing loss with a threshold of 45 dB HL (right ear), respectively, 35 dB HL (left ear) at 4 kHz, and 40 dB HL (right ear), respectively, 20 dB HL (left ear) at 8 kHz. Since this reduced sensitivity was within the attenuated frequency response of the ER3 devices, the data of this listener were not excluded from the study. All subjects were familiar with magnetoencephalography (MEG) recording sessions and gave informed consent after the aim of the study was explained. The experiment was part of a larger research project on temporal processing of the auditory system, which was approved by the local ethics committee of the University of Heidelberg.

Stimuli

The stimuli were white noise bursts with a total length of 100 ms. All stimuli were generated on-line (“running noise”) to eliminate artifacts due to the fine structure of the sounds. The onsets and offsets of the noise bursts were tapered by a 1-ms Hanning gate. Silent periods of 3, 6, 10, and 30 ms were inserted after the leading noise burst. To investigate the influence of the temporal position of the gap, the duration of the leading noise burst was studied in three separate recording sessions, where the gap occurred after 5, 20, and 50 ms. These conditions are indicated by the labels L5, L20, and L50, respectively. The offset of the leading noise burst and the onset of the trailing noise burst were also windowed by a 1-ms Hanning gate. In each session, continuous noise bursts without any gap served as a control stimulus. A 1-ms Hanning gate was imposed at the beginning and the end of this 100-ms stimulus. An interstimulus interval (ISI) of 250 ms with an additional jitter of 50 ms was employed to separate the noise bursts from each other. Within sessions, stimuli were presented in a pseudo-random order.

Stimuli were generated digitally with a sampling frequency of 44.1 kHz. D/A-conversion was carried out using a Soundblaster soundcard connected to a Pentium II computer. The sounds were presented diotically with a custom-made sound list processor at a level of 65 dB SPL (linear) via ER-3 earphones (Etymotic Research) connected to 90-cm plastic tubes and foam earpieces. The level was adjusted using a Bruel and Kjaer sound level meter type 2203 equipped with an artificial ear (2 cc) type 4152.

Data recording

Prior to recording, the head position was determined using four coils attached to the scalp. Additionally, 32 surface points on the scalp were digitized to match the MEG head coordinate system with individual T1-weighted MRI. For all subjects, MRI scans were available. The images were obtained using a Siemens Symphony 1.5 T scanner. Three-dimensional (3D) reconstructions of the 176 (1-mm voxel) slices were computed using the BrainVoyager software (version 4.4, Brain Innovation, Maastricht, The Netherlands).

Magnetic fields were acquired with a Neuromag-122 whole head MEG system (Ahonen et al. 1993) inside a magnetically shielded room (IMEDCO). Subjects sat in an upright position and were watching a silent movie of their own choice. They were instructed not to pay attention to the acoustic stimuli. MEG registration lasted for about 30 min in each session. Data were recorded at a sampling rate of 1,000 Hz and filtered on-line with a bandwidth of 0.01–330 Hz. During off-line analysis, single sweeps with an MEG signal exceeding a peak level of 8,000 fT or with a gradient of 800 fT/sample were rejected prior to averaging. For each stimulus condition, about 830 single sweeps covering the range from 50 ms before to 300 ms after stimulus onset were averaged.

Source analysis

Spatio-temporal source modeling (Scherg 1990; Scherg and von Cramon 1986a) was applied using the BESA2000 software package (MEGIS Software, Gräfelfing, Germany). The center of the spherical
indicate whether the derived in an adaptive two-alternative forced-choice task using a respectively. After an initial training run, this procedure was carried 100 ms. The step size was varied using a factor of 0.8 or 1.2, silent period by pressing a button. The duration of the noise bursts was, gap detection thresholds were obtained for each leading noise burst, and orientations of the three independent source models in a second step and used these mean parameters as a final model for all 15 experimental conditions (length of leading noise burst: 50, 20, and 5 ms and gaps of 0, 3, 6, 10, and 30 ms). These steps were computed for each subject individually. Source waveforms of all conditions were derived from this model based on the assumption that the P37m is evoked by the same generators within Heschl’s gyrus, i.e., the location and orientation of the equivalent dipole remain constant.

To separate the small middle latency P37m response evoked by the on-response to the noise burst following the gap from the large overlapping P1 and N1 responses elicited by the leading noise burst, we band-pass filtered the source waveforms using a digital second-order Butterworth zero-phase filter with a passband from 20 to 80 Hz (MATLAB 6.0). Grand average source waveforms were computed for each condition and both hemispheres separately. Finally, difference waveforms were computed to derive the specific response elicited by the gap. The source waveform of the control condition without a gap was subtracted from the source waveforms of the gap conditions. To assess the significance of the resulting P37m amplitude evoked by the second noise burst, a permutation test for waveform differences, introduced by Blair and Karniski (1993), was applied. This distribution-free method produces \( P \) values without any assumption about a particular correlation structure of the waveforms. The statistic was based on the entire waveform, including the negative deflection preceding the P37m, the positive peak, and the following negative deflection of the MAEF complex as indicated by the vertical lines in the L20 condition in Fig. 4. The output of this procedure is a single multivariate statistic, denoted as \( t \)-sum. Critical \( t \) intervals for the P37m latencies were computed in a separate statistical evaluation using a bootstrap resampling procedure (Efron and Tibshirani 1993) since the individual source waveforms did not allow to derive the P37m peak in most subjects for conditions with short gap durations reliably. Therefore the latency and amplitude of the P37m was determined for each of the 1,000 independent bootstrap samples generated by sampling with replacement 12 times from the original data set. The critical \( t \) intervals of the latencies and amplitudes were derived from the resulting distribution of the parameters.

After computing the dipole fits, the dipole locations of the model were projected onto the individual 3D MRI reconstructions and transformed into coordinates according to the stereotactic space of Talairach and Tournoux (1988). The mean dipole positions of all subjects were finally projected onto the axial map provided by Leonard et al. (1998) to visualize the average position of the bilateral P37m dipole.

Psychoacoustics

After all three MEG recordings were completed, psychophysical gap detection thresholds were obtained for each leading noise burst length condition (L50, L20, and L5) separately. Thresholds were derived in an adaptive two-alternative forced-choice task using a three-down/one-up procedure (Levitt 1971). At the beginning of each run, the initial gap duration was set to 50 ms. The subject had to indicate whether the first or second noise burst of a pair contained a silent period by pressing a button. The duration of the noise bursts was 100 ms. The step size was varied using a factor of 0.8 or 1.2, respectively. After an initial training run, this procedure was carried out without feedback and ended after 14 reversals. The threshold of each run was determined by averaging the last eight reversals of each session. The final thresholds were based on two runs for each leading noise burst condition. Friedman’s nonparametric ANOVA for repeated measurements (Sprent and Smeeton 2001) was employed to perform the statistical comparisons of the thresholds using the SAS software (version 8). All analyses included pairwise comparisons with simultaneously adjusted \( \alpha \)-errors based on the Holm procedure (Holm 1979).

RESULTS

Source analysis

Principal components analysis (PCA) of the individual gradient waveforms evoked by the control condition confirmed that, for 11 of 12 subjects, the first component accounted for \( >80\% \) of the variance of the initial P37m. The contribution of the second component was \( <10\% \). Thus a dipole solution with one equivalent dipole in each hemisphere served as an adequate spatio-temporal model for the P37m. The projection of the equivalent dipoles for each leading noise burst condition, as well as the final model based on the mean coordinates and orientations (Fig. 1, white dots) onto the probabilistic map of Leonard et al. (1998), showed that the dipole sources of the BESA models were located bilaterally in the center of Heschl’s gyrus (Fig. 1).

The resulting grand-average source waveforms of the unfiltered data are shown in Fig. 2. The comparison of the left and right hemisphere data exhibited a very similar pattern for all conditions. In the no-gap conditions, the waveforms showed a typical middle latency on-response with an initial prominent P37m followed by a second positivity at about 63 ms. The noise burst offset was followed by an off-response that overlapped with the P200m due to the short duration of the noise bursts. The reliability of the middle latency on-response is shown by the source waveforms of the control condition without a gap that was recorded in the L50, L20, and L5 conditions separately. The arrows in Fig. 2 point at the specific responses evoked by the gap. Compared with the overall on-response, these deflections exhibit a rather small amplitude. However, it shows an increasing magnitude for longer gap durations for all leading noise burst conditions. To separate the specific middle latency complex evoked by the gap from the overlapping late AEF activity evoked by the onset (Fig. 3), we applied a zero-phase band-pass filter of 20–80 Hz.

![FIG. 1. Mean Talairach coordinates of the equivalent dipoles for the “no-gap” stimulus of all 3 experimental leading noise burst conditions based on data of all 12 subjects. Talairach coordinates are projected onto the probabilistic map provided by Leonard et al. (1998). The cross represents the mean values of the 3 dipole fits; the length of the error bars indicates SE. The mean coordinates locate near the central aspect of Heschls gyrus in both hemispheres.](http://jn.physiology.org/doi/fig/10.22033/jn.2241)
The visual inspection of the filtered source waveforms evoked by noise bursts with a gap that occurred 50 ms after onset clearly showed these additional peaks following the P37m-P63m complex. In the L20 condition, the additional peak followed the ON-response and is clearly visible for the 6-ms gap duration. In the L5 condition, the ON-response and the gap response merge, and it is difficult to separate the effect of the 3- and 6-ms gap.

Subtracting the response of the control condition (continuous 100-ms noise bursts) from the gap conditions resulted in waveforms representing the specific MAEFs elicited by the gap. The difference waveforms that are aligned to the onset of the noise following the gap are shown in Fig. 4. The comparison of the MAEF morphologies with the onset response in the control condition (‘no gap,’ plotted as a gray line above the difference waveforms) indicates that the gap response is largely determined by the middle latency ON-response to the trailing noise burst that occurred at about 37 ms. Across all leading noise burst conditions, the latencies and amplitudes evoked by the noise burst without a gap exhibited comparable values (Fig. 5).

It should be noted that the MAEF morphology of the specific gap response in the L50 condition with long gap durations is distorted due to the temporal overlap of the off-response of the control condition and the ON-response of the trailing noise burst. However, this overlap occurs for gap durations that are far above the neuromagnetic and psychoacoustic thresholds of the L50 condition.

As was expected from animal and behavioral data, the current data showed that longer gaps are needed to evoke a significant P37m when the duration of the leading noise burst was decreased.

The detailed statistical analysis of the P37m ON-response to the trailing noise burst is shown in Table 1. Table 1 includes the statistics of the pooled data of the left and right hemispheres as well as separate tests for each hemisphere. The analysis of the pooled data showed that all gaps of the L50 condition, including the shortest silent interval of 3 ms, evoked a significant P37m. However, when the duration of the leading noise burst was reduced, the P37m magnitude decreased and failed to reach significance for 3-ms gaps in the L20 and L5 conditions. In both of these conditions, gaps of 6 ms resulted in a significant response. The additional analysis for the left and right hemisphere data showed a very similar pattern except that the test for differences of the right hemisphere source waveforms failed to reach significance for 3-ms gaps in L50 and for 6-ms gaps in L5. Since this result might indicate a global difference of the left and right P37m deflection, posthoc comparisons of the left and right hemisphere waveforms were carried out to check for significant differences of the original waveforms. As for the tests described above, the permutation test was based on the critical interval including the P37m with its negative side-bands. However, neither for the gap durations of 3 and 6 ms in the L50 nor for the durations of 3 and 6 ms in the L5 condition were any significant differences in the source waveform magnitude between hemispheres observed (L50, gap 3 ms: subtr = 16.73, not significant; L50, gap 6 ms: not significant...
paired comparisons with an adjusted $\alpha$-error indicated that thresholds differed significantly between each of the leading noise burst durations ($L50$ vs. $L5$: $P < 0.001$; $L50$ vs. $L20$: $P \leq 0.05$; $L20$ vs. $L5$: $P < 0.05$).

**Discussion**

The results of the study can be summarized as two main findings. First, the reduction of the leading noise burst duration resulted in larger neuromagnetic gap thresholds derived from MAEF source waveforms, and for all conditions, we observed increased amplitudes for longer gaps. Second, the pattern of increasing psychoacoustic thresholds for decreasing leading noise burst durations reflected the observed neuromagnetic gap thresholds.

**Spatio-temporal source modeling**

All neuromagnetic analyses were based on virtual source waveforms (Scherg and von Cramon 1986) derived from a spatio-temporal source analysis with one equivalent dipole in each hemisphere. PCAs of the gradiometer waveforms for each subject indicated that the inclusion of further dipoles would not result in a significant improvement of the model for the P37m.

Although such a spatio-temporal source model is a simplification of specific temporally overlapping physiological events in different laminae in the central aspect of Heschl’s gyrus, it is in line with earlier reports of a model for the middle latency far field data (Scherg 1990; Scherg and von Cramon 1986a). These reports showed that the MAEF complex evoked by transient sounds could be described sufficiently by a tangential and a radial dipole in each hemisphere. However, since the MEG does not record activity elicited by radially oriented sources, a

![FIG. 4. Difference source waveforms obtained by subtracting the response of the control condition without a gap (0 ms) from all 4 gap conditions to extract the specific on-response evoked by onset of the trailing noise burst following the silent period. All source waveforms are aligned to the onset of the trailing noise burst after the gap. Gray source waveforms on top of each run represent response to the control stimulus without a gap. Note the increasing amplitude of the ON -response with increasing gap duration. Vertical lines in the middle row depict the critical interval used for the statistical evaluation of the P37m summarized in Table 1. Note that the difference of the specific gap response in the L50 condition with long gap durations is due to the temporal overlap of the OFF-response of the control condition and the ON-response to the 2nd noise burst.](http://jn.physiology.org/)

![FIG. 5. MAEF peak amplitudes of the P37m evoked by onset of the leading noise burst (A) and onset of the trailing noise burst following the gap as a function of gap duration (B). Vertical lines indicate the bootstrap-based Student’s $t$-intervals. All parameters are based on the average of the left and right hemisphere data. The $t$-intervals indicate that amplitudes in all conditions with a 50-ms leading noise burst represent significant deflections, whereas for shorter leading noise bursts, the response failed to reach significance for the shortest gaps of 3 ms. C and D: latency of this MAEF on-response to the leading and trailing noise burst. Amplitude and latency measures of the overall on-response show the high replicability of the P37m.](http://jn.physiology.org/)
solution with one equivalent dipole in each hemisphere was regarded as an adequate model to describe the initial P37m ON-response. Furthermore, no significant activity has been observed in MAEF transient and periodic responses in the antero-posterior tangential direction orthogonal to the main orientation of the P37m that corresponds to the P37m following noise onset (Gutschalk et al. 1999; Schneider et al. 2002).

Several findings indicate that the P37m is evoked near or at the level of primary auditory cortex. First, the mean location of the left and right dipolar sources was near the medial portion of Heschl’s gyrus when referred to the probabilistic map provided by Leonard et al. (1998). This corresponds to the coordinates of the left and right hemispheres. The waveform morphology elicited by broadband noise bursts parallels the early pattern of the late AEPs in the same hemisphere (Scherg and von Cramon 1986b, 1989). In contrast, patients with extended lesions in the auditory cortex showed an overall decrease of middle and late auditory evoked potentials in the affected hemisphere. This specific behavior indicates that MAEPs reflect the initial activation of the primary auditory cortex.

The comparison of grand mean source waveforms of the control condition without a gap revealed a high replicability of the MAEF responses evoked by broadband noise bursts in the left and right hemispheres. The waveform morphology elicited by broadband noise bursts parallels the early findings of Hari et al. (1987) and Joutsiniemi et al. (1989) and the responses of a closely related late-gap detection task (Rupp et al. 2002).

The neurophysiological gap thresholds of this study are very similar to the initial ON-response of the noise burst. As shown for the grand mean difference waveforms in Fig. 4, a prominent OFF-response that is elicited by noise burst offsets could not be identified. This is in agreement with the observations of Eggermont (1999) and Guo and Burkard (2001), who reported that, for shorter temporal gaps, the ON-response was abolished by the ON-response. Therefore in this study, neurophysiological gap thresholds were based on the significance of the ON-response evoked by the trailing noise burst.

**Electrophysiological effects of temporal gap placement**

For the collapsed data of the left and right hemispheres, the neural gap thresholds derived from the significance of the P37m ON-response to the trailing burst showed an increase from 3 to 6 ms when the leading noise burst duration was decreased from 50 to 20 ms. A further decrease of the leading noise burst to 5 ms resulted in smaller responses, but according to the permutation tests, the P37m still indicated a significant response after a gap duration of 6 ms. Thus the small neuro-magnetic gap threshold of the L50 condition is comparable to

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**Table 1. Multivariate t-statistic (omnibus test) based on the permutation test (Blair and Karniski 1993) of the P37m deflection for the difference waveforms as shown in Fig. 3 of both hemispheres for all gap conditions**

<table>
<thead>
<tr>
<th>Gap duration, ms</th>
<th>Left Hemisphere</th>
<th>Right Hemisphere</th>
<th>Left + Right/2</th>
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<tbody>
<tr>
<td></td>
<td>sumt</td>
<td>maxt</td>
<td>sumt</td>
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<tr>
<td>Leading Noise Burst Duration 50 ms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>65.13***</td>
<td>9.20***</td>
<td>24.54**</td>
</tr>
<tr>
<td>6</td>
<td>55.01***</td>
<td>4.50**</td>
<td>61.80**</td>
</tr>
<tr>
<td>10</td>
<td>70.23***</td>
<td>4.20**</td>
<td>67.15**</td>
</tr>
<tr>
<td>30</td>
<td>48.61**</td>
<td>-3.41*</td>
<td>47.57**</td>
</tr>
<tr>
<td>Leading Noise Burst Duration 20 ms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>14.73**</td>
<td>-1.23**</td>
<td>23.50**</td>
</tr>
<tr>
<td>6</td>
<td>45.11***</td>
<td>-5.47***</td>
<td>41.29**</td>
</tr>
<tr>
<td>10</td>
<td>57.86***</td>
<td>-4.78***</td>
<td>41.38**</td>
</tr>
<tr>
<td>30</td>
<td>85.69***</td>
<td>5.64**</td>
<td>62.19**</td>
</tr>
<tr>
<td>Leading Noise Burst Duration 5 ms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>12.85**</td>
<td>-1.47**</td>
<td>29.84**</td>
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</tr>
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<td>-5.73**</td>
<td>42.78**</td>
</tr>
<tr>
<td>30</td>
<td>48.52***</td>
<td>-3.40**</td>
<td>37.05**</td>
</tr>
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The critical interval included the most negative deflection before and after the positive peak. Due to this selection, negative and positive differences contributed to the multivariate statistic. The max values represent the largest individual $t$ values within the interval. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. 

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**Fig. 6. Individual psychometric gap detection thresholds for all 12 subjects as a function of the leading noise burst duration (gray lines). Black line represents mean thresholds. Vertical bars indicate SE. Individual data clearly show that all subjects exhibited larger thresholds in the early-gap condition (L5) compared with the late-gap condition (L50).**
the findings of the neuromagnetic late-gap detection study (Rupp et al. 2002), where a significant P37m on-response was derived for 3-ms gaps inserted in the middle of a 600-ms broadband noise burst. Furthermore, the comparison to the late-gap detection responses exhibited only minor differences in the resulting MAEF morphology due to the different total length of the stimuli.

This increase of the neuromagnetic thresholds observed for decreasing leading noise burst durations reflects the behavior of thresholds derived from MU activity by Eggermont (1999, 2000). He first showed that longer gap durations are necessary to evoke an on-response to the trailing noise when the leading noise burst is shortened. However, in comparison with these MU data reported by Eggermont (2000), the neuromagnetic recordings of this study exhibited a completely different behavior. First, the mean neural gap thresholds derived from SU and MU recordings of the cat auditory cortex are about one order of magnitude larger compared with the significance threshold of the P37m on-response of the current data, and second, we found a closer relationship of the difference source waveform morphologies for the different leading noise burst conditions.

In contrast to these early-gap results, Eggermont reported a correspondence of gap-evoked SU, MU, and LFP mean values with human psychoacoustic thresholds when late-gap stimuli were administered. Based on these observations, he concluded that LFPs are a good predictor for the neural representation of temporal features in AI.

Since Eggermont was able to show that the lower tail of MU and LFP distributions in AI reflect behavioral data observed in human listeners, he refers to the lower envelope principle introduced by Parker and Newsome (1998). This principle states that sensory thresholds are determined by a few sensory units that exhibit the lowest thresholds. Eggermont (2000) explains the increasing gap duration function for shorter leading noise burst durations with intrinsic properties of cortical cells.

The recovery functions of the trailing burst onset response, as displayed in Fig. 5, showed that the amplitudes of the P37m response for 10-ms gaps of all leading noise burst conditions did not increase significantly when the gap duration was increased to 30 ms. Thus the similarity of the P37m on-responses following the gap exhibited a closer relationship for short gaps compared with the steep increase of neural gap thresholds from L50 to L5 reported by Eggermont (2000). However, as can be seen in Fig. 4, a complete recovery after a gap duration of 30 ms was not observed in our data. This is in line with the findings of Brosch and Schreiner (1997), who reported average maximal forward masking effects of 143 ms.

Empirical evidence is given that the discrepancies between neurophysiological thresholds in cat auditory cortex on the one hand and psychophysical and neuromagnetic thresholds derived from human listeners on the other hand might be due to the use of anesthetized animals. This view is based on several observations. Zurita et al. (1994) showed that the peak firing rate of cortical SU spikes evoked by white-noise bursts were decreased after the application of ketamine. This rate reduction is in line with the data of Eggermont (1995), who found in the auditory cortex of ketamine anesthetized cats neurophysiological thresholds in a double click paradigm of about 50 ms. This is in contrast to psychoacoustic fusion thresholds in human listeners of about 2–3 ms reported by Scharf and Buus (1986). Even lower thresholds of <1 ms were observed by Krumbholz and Wiegrehle (1999) in a “one-versus-two” discrimination task. These values are closely related to neuromagnetic thresholds derived in a similar task that was conducted to assess the relationship between psychoacoustic thresholds and middle-late latency responses (Rupp et al. 2000). The analysis of the grand-average difference source waveforms in this earlier study showed that the second tone of a pair evoked a small but significant N19m-P30m complex when the tones were separated by silent intervals of 1 and 4 ms. These neuromagnetic thresholds mirror the psychoacoustic lower limits of about 1.5 ms observed in the same subjects. Neurophysiological data that support to a large degree the correspondence of neuromagnetic and single unit responses are provided by Fitzpatrick et al. (1999), who recorded neural responses along the auditory pathway to paired clicks in unanesthetized animals. Although the recovery times increased systematically along the auditory pathway from the auditory nerve to AC, neurons with short recovery times exhibited a significant response with a recovery rate of 50% to the second click when the inter-click-interval (ICI) was about 2 ms.

Similar relationships of the functional properties are given for studies using continuous click trains. Goldstein et al. (1959) found an upper limit of phase-locked evoked potentials in the AC of awake cats around 200 Hz that was substantially decreased after the application of anesthesia. Steinschneider et al. (1998) showed that MU activities and current source densities in awake monkeys exhibited comparable high modulation transfer rates with an upper limit of 100–200 Hz for high best frequency neurons. This observation is in line with data from intracellular recordings provided by de Ribaupierre et al. (1972). They showed that a small fraction of single neurons exhibited an upper limit of locking to clicks of >300 Hz with
a median between 50 and 100 Hz. Comparable rates were found for trains of repetitive 1- to 2-ms noise bursts.

Again, these neurophysiological modulation transfer rates are closely related to neuromagnetic steady-state responses. Gutschalk et al. (1999) used click trains with rates of 32.3–52.6 Hz to deconvolve the N19-P30 complex elicited by every single click and observed only little refractoriness of the response compared with the transiently recorded MAEF. Similar results were found with amplitude-modulated sinusoids compared with single tone pips (Schneider et al. 2002).

However, it is important to note that contrary to the SU, MU, and LFP data reported above, the MEG source activity is recorded on a rather macroscopic level based on the excitatory postsynaptic potentials (EPSPs) of ≥300,000 units (Williamson and Kaufman 1990). Therefore the ensemble excitation might reflect the activity of two groups of neurons: those that fire to the onset of the leading burst and a disjunctive population that fire to the onset of the second burst.

Thus MAEF source waveforms derived from far field recordings do not reflect a one-to-one relationship of current source densities (CSD) or SU or MU activities. Surface-recorded AEs represent the compound sum of current sources and sinks evoked in different laminae (Steinschneider et al. 1992, 1994). Due to this complex generator structure, it is difficult to determine whether the P37m reflects postsynaptic potentials induced by cortical cells in lamina III or if it is driven by thalamo-cortical fibers. However, an extended series of experiments on voice onset times with intracranial recordings in awake monkeys and humans (Steinschneider et al. 1994, 1999) suggests a correspondence between the CSD profiles observed in different laminae and specific deflections recorded at the cortical surface of awake human listeners. Steinschneider et al. (1994) used synthesized syllables to investigate the temporal encoding of VOT in thalamocortical fibers and A1 cells. They found a large positive component around 28 ms in A1 of the monkey. The corresponding laminar CSD profiles show that this P28 is coherent to the second current sink, which is assumed to be partially generated by pyramidal cells in the upper lamina III. Thus the authors suggest that this deflection is equivalent to the positive peak around 40 ms reported by Kaukoronta et al. (1987) that was evoked by vowel onsets. Since this neuromagnetic component is comparable to the on-response to noise bursts of the present data, the P37m very likely represents an early response largely evoked by cortical activity.

The statistical evaluation of the left and right hemisphere data presented in Table 1 revealed a higher temporal resolution for the left hemisphere in the L50 and L5 conditions. This parallels earlier findings on neuromagnetic thresholds in a late-gap detection task (Rupp et al. 2002), where a significant on-response near the perceptual threshold was only observed in the left hemisphere. However, additional posthoc tests to assess the significance of a different P37m of the left and right hemisphere in this study did not reveal any global effects between the original source waveforms. Thus our data do not provide conclusive evidence to support the view of a global left hemisphere advantage in gap detection.

Relation of neural and behavioral gap functions

As expected, the psychoacoustic thresholds of this study were a function of the leading noise burst duration. When the duration of the leading noise burst was decreased, significantly longer gaps were needed for the detection of a discontinuity of the sound. Both the increase of thresholds as well as the increase in variability of these parameters is closely related to the behavioral data of Snell and Hu (1999), which are shown in Fig. 7. They observed the lowest thresholds of about 2 ms for a leading noise burst duration of 40 ms. The decrease of the leading noise burst duration to 20 ms resulted in a significant threshold increase to about 3 ms. These values are comparable to our data. We observed a significant increase from 2.4 to 3.2 ms when the duration of the leading noise burst was reduced from 50 to 20 ms. The gap threshold of 5.3 ms obtained in the L5 condition cannot be compared with the data provided by Snell and Hu since the shortest leading noise burst duration in their study was 10 ms. However, they reported comparable thresholds of 6.8 and 4.2 ms for inexperienced and experienced listeners, respectively, for leading noise bursts of 10-ms duration. Thus it can be concluded that the L5 thresholds of 5.6 ms of the current study are between values that can be expected for experienced and inexperienced listeners. This is in line with the fact that most of our subjects had participated in other experiments on temporal acuity and duration discrimination tasks (Rupp et al. 2000, 2002; Sieroka et al. 2003) on the one hand, but on the other hand, they represented inexperienced listeners in the sense that they were not performing psychoacoustic discrimination tasks on temporal acuity frequently.

Furthermore, Snell and Hu (1999) discussed the influence of attentional effects on gap thresholds. The middle latency AEF data of this study, however, were recorded in sessions when the subjects watched a silent movie of their own choice and did not attend to the auditory stimulation. Nevertheless, a close correspondence between neuromagnetic gap thresholds and psychoacoustic thresholds derived from a 2-AFC task was observed.

In summary, the findings of the current early-gap detection study indicate that neuromagnetic MAEF recordings might serve as a powerful and objective tool to further investigate the effects 1) of age, 2) of long-term training, and 3) of attention on the temporal resolution of the primary auditory cortex noninvasively.

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References

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