

Stimulus intensity affects early sensory processing: Sound intensity modulates auditory evoked gamma-band activity in human EEG

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Abstract

We studied the effect of different sound intensities on the auditory evoked gamma-band response (GBR). Previous studies observed oscillatory gamma activity in the auditory cortex of animals and humans. For the visual modality, it has been demonstrated that the GBR can be modulated by top-down (attention, memory) as well as bottom-up factors (stimulus properties). Therefore, we expected to find a sound intensity modulation for the auditory GBR.

21 healthy participants without hearing deficits were investigated in a forced-choice discrimination task. Sinusoidal tones were presented at three systematically varied sound intensities (30, 45, 60 dB hearing level). The results of the auditory evoked potentials were predominantly consistent with previous studies. Furthermore, we observed an augmentation of the evoked GBR with increasing sound intensity. The analysis indicated that this intensity difference in the GBR amplitude most likely arises from increased phase-locking.

The results demonstrate a distinct dependency between sound intensity and gamma-band oscillations. Future experiments that investigate the relationship between auditory evoked GBRs and higher cognitive processes should therefore select stimuli with an adequate sound intensity and control this variable to avoid confounding effects. In addition, it seems that gamma-band activity is more sensitive to exogenous stimulus parameters than evoked potentials.

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1. Introduction

Synchronous neuronal firing in the range from 30–80 Hz appears to be involved in binding different features of an object so that it is perceived as a single, coherent one (Eckhorn et al., 1988; Singer, 1993; von der Malsburg, 1995). This phenomenon is well investigated for animals and humans in the visual modality (Gray et al., 1989; Singer and Gray, 1995; Tallon-Baudry and Bertrand, 1999). Furthermore, the individual stimulus features such as size, spatial frequency, and contrast have a noticeable influence on the human gamma activity (Busch et al., 2004; Tzelepi et al., 2000; Schadow et al.,

submitted for publication to IJP). The mentioned studies reported a systematic variation of gamma-band amplitude with changing stimulus features.

Different types of oscillatory activity have been distinguished in the auditory, visual, and somatosensory modalities. The evoked gamma-band response is characterized by precise phase-locking to stimulus onset and can be detected by averaging the single trials. In the auditory system, the evoked gamma-band response has been observed at 20–130 ms after stimulus onset. In contrast to the evoked gamma activity, induced responses jitter in latency from trial to trial (non-phase-locked) and are thus cancelled out by classic averaging techniques. For this reason, specific analysis methods are required for detecting the induced gamma-band response which occurs in a later time interval around 200–400 ms (Galambos, 1992; Tallon-Baudry and Bertrand, 1999).

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The auditory evoked gamma-band response (GBR) has been investigated with different methods in animals and humans (Başar et al., 1987; Pantev et al., 1991; Galambos, 1992; Başar-Eroglu et al., 1996). A number of studies argue about whether the auditory evoked gamma-band activity represents an independent brain response functionally distinct from the auditory middle latency response (MLR) and long latency response (e.g. N1) (Başar et al., 1987; Bertrand and Pantev, 1994; Pantev, 1995; Jacobson et al., 1998; Müller et al., 2001). Since several studies observed a similar amplitude increase with an increasing interstimulus interval for evoked gamma-band responses as shown for the MLR and long latency response (Makeig, 1990; Pantev et al., 1993), Başar et al. (1987) reasoned that the 40 Hz response is a consistent part of the auditory evoked potential. However, dipole localizations suggested that generators underlying the gamma-band field (GBF) are spatially distinct from those underlying the MLR Pa component as well as the N100 (Pantev et al., 1993). In this regard, the spatial separation of the GBF, MLR, and N100 provides evidence that they may arise from different processes in the auditory pathway (Pantev, 1995).

Animal studies with intracranial recordings have shown oscillations with a frequency around 40 Hz, both in the primary and secondary auditory cortex that occurred spontaneously and in response to sensory stimulation (Franowicz and Barth, 1995; MacDonald and Barth, 1995; Brett et al., 1996; Brosch et al., 2002). In humans, GBRs elicited by auditory stimulation were intensively studied in a variety of perceptual and cognitive tasks (Karakas and Başar, 1998; Crone et al., 2001; Kaiser and Lutzenberger, 2005b; Karakas et al., 2006). In different experiments, gamma-band activity was functionally related to Gestalt perception and attention as well as memory processing (Tiitinen et al., 1993; Yordanova et al., 1997; Knief et al., 2000; Debener et al., 2003; Kaiser and Lutzenberger, 2005a). However, the effects of auditory stimulus features on gamma-band activity such as loudness, pitch, timbre, or the combination of multiple frequencies have not yet been reported. Knowing and controlling such effects is necessary even for investigations of auditory cognition in order to yield optimal gamma-band responses and not to confound task (cognitive) effects with stimulus effects (see Busch et al. [2004] for a similar discussion in the visual modality).

Processing of different sound intensities has already been investigated for auditory evoked potentials (AEPs). These studies consistently found a strong intensity dependency of the early AEP (Rapin et al., 1966; Beagley and Knight, 1967; Polich et al., 1996; Carrillo-de-la-Peña, 1999; Neukirch et al., 2002). All of them have reported a shortening of N1 latency and a pronounced increase of the N1–P2 peak-to-peak amplitude as the intensity of pure sinusoidal tones was increased. This loudness dependence phenomenon has also attracted much interest in psychiatric research, since several studies examined the serotonergic modulation of the cortical loudness dependency (Hegerl and Juckel, 1993; Hegerl et al., 2001; Debener et al., 2002). While Hegerl and colleagues stated that low serotonergic neurotransmission is associated with an enhancement in N1–P2 amplitude with increasing stimulus intensity, recent studies have demonstrated contradictory findings (Dierks et al., 1999;

Debener et al., 2002; Massey et al., 2004). These studies manipulated the cerebral levels of serotonin by using tryptophan depletion and did not find significant effects of tryptophan depletion on intensity dependence of AEPs. Thus, it remains questionable whether the loudness dependency of AEPs is a specific biological marker of serotonergic activity.

The present study compared gamma-band activity in response to different sound intensity levels of a pure sinusoidal tone. This study represents a counterpart to the visual experiment analyzing the effects of stimulus contrast (Schadow et al., submitted for publication). We analyzed the gamma-band responses in an early and late time interval. In the early time window, evoked and total GBR as well as the strength of phase-locking were calculated. Presenting the phase-locking values and the total GBR completes the description of the evoked GBR and might give an important explanation for amplitude differences in the early GBRs (Busch et al., 2006). These three measures might resolve the question of whether stronger evoked gamma-band responses arise from stronger phase-locking of ongoing oscillatory activity or from signal increases. Based on the theoretical considerations, we expected to find enhanced GBRs with increasing intensity of the auditory stimulus. In addition, we aimed to replicate the aforementioned results for auditory evoked potentials.

2. Method

2.1. Participants

Twenty-one paid subjects (13 females, 8 males, mean age 26.2 ± 5 years) participated in the study. They had no history of hearing impairments and showed no signs of psychiatric or neurological disorders. All subjects received a written task instruction and gave informed consent to participate. Two subjects were excluded from the entire data analysis due to numerous eye artifacts. The ethical principles of the Declaration of Human Experimentation (1964) concerning human experimentation were followed.

2.2. Stimuli and task

Two pure sinusoidal tones (2000 Hz, 4000 Hz) were generated using Adobe Audition V1.0 (Adobe Systems Inc., 2004) and delivered binaurally through insert earphones (EARTone 3A). The duration of each stimulus was 500 ms (10 ms rise and fall time) with a randomized interstimulus interval (ISI) between 1200–2000 ms. For each participant and each sine tone, the individual hearing threshold for the left and the right ear was determined in intensity steps of 1 dB. Based on the individual hearing level (HL), three intensities (30, 45, 60 dB) were selected for the high and the low frequency tone. A calibrated attenuator was used to control the sound levels (Tucker-Davis Technologies, model PA5). This attenuator has two channels — one for each ear. The attenuator is set before the presentation of every sinusoidal tone. Thus, we can adjust for each ear and each tone individually.

The present experiment was constructed as a forced-choice discrimination task. The frequent stimulus ($p=0.8$) was a

2000 Hz tone, whereas a 4000 Hz tone served as the infrequent stimulus. The experimental session consisted of 300 frequent stimuli (100 for each intensity) and 75 infrequent stimuli (25 for each intensity) which were presented in a pseudorandomized order. Only the frequent stimuli were included in the present analysis.

Since it has been demonstrated that stimulus-related motor activation modulates the gamma-band response (De Pascalis and Ray, 1998; Yordanova et al., 2001, 2002), all stimuli required a motor response to avoid confounding effects. Participants were instructed to press a button with their right index finger in response to the infrequent stimuli and another button with their left index finger in response to the frequent stimuli. During the entire experimental session, subjects were instructed to fixate a cross in the center of the screen to avoid eye movement artifacts. Two breaks were included. The length of each break was individually determined by the participant.

2.3. Data acquisition

EEG was recorded with a BrainAmp amplifier (Brain Products, Munich), using 32 sintered Ag/AgCl electrodes mounted in an elastic cap (EasyCap, Falk Minow Services, Munich). The electrodes were placed according to the 10–10 system, with a nose-tip reference and ground electrode between Fz and Cz. Eye movement activity was monitored with an electrode placed suborbitally to the right eye. Electrode impedances were kept below 5 kΩ. Data were acquired with

a band-pass filter of 0.016–250 Hz and a sampling rate of 500 Hz with an amplitude resolution of 16 bit, i.e. 0.1 μV resolution and ±3.28 mV dynamic range. Stimulus markers and EEG were stored on hard disk for further analysis. The EEG was recorded while participants sat in an electrically shielded, sound-attenuated cabin. The monitor was placed outside behind an electrically shielded window. All devices inside the cabin were operated on batteries to avoid interference of the line frequency (50 Hz in Germany). Digitized EEG data were transferred to a computer outside the cabin using a fiber-optic cable. Averaging epochs lasted from 200 ms before to 1000 ms after stimulus onset for AEPs and evoked gamma-band responses. Baselines were calculated in the interval from –200 ms to –100 ms and subtracted before averaging. An automatic artifact rejection was computed which excluded trials from averaging if the standard deviation within a moving 200 ms time interval exceeded 40 μV. Afterwards, all epochs were also visually inspected for artifacts and rejected when eye movements, electrode drifts, or electromyographic activity occurred. Whereas data analysis was performed on unfiltered data, AEPs are displayed low-pass filtered at 20 Hz.

2.4. Data analysis

2.4.1. Behavioral data

Responses were scored as correct if the correct button was pressed within a time window lasting from 200 to 2500 ms after the stimulus onset. False trials were rejected from the behavioral

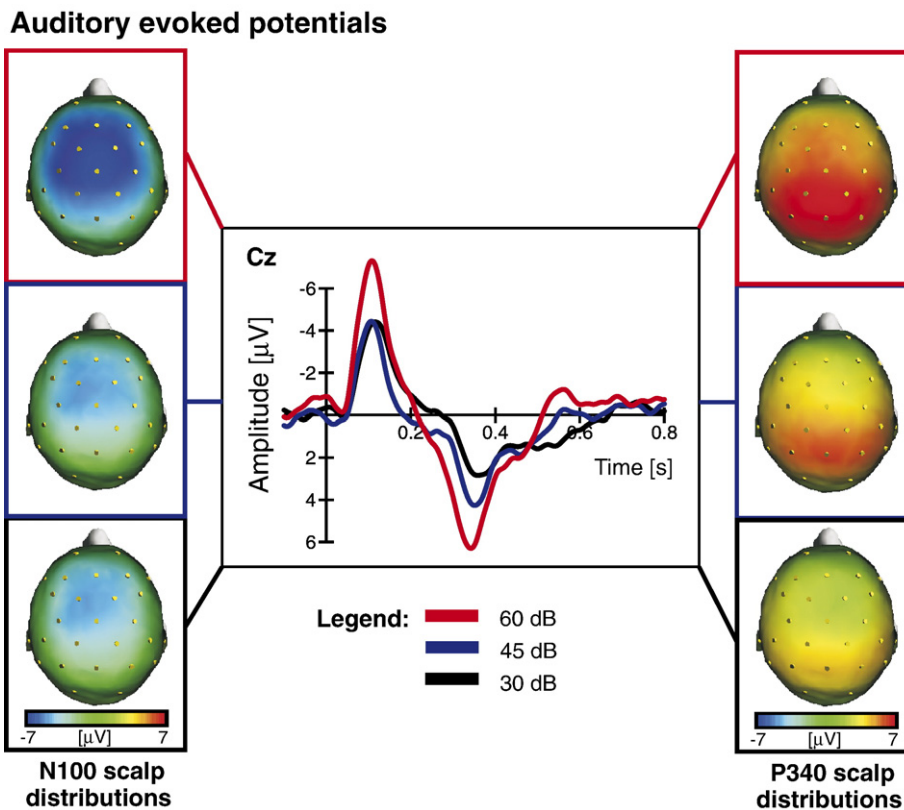


Fig. 1. Left column: Scalp distributions of the N100 at its peak latency (108 ms). Middle column: Auditory evoked potentials at electrode Cz for 60 dB HL (red), 45 dB HL (blue), and 30 dB HL (black) sine tones. Right column: Scalp distributions of the P340 at the peak latency (342 ms).

data analysis, as well as trials in which the response time (RT) exceeded two standard deviations from the mean.

2.4.2. Auditory evoked potentials

The statistical analysis of AEPs was performed after channels which exhibited the strongest activity were pooled into a fronto-central region of interest (ROI) (F3, Fz, F4, Fc5, Fc6, Fc1, Fc2, C3, C4, Cz, Cp1, Cp2 — see the N100 scalp topographies in Fig. 1). Two AEP components were defined as peak amplitudes in the time interval from 60 ms to 160 ms (N100) and 290 ms to 400 ms (P340)¹. Similar to previous studies, the analysis of the loudness dependence phenomenon was based on the peak-to-peak amplitude of the N100–P340 complex. This peak-to-peak amplitude as well as N100 amplitude and latency were analyzed using a repeated measures ANOVA with the factor INTENSITY (3 intensity levels). *F*- and *p*-values were reported as well as effect sizes of selected comparisons (partial eta-squared — η_p^2)². In order to ensure that all values that entered into the ANOVA were normally distributed, the Kolmogorov–Smirnov test was applied. The analysis for each variable revealed *p*-values that were $>.20$. The Greenhouse–Geisser correction, an adjustment used in univariate repeated measures when the sphericity assumption is violated, was applied for all ANOVA models. Post hoc *t*-tests of specific comparisons of significant ANOVA effects were calculated. All post hoc tests were Bonferroni corrected for multiple comparisons.

2.4.3. Early and late gamma-band responses

For the analysis of the gamma-band activity, a wavelet transform with a width of 12 cycles based on Morlet wavelets was applied (Herrmann et al., 1999). To analyze the evoked GBR phase-locked to the stimulus, the wavelet transform was applied to the averaged event-related potentials. However, for the non-phase-locked portion of the GBR, each trial was first transformed in the frequency domain and then the resulting wavelet transforms were averaged. This measure represents the total activity comprising the phase-locked and non-phase-locked part of the GBR. Additionally, the amount of phase-locking across trials was computed. The absolute value yields a number between 0 and 1 determining the degree of phase-locking, where 1 indicates perfect phase alignment across trials and values close to 0 reflect a high phase variability. From the obtained time–frequency representations, the average from the baseline between 200–100 ms before stimulus onset was subtracted.

Since previous studies have shown that the frequency of oscillatory brain activity varies notably between subjects, the frequency used for the wavelet analysis was individually adapted by the time–frequency representation of the signal at Cz (Busch

et al., 2004; Klimesch, 1999). The individual gamma frequency was defined as the highest peak in response to the 60 dB tone in a time interval between 20 and 90 ms (early GBR) as well as 200 and 600 ms (late GBR) after stimulus onset in the gamma frequency range. However, the time–frequency planes did not reveal any late gamma-band activity in the selected time interval that exceeded the noise level. Therefore, further statistical analyses and the description of the results were only related to the early gamma-band activity. If no clear GBR peak was visible, a frequency of 40 Hz was chosen for analysis (as done previously, e.g. Herrmann et al., 2004). This had to be done for two subjects in the early time interval. The peak frequencies of the individually identified evoked GBRs ranged from 26 Hz to 65 Hz (mean 42.6 Hz, SD=11.7 Hz). For the statistical analysis, early GBRs were defined as the peak amplitude of evoked gamma activity, the phase-locking and total gamma activity in the time interval between 20 and 90 ms, which turned out to be the peak interval in the time–frequency planes. Thereby, channels were pooled into a ROI comprising the following seven central electrodes which exhibited the strongest GBRs: FC1, FC2, C3, C4, Cz, Cp1, Cp2 (see the scalp topographies in Fig. 2). We performed a repeated measures ANOVA using the factor INTENSITY (3 intensity levels). The Kolmogorov–Smirnov test applied to each variable revealed *p*-values that were $>.20$. Post hoc *t*-tests of specific comparisons of significant ANOVA effects were additionally calculated (60 dB vs. 45 dB, 60 dB vs. 30 dB, and 45 dB vs. 30 dB). For all ANOVA models the Greenhouse–Geisser correction was applied and post-hoc *t*-tests were Bonferroni corrected.

3. Results

3.1. Behavioral data

Participants easily performed the task with high accuracy (2.4% errors). The error rates were not influenced by sound intensity ($F [2, 36]=1.702, p=0.205$). The responses to the 45 dB tone (meanRT=421 ms) were somewhat faster than to the 60 dB (meanRT=439 ms) and 30 dB (meanRT=432 ms) tone, however, this difference was not significant ($F [2, 36]=2.858, p=0.097$).

3.2. Auditory evoked potentials

The AEPs of all conditions were characterized by a first negative peak at a latency at 100 ms (N100) followed by a positive peak at approximately 340 ms latency (P340, Fig. 1). For all conditions the strongest N100 responses were observed at fronto-central sites, while the P340 responses were strongest at posterior-central electrodes (see the scalp topographies for the N100 and P340 in Fig. 1). Peak-to-peak amplitudes of the N100–P340 were larger for higher stimulus intensities ($F [2, 36]=6.441, p<0.05, \eta_p^2=0.264$). Post hoc comparisons revealed a significant effect for the 60 dB vs. 30 dB tone condition ($t[18]=-3.004, p<0.05$). Post hoc tests between 60 dB vs. 45 dB and 45 dB vs. 30 dB revealed no significant differences, although the data showed a statistical trend for larger amplitudes at higher sound intensities. In contrast,

¹ Note, that this ERP component is referred to as P2 in many sensory experiments. The latency of the P2 component could extend to frequently presented stimuli, if the task requires a motor response to infrequent (target) stimuli (Starr et al., 1997). Thus, we designated this component P340 to account for the later latency.

² The η_p^2 is the proportion of the effect and the error variance that is attributable to the effect (Pierce et al., 2004).

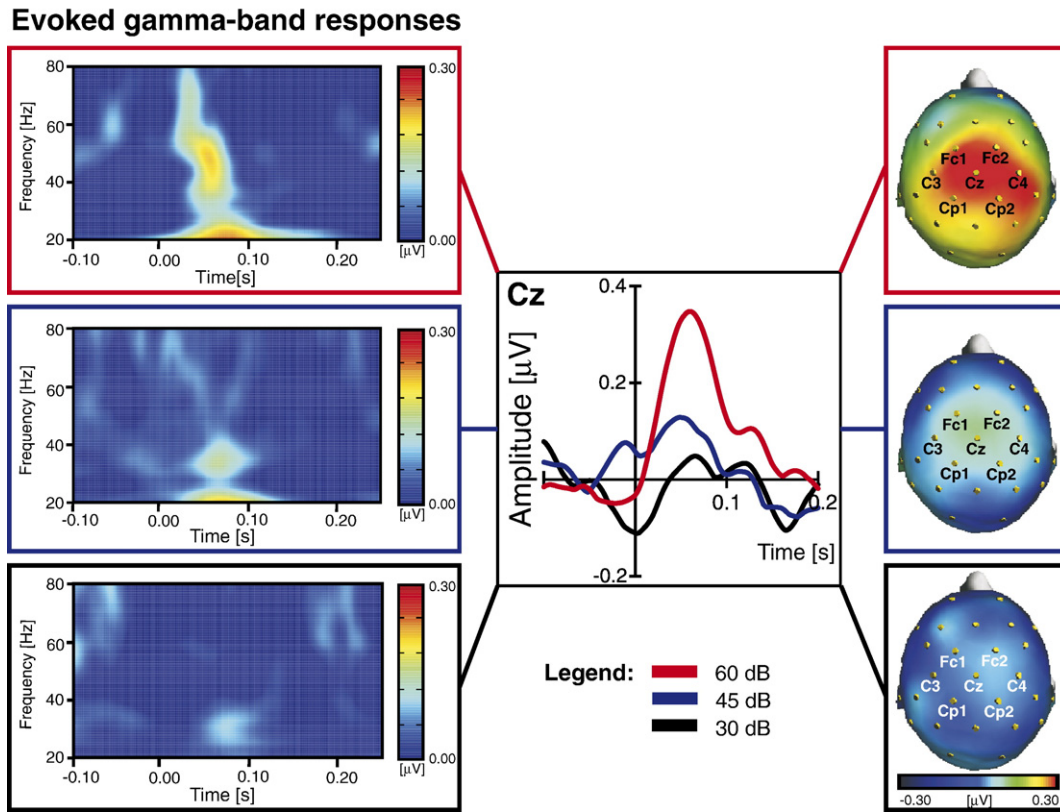


Fig. 2. Left column: time–frequency plots at electrode Cz for 60 dB HL (red), 45 dB HL (blue), and 30 dB HL (black) sine tones. Middle column: Time courses of the individually adapted wavelet transforms at electrode Cz. Right column: Scalp distributions of the gamma peak at 61 ms for all conditions.

no significant effect of stimulus intensity was found for N100 amplitudes ($F [2, 36]=0.122, p=0.858, \eta_p^2=0.007$). Instead, N100 latencies were shorter for higher sound intensities ($F [2, 36]=4.574, p<0.05$). Post hoc tests yielded only a significant effect between 60 dB vs. 30 dB ($t[18]=3.265, p<0.05$), but not for the remaining comparisons (60 dB vs. 45 dB and 45 dB vs. 30 dB).

3.3. Early gamma-band responses

The wavelet analysis revealed an increase in evoked gamma-band activity for higher sound intensities. This is illustrated in

Fig. 2 by the baseline-corrected time–frequency plots and the time courses of the individually adapted wavelet transforms for all intensity conditions. The ANOVA of the peak amplitudes yielded a main effect of INTENSITY ($F [2, 36]=9.276, p=0.001, \eta_p^2=0.339$; Fig. 2) with larger amplitudes for stimuli with the highest sound intensity. Post hoc comparisons revealed significant differences between the 60 dB vs. 30 dB ($t[18]=-4.092, p=0.003$) and the 60 dB vs. 45 dB ($t[18]=-3.039, p<0.05$) condition, but not between the middle and the lowest intensity ($t[18]=-1.031, p=0.948$). The electrode Cz and adjacent leads show the largest amplitudes compared to frontal and occipital areas. This is explicitly apparent for the middle

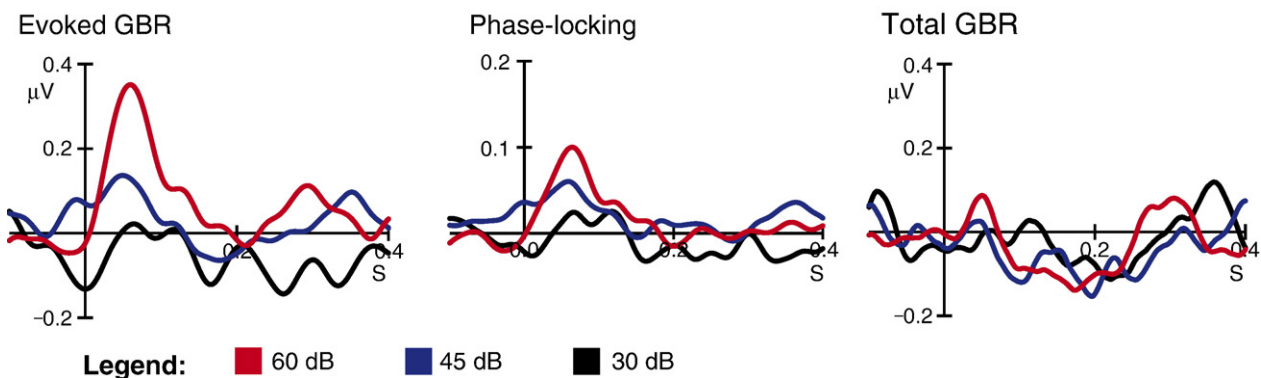


Fig. 3. Time courses for the evoked GBR, phase-locking, and total GBR (containing the phase-locked and non-phase-locked parts of the GBR) at electrode Cz. All displayed time courses were baseline corrected.

and the highest intensity (see scalp distributions in Fig. 2). The analysis of the GBR peak latency revealed no significant main effect of INTENSITY ($F [2, 36]=0.812, p=0.446$).

Fig. 3 displays the time-courses of evoked GBR, phase-locking, and total GBR (containing the phase-locked and non-phase-locked parts of the GBR) in comparison. For the evoked GBR, the amount of phase-locking was significantly larger for sine tones with higher sound intensities ($F [2, 36]=5.997, p=0.009$), whereas the analysis of the total GBR, an index of signal power, revealed no INTENSITY effect ($F [2, 36]=0.694, p=0.506$). Thus, the increase in evoked GBR is most likely based on stronger phase-locking. Interestingly, in the grand average across all subjects the frequency of the evoked gamma-band response was higher for the 60 dB tone (47 Hz) than for the 45 dB (35 Hz) and 30 dB tone (30 Hz). However, the ANOVA did not turn out to be statistically significant ($F [2, 20]=2.237, p=0.140$).

3.4. Comparison of AEPs and evoked GBRs

The effects of sound intensity level were compared for the N100, N100–P340 complex, and GBRs. To this end, the amplitude value of the lowest sound intensity was set to 100%. Subsequently, the increase in response to the intermediate and the loudest stimulus relative to 30 dB tone was calculated (see Fig. 4). It stands out that the amplitudes of GBRs as well as all AEP components exhibit an enhancement with intensity of the sine tones. Nevertheless, a difference between auditory evoked potentials and gamma oscillations is apparent, indicating an enhanced intensity effect for the evoked gamma-band activity particularly with regard to the 60 dB HL tone. This is also reflected in the larger effect size of the evoked GBR ($\eta_p^2=0.339$) compared to the AEPs (N100–P340: $\eta_p^2=0.264$, N100: $\eta_p^2=0.007$).

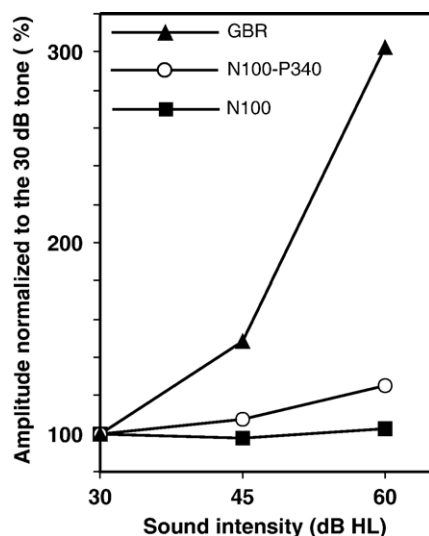


Fig. 4. Increase of amplitude for AEP components (N100–P340 and N100) and auditory evoked GBRs with increasing sound intensity.

4. Discussion

The purpose of the present study was to investigate the influence of sound intensity on gamma-band activity and to replicate existing reports of such effects on auditory evoked potentials.

4.1. Auditory evoked potentials

We found the strongest response pattern for auditory stimuli at fronto-central electrodes, which is in line with previous studies of auditory evoked potentials (Woods, 1995). Dipole source analyses of the N1–P2 complex have explained this topography by two dipoles per hemisphere: a tangential dipole located in the superior temporal plane including the primary auditory cortex and a somewhat later activity of a radial dipole situated near the lateral temporal cortex (secondary auditory areas, Scherg and von Cramon, 1985, 1986; Pantev et al., 1991; Hegerl et al., 1994).

The AEP results of our study agree in most instances with those of Rapin et al. (1966), Beagley and Knight (1967), and Carrillo-de-la-Peña (1999). Similar to those studies, we found the expected enhancement of amplitude as a function of sound intensity. The results demonstrate a stronger intensity dependency of the peak-to-peak amplitude of N100–P340 compared to the N100. Contrary to our expectations and to previously mentioned studies, the enhancement of N100 amplitude did not reach statistical significance. One explanation, which Näätänen and Picton (1987) discussed in a review about the N100 wave, might be that the change in amplitude with increasing intensities varies greatly among subjects. This was also the case in our study. In some subjects, we observed an increasing N100 amplitude with enhanced sound intensity, whereas others showed no clear differences or the inverse effect in N100 amplitude, especially for the 45 and 30 dB sine tone. Therefore, some studies classified the subjects into "augmenters" and "reducers" and attempted to associate these groups with aspects of personality and psychopathology (Buchsbaum, 1976). Nevertheless, the augmenting/reducing approach and its functional relevance is still under debate (for more details refer to the critical review of Carrillo-de-la-Peña, 1992).

Moreover, our study confirmed the N100 latency dependence on stimulus intensity (Rapin et al., 1966; Beagley and Knight, 1967). Our data showed longer N100 latencies at low intensity levels. However, post hoc comparisons revealed only a significant effect between 60 dB vs. 30 dB, but not between the other sound intensities. One explanation for this result might be the frequency of the sine tone. Rapin et al. (1966) only observed a prolongation of N100 latency for low frequencies (250 Hz) but not for higher frequencies (1000, 6000 Hz). For the 1000 Hz tone the latency effect was extremely reduced and for the 6000 Hz tone there was no significant latency modulation by intensity. In our experiment, we chose a frequency of 2000 Hz for the frequent sine wave tone. This frequency lies exactly between the low and high frequency tones mentioned by Rapin et al. (1966). Hence, their finding might elucidate why we did not find such an obvious latency effect between the two highest sound intensities.

4.2. Evoked gamma-band responses

The present study demonstrates that auditory gamma activity in scalp-recorded human EEG can be detected using sine tones of a specific sound intensity and is additionally influenced by the stimulus intensity. It has been demonstrated that the processing demands of a task modulate the gamma-band activity (Yordanova et al., 1997; Senkowski and Herrmann, 2002; Simos et al., 2002). Thus, the fact that our participants had to perform a discrimination task might have contributed to our results. However, we assume that the intensity dependence also occurs in a fully passive listening condition. The evoked gamma-band activity following the highest intensity (60 dB HL) had a mean latency of 60 ms after stimulus onset with strongest responses at central electrodes. Given that auditory evoked potentials of this latency range stem from the auditory cortex and that generators in the auditory cortex result in maximum amplitudes over electrode Cz, it seems plausible to assume that the auditory evoked GBR is generated in or near the auditory cortex. This is in line with a previous study by Pantev et al. (1993), who reported that the generators of auditory gamma-band activity are located in the supratemporal auditory cortex which explained the strongest activity at central leads.

In contrast to the highest sound intensity (60 dB HL), lower ones (30 and 45 dB HL) evoked only very low gamma-band responses. Three possible mechanisms could account for this result. Either more neurons might respond to the louder sound (i), or the same number of neurons with higher interneuron synchronization (ii), or the same number of neurons with higher synchronicity to stimulus onset (intertrial synchronization-iii). Both (i) and (ii) would result in an increase of total gamma-band activity which we did not observe. Only the last possibility (iii) is in accordance with the observed data. We found a higher phase-locking to stimulus onset for the high intensity stimulus. Thus, we assume, that the condition difference of sound intensity in the evoked time-domain signal results from increased phase-locking. This interpretation is in line with previous findings in the visual domain (Busch et al., 2006). In their study, bottom-up factors modulated only the phase-locking, whereas top-down factors modulated the power of the early evoked GBR. The intensity variation of our study represents such a bottom-up modulation. Therefore, it was to be expected to find the observed increase in phase-locking for higher sound intensities.

Phase-locking represents a measure across trials and cannot be seen in a single trial. This raises the question of which neural mechanism could modulate such an intertrial synchronization. Loud stimuli have been demonstrated to result in an earlier latency of the first spike that can be recorded in response to a stimulus (Heil, 2004). This so-called first-spike-latency is believed to be an important code for the brain. At the same time that first-spike-latency is reduced in response to loud stimuli, the standard deviation of latencies across trials decreases (Heil and Irvine, 1997). This is illustrated in Fig. 5 and offers a potential explanation for the increased phase-locking observed for loud stimuli: The standard deviation of the first-spike-latency represents the variability across trials, i.e. it represents a similar

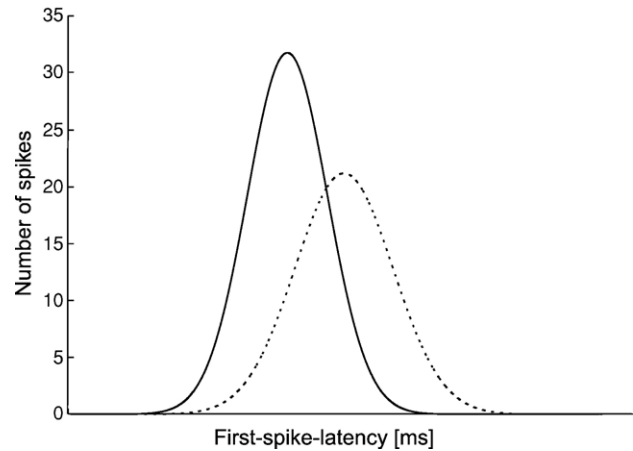


Fig. 5. First-spike-latency of auditory neurons. In response to low-intensity sounds (dotted line), first-spike-latency is longer than in response to high-intensity sounds (solid line). At the same time, the standard deviation of latencies decreases. This potentially explains why we observed an increased phase-locking for high-intensity sounds.

measure to our phase-locking. The more narrow the standard deviation becomes, the higher the synchronization of the first spike to stimulus onset must be. Other recordings have also revealed an increased phase-locking in response to loud stimuli, however for the first recordable spike. Therefore, it seems plausible to also expect such an effect for further measures such as evoked gamma activity. Even though we do not want to argue that the first spike in the auditory cortex would evoke a GBR that can be recorded at the scalp, it seems probable that subsequent stages of processing also reveal more narrow latency distributions in response to increased sound intensity if the first spike does. Thus, we believe that our enhanced phase-locking in response to loud stimuli is a result of shorter first-spike-latency, even though the latter cannot be recorded at the scalp.

While we think that our increase in evoked gamma-band activity in response to high intensity stimuli is due to enhanced phase-locking to the stimuli, other studies investigating sound level dependent processing found different phenomena. On the one hand, a larger number of neurons fire at higher sound intensities due to their tuning curves, which are narrow for low but wide for high intensities (Pickles, 1988). On the other hand, fMRI studies exhibited a systematic increase in the extent of activated voxels and BOLD signal intensity with enhanced sound intensity (Brechmann et al., 2002; Hart et al., 2003; Mulert et al., 2005), implying a larger number of neurons being active in response to higher intensity.

One type of neurons in the auditory cortex reveals a monotonic increase in their firing rate in response to higher sound intensities and is therefore called monotonic neuron (Pfungst and O'Connor, 1981). Thus, one might expect the frequency of the GBR to increase at higher sound intensities. While this effect did not reach significance in our data, there was a tendency in this direction: 30 Hz, 35 Hz, and 47 Hz for 30 dB, 45 dB, and 60 dB, respectively.

Furthermore, the present study provides new contributions to the frequently discussed question of why some research groups failed to find any gamma-band activity (Menon et al., 1996;

Juergens et al., 1999). A key factor that seems to be most important in eliciting a strong response in the auditory gamma-band is the sound intensity of stimuli. These results are supported by studies that investigated additional parameters affecting the auditory evoked GBR. First, the GBR decreases as a function of shortening the ISI (Pantev et al., 1993; Pantev, 1995). Auditory evoked GBR is best elicited with long ISIs around 2 s. Second, tone-burst stimuli evoked a GBR in as few as 33% of normal subjects, while noise-burst stimuli elicited a GBR in as many as 80% of normal subjects (Jacobson et al., 1998). Furthermore, Crone et al. (2001) investigated changes in the gamma-band during auditory tone and phoneme discrimination by electrocorticographic recordings. Those data showed a greater augmentation in gamma power during phoneme discrimination than during tone discrimination. Apparently, stimuli such as noise and speech contain more frequencies and temporal changes which have to be processed and therefore require a higher demand of integration of neuronal assemblies than processing pure tones.

According to the abovementioned findings, gamma oscillations seem to be very sensitive to experimental conditions. Hence, sound stimuli with a greater spectral and temporal complexity presented with a sound intensity of 60 dB HL or higher and an ISI around 2 s are most suitable to evoke a measurable GBR at the scalp. The present study cannot provide evidence about how the GBR amplitude is associated with intensity levels higher than 60 dB HL. Future research should consider more than three intensity levels across a wider range, which would yield more reliable results (Beauducel et al., 2000). Our results concerning sound intensity effects could be particularly important for auditory paradigms investigating top–down influences on gamma-band activity. Thus, potential confounds with bottom-up factors such as sound intensity are avoidable. Interesting in this context would be a study combining both bottom-up and top–down aspects to resolve the question under which circumstances top–down influences can be optimally observed in auditory GBRs. Such a study for the visual system was already conducted by Busch et al. (2006), who examined both stimulus size and attention in one task. The results indicated that attention effects on visual GBRs only occur if the stimulus covers a sufficiently large area.

4.3. Comparison of AEPs and evoked GBRs

When comparing the effects of stimulus intensity on gamma-band responses and auditory evoked potentials, it is apparent that GBRs are modulated considerably stronger and earlier than AEPs. A similar pattern has been demonstrated in the visual domain (Busch et al., 2004), where visually evoked GBRs are modulated stronger and earlier by stimulus size and eccentricity than visual evoked potentials. This difference between GBRs and AEPs supports the notion, also proposed by Bertrand and Tallon-Baudry (2000), that both reflect independent neuronal and possibly functional mechanisms.

4.4. Conclusion

The present study revealed that the auditory evoked GBR is modulated by sound intensity and much more so than AEPs. It has

been argued that gamma activity is essential for human cognition involved in binding, perception, and memory processes (Singer and Gray, 1995; Keil et al., 1999; Tallon-Baudry and Bertrand, 1999; Engel et al., 2001).

These findings may help to design future auditory experiments dealing with gamma oscillations as a central issue. Future experiments should clarify whether other auditory stimulus features affect 40 Hz oscillations. In addition, most natural sounds are not, however, well approximated by sinusoidal tones of a particular frequency as used in our study. Thus, it is of considerable interest to investigate spectrally more complex environmental sounds and their evoked responses.

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