Stimulus-Related Gamma Oscillations in Primate Auditory Cortex

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Brosch, Michael, Eike Budinger, and Henning Scheich. Stimulus-related gamma oscillations in primate auditory cortex. J Neurophysiol 87: 2715–2725; 2002; 10.1152/jn.00583.2001. With a multielectrode system, we explored neuronal activity in the gamma range (>40 Hz) in the primary and caudomedial auditory cortex of six anesthetized macaque monkeys. Stimuli were tone bursts of 100- to 500-ms duration that were presented at sound pressure levels of 40–60 dB and were varied over a wide range of frequencies. These stimuli induced gamma oscillations, not phase-locked to the onset of stimulation, in 465 of 616 multunit clusters and at 321 of 422 sites at which field potentials were recorded. Occurrence of gamma activity was stimulus dependent. It was mostly seen when the stimulus was at the units’ preferred frequency. The incidence of gamma activity decreased with increasing difference between stimulus frequency and preferred frequency. Gamma activity emerged 100–900 ms after stimulus onset with highest incidence ~120 ms. Amplitudes of stimulus-induced gamma oscillations in field potentials were, on average, almost twice the amplitude of spontaneously occurring gamma oscillations. Gamma activity at different sites within the primary and the caudomedial auditory field could be synchronized at near-zero phase. Synchrony depended on the spatial distance and on the receptive fields similarity of pairs of units. It decreased with increasing distance between recording sites and increased with similarity of preferred frequencies of the pairs of units. The results indicate that stimulus-induced gamma oscillations originate from sources in the auditory cortex. They further suggest that gamma oscillations may provide a mechanism utilized in many parts of the sensory cortex, including the auditory cortex, to integrate neurons according to the similarity of their receptive fields.

INTRODUCTION

High-frequency brain rhythms >30 Hz (gamma oscillations) are thought to be involved in visual, auditory, tactile, and motor processing (for review, see Eckhorn 1999; Freeman 1998; Gray 1999; Singer 1999; Tallon-Baudry and Bertrand 1999). Two types of gamma oscillations have been distinguished, evoked and induced gamma oscillations (Galambos 1992). Evoked gamma oscillations are precisely phase-locked to the onset of sensory stimulation and are present during the initial 100-ms period after stimulus onset. A particular type of evoked gamma oscillation provides the steady-state response, which is elicited at greatest amplitudes by periodic stimulation at a frequency of ~40 Hz (Galambos et al. 1981). Evoked gamma oscillations have been implicated with attentional processes (Sheer 1989; Tiitinen et al. 1993), vigilance, and consciousness (Llinas and Ribary 1993; May et al. 1994) and with the temporal binding of successive sensory events (Joliot et al. 1994). Induced gamma oscillations are characterized by poor temporal locking to stimulus onset and occur ~200–400 ms past stimulus onset. Induced gamma oscillations are task dependent (Bertrand et al. 1998; Marshall et al. 1996; Sheer 1989) and are related to associative learning (Miltner et al. 1999), sensory/motor integration (Murthy and Fetz 1992; Salenius et al. 1996; Sanes and Donoghue 1993), feature binding (Eckhorn 1999; Eckhorn et al. 1988; Gray 1999; Gray and Singer 1989; Singer 1999), and object representation (Pantev 1995; Tallon-Baudry and Bertrand 1999).

The neural basis of gamma oscillations has been investigated most extensively in the visual system (Eckhorn 1999; Gray 1999; Singer 1999). In these reviews, it is stated that gamma oscillations can be found in discharges and local slow wave field potentials recorded in the retina, thalamus, and various areas of the visual cortex in anesthetized and awake cats and monkeys. The occurrence, amplitude, and frequency of gamma oscillations can be modified by the visual stimulus and by electrical stimulation of the mesencephalic reticular formation and are related to behavioral tasks (Amzica et al. 1997). Gamma oscillations at different parts of the visual system can be synchronous, and their synchrony is related to the similarity of stimulus elements. Compared with the visual system, as well as to the olfactory system (Freeman 1998), little is known about gamma oscillations in the auditory cortex. Although there is an increasing number of studies reporting acoustically evoked gamma oscillations in human electro- and magnetoencephalographic (EEG and MEG) signals, there are relatively few reports that have actually observed gamma oscillations in the neural activity in the auditory cortex. Except for a recent observation in the human electrocorticogram (Crone et al. 2001), most of our current knowledge is based on epidural recordings in rodents. In a series of experiments in lightly anesthetized rats, Barth and coworkers (Barth and MacDonald 1996; Franovicz and Barth 1995; MacDonald et al. 1996, 1998; Sukov and Barth 2001) have found gamma oscillations with a frequency of ~40 Hz in the primary (AI) and secondary (AII) auditory cortex. The gamma oscillations at different sites within the same area were highly synchronized with no phase lag, whereas there was a phase lag of ~2 ms between AI and AII. Gamma oscillation occurred in the ongoing activity but could also be evoked by electrical stimulation of the posterior intralaminar nucleus of thalamus. Moreover, ongoing gamma oscillations were inhibited by click stimuli but reappeared after the evoked potential at enhanced amplitudes. Recently gamma oscillations have also been found in slice preparations of rat and mouse auditory cortex, where they could be evoked by electrical stimulation of thalamic afferents (Metherate and Cruikshank 1999).

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The goal of the present study is to elucidate properties of \( \gamma \) oscillations in the auditory cortex in more detail. This is important because of the increasing interest in the functional role of \( \gamma \) oscillations in EEG and MEG signals of humans. Because of their similarity to humans in terms of anatomy and physiology, experiments were carried out in macaque monkeys in which we addressed the following questions: are \( \gamma \) oscillations induced by specific acoustic stimuli? What is the relation between \( \gamma \) oscillations occurring in slow wave field potentials and in spike trains? Are \( \gamma \) oscillations at different cortical sites correlated, and if so, is correlation related to the frequency selectivity of units? Are \( \gamma \) oscillations precisely or loosely locked to acoustic stimuli?

**METHODS**

**Animal preparation**

Data are from six experiments performed on *Macaca fascicularis* (2.5–4.2 kg). The surgical procedure was initiated by injections of atropine (0.5 mg/kg) and a mixture of ketamine HCl (4 mg/kg) and xylazine (5 mg/kg IM). Thereafter we performed a tracheotomy and an extensive craniotomy over the left auditory cortex, which included the lateral inferotemporal sulcus and parts of the central sulcus. In three animals, we aspirated parts of the parietal cortex overlaying the lateral inferotemporal sulcus and parts of the central sulcus. In the other animals, electrodes penetrated the supratemporal plane almost at a right angle. In the other animals electrodes first entered the parietal cortex at an angle of about 45° before they arrived in the auditory cortex. Most recordings were made 200–600 \( \mu \)m after the first observation of neural discharges in the supratemporal plane and thus were presumably made from upper cortical layers. The first electrode penetrations were from AI. Consecutive penetrations were done from adjacent locations in AI and the caudomedial auditory field (CM) by moving the electrode array along the mediolateral axis in steps of 330 \( \mu \)m or along the rostrocaudal direction in steps of 2.33 mm. Areal locations of recording sites was assessed by inspecting the gradient of best frequency (see following text) as well as the cytoarchitectonic features and the parvalbumin staining of brain sections relative to dye stained recording sites (Kosaki et al. 1997).

**Acoustic stimuli**

Acoustic search stimuli (tone pips, frequency sweeps, and noise bursts) were produced with a waveform generator (Tucker-Davis Technologies, model WG1). For quantitative analyses, acoustic signals were generated digitally in a computer (Pentium-PC interfaced with an array processor AP2-card, Tucker-Davis Technologies) at a sampling rate of 100 kHz and with a dynamic range of 88 dB and D/A converted to an analog signal (Tucker-Davis Technologies, model DA1). Aliasing was reduced with a low-pass filter set at a cutoff frequency of 35 kHz (Tucker-Davis Technologies, model FT5). Signal amplitude could be controlled over a 100-dB range by passive attenuators (Tucker-Davis Technologies, model PA4). Signals were then passed through an equalizer (SEA 4500; Conrad Electronics) to compensate for the frequency response of the sound system, amplified (Pioneer, model A202), and coupled to a free-field loudspeaker (Manger), which was located on the right frontal side of the animal at a distance of 1 m. The sound pressure level (SPL) was measured with a free-field 0.5-in microphone (GRAS, 40AC) located close to the monkey’s ear and a spectrum analyzer (Rion, SA 77). The output of the sound delivering system varied 10 dB in the frequency range of 0.2–35 kHz. At SPL <90 dB, harmonic distortion was \( \geq 36 \) dB below the signal level.

The frequency tuning of units was measured by presenting 400 single pure tones at 40 frequencies (each repeated 10 times) with a duration of 100 ms in pseudo-random order. Frequencies were equidistantly spaced on a logarithmic scale and covered a range of two to eight octaves, centered on the best frequencies of the neurons recorded simultaneously on the seven electrodes. Best frequency (BF) was defined as the tone that elicited the highest number of action potentials during the tone presentation; it ranged between 0.07 and 31.7 kHz in different units. For each recording, all tones were presented at the same SPL, which varied between 40 and 60 dB. Tone duration was 100 ms (including 5-ms rise and fall time) and intertone interval was 1,375 ms, except for *monkey E*, where it was 1,078 ms. Often measurements were repeated with tones of longer duration (300 or 500 ms).

**Data analysis**

Off-line data analyses were carried out with Brain Wave Common Processing version 5.0 (DataWave Technologies) and MATLAB 4.0 (Mathworks). Spectral and temporal properties of \( \gamma \) oscillations were analyzed from field potentials. The stimulus-specificity of \( \gamma \) oscillations was examined from the spike trains of units.

**FIELD POTENTIALS.** To assess the effect of pure tone stimulation on the spectral composition of field potentials, we compared different
short-time spectra with the spectrum of ongoing activity. This analysis was performed on 70 trials. In 10 of these trials, the tone was at the frequency that evoked the greatest middle-latency potential, which was measured as the amplitude between the first positive and the first negative deflection in this potential. To increase the power of our statistical tests, we included another 60 trials for this analysis in which we presented tones with the six frequencies closest to the tone frequency evoking the largest middle-latency potential. The field potential record of each of the 70 trials was divided into 59 overlapping 64-point (98.3 ms) time windows with a shift interval of 16 points. In monkey E, the trial length of 1,178 ms accommodated 47 time windows. Each time window was tapered with a three-term Blackman-Harris window (Harris 1978) to reduce the high-frequency artifacts induced by the sectioning of the data. A discrete Fourier transform algorithm then yielded the complex spectrum, providing amplitude and phase information of different spectral components of the signal. The frequency resolution of the spectral estimates was 10.17 Hz. The lowest frequency bin ranged from 0 to 10.17 Hz with a center frequency of 5.08 Hz. The zero time bin started 49.15 ms before and ended 49.15 ms after stimulus onset. For an easier reading, values of time and frequency bins are rounded in the remainder of this article.

From the 70 complex spectra of each time window, we next calculated two different average amplitude spectra. In the first spectrum, phase differences between the 70 spectra were neglected. This was done by calculating the absolute value from each spectrum before they were averaged. This procedure, hence, revealed the mean amplitude of different frequency components of the field potential whether or not they had the same phase relation to stimulus onset in each trial. In the second spectrum, phase information of the different spectra was preserved by averaging the complex spectra without taking the absolute value prior to calculating the amplitude spectrum. This second procedure, hence, yielded only those frequency components that were phase-locked to stimulus onset in each trial.

For each 98.3-ms time window, we then assessed whether stimulation had modified the amplitude in individual frequency bins. This was done by employing t-tests separately for all frequency bins in which we compared the distribution of the amplitudes of the 70 trials of a given time window with the corresponding distribution of ongoing activity. The latter was estimated by analyzing the time window immediately before onset of stimulation, which corresponded to the time window 1,361–1,475 ms after onset of stimulation because of the cyclic stimulation. This time window provided a good estimate of ongoing or spontaneous activity because the field potential was no longer influenced by the preceding stimulus, in accordance with previous studies of the auditory-evoked potential (Franowicz and Barth 1995; Ohl et al. 2000). To account for the multiple comparisons performed on the 20 frequency bins between 5.1 and 198.4 Hz, a frequency bin was deemed to be significantly modified by the stimulus if the P value of the t-test was <0.0001.

The similarity of pairs of simultaneously recorded field potentials was assessed by compiling average coherence spectra for three time windows, namely 0–300 ms before and 0–100 and 100–400 ms after stimulus onset. This analysis was performed on the responses to the seven tones closest to the mean of the tones that evoked the greatest amplitude of the middle-latency auditory-evoked potential at the two recordings sites. The signal in each time window was sectioned into overlapping 64-point (98.3 ms) periods with a shift interval of 16 points, tapered with a three-term Blackman-Harris window, and Fourier transformed. Subsequently the cross spectrum was calculated by multiplying the complex spectra of the two field potentials. Last the squared coherence was calculated by dividing the square of the mean of all cross spectra through the average power spectra of the signal pair. With this method, identical signals are found to have a coherence value of 1, whereas statistically independent signals have a coherence of maximally $1 - (1 - \alpha)\sqrt{(1/(N - 1))}$ (Rosenberg et al. 1989), where N is the number of time windows and \( \alpha \) was set to 0.99. The phase relation between frequency components of two field potential recordings was determined by the inverse tangent of the ratio of the imaginary and real part of the average cross spectrum. This value was divided by the frequency to give the average phase shift in milliseconds of a specific frequency component of two signals.

RESULTS

\( \gamma \) oscillations were observed both in field potentials and in spike trains recorded from the auditory cortex of the macaque. Figure 1A shows individual field potential traces from the caudomedial field in response to 10 presentations of a 760-Hz tone burst. Inspection of these traces revealed a period with high-frequency oscillations that emerged after the middle-latency-evoked potential complex and lasted for several hundred milliseconds. Onset, frequency, and amplitude as well as duration of these high-frequency oscillations varied considerably from trial to trial, indicating that these oscillations were not phase-locked to stimulus onset. This was also reflected in the average of the 10 field potential traces (Fig. 1A, bottom), which showed little indication of high-frequency oscillations. The average was rather dominated by a middle-latency-evoked potential, indicating that this component of the field potential was precisely locked to the onset of stimulation.

Because high-frequency oscillations varied considerably in frequency over time and were not phase-locked to stimulus onset, the spectral composition of field potentials was quantitatively assessed by adding the amplitude spectra of short data segments of the 10 individual trials (see METHODS). The resulting average amplitude spectra showed that, during the period 100–400 ms after stimulus onset, the field potential had considerable power in the range of 41–71 Hz, i.e., in the \( \gamma \) range (Fig. 1C). This was in contrast to the initial 100 ms after stimulus onset and to ongoing activity (estimated by analyzing the 300-ms period before stimulus onset), when the amplitude of the spectral components decreased monotonically with increasing frequency.
The period of enhanced $\gamma$ oscillations in the field potential coincided with the late part of the spike response of a unit that was recorded in parallel with the field potential (Fig. 1B). The temporal structure of the spike train was analyzed with the autocorrelation technique for the period 100–400 ms after stimulus onset. The oscillatory structure of the autocorrelogram indicated that the unit had a periodic discharge pattern, which was characterized by a significantly increased number of interspike intervals in the range of 12.5 and 22.2 ms (corresponding to frequencies between 45 and 80 Hz; Fig. 1D). This was shown by calculating the amplitude spectrum of the autocorrelation (Fig. 1E) and comparing this spectrum to the spectrum of the autocorrelation of a spike train with Poisson-distributed interspike intervals and a mean equal to that of the spike train shown in Fig. 1B.

$\gamma$ oscillations in field potentials

Figure 2 depicts the average time course of frequency-specific increases of field potentials seen at 422 sites in the auditory fields AI and CM. The time course was determined by dividing the 1,475-ms-long field potential traces into 59 overlapping time windows of 98 ms duration and finding in each time window which spectral components of the field potential were significantly increased over corresponding components of ongoing activity (see METHODS). During ongoing activity, there was little $\gamma$ activity; the spectral power decreased monotonically with increasing frequency (Fig. 2, inset). Our analysis was performed on the responses to the six tones closest to the largest middle-latency-evoked potential and the tone that elicited the largest middle-latency-evoked potential. The gray level
of each pixel is proportional to the number of cases with a significant amplitude increase in the frequency bin specified on the ordinate and in the time bin specified on the abscissa. This analysis revealed that acoustic stimulation increased field potential amplitudes in the time bins 0–909 ms after stimulus onset. During this period, the spectral distribution of increases of field potential amplitudes varied considerably. Initially, i.e., 49 ms after stimulus onset, most recording sites exhibited increased field potential amplitudes in the frequency bins between 20 and 41 Hz. These frequencies corresponded to the temporal structure of the middle-latency-evoked potential (cf. Fig. 1). At a number of sites, the amplitude increase in the 20- to 41-Hz band was accompanied by increases in other frequency bands, especially in the range 41–102 Hz. After this period, the spectral distribution of increased field potential amplitudes changed notably. There were markedly fewer sites with a low-frequency increase; rather most sites exhibited increases at frequencies between 41 and 102 Hz. This period with high frequencies started ~100 ms after stimulus onset and lasted maximally 800 ms. In the present report, we therefore considered a cortical site to exhibit stimulus-induced oscillations if the neural signal contained a frequency component >40 Hz.

Results similar to those shown in Fig. 2 were found for the dominant frequency of the field potential, i.e., the frequency bin whose amplitude was maximally increased over that of ongoing activity (Fig. 3). During the initial 100 ms after stimulus onset, the dominant frequency was mostly ≤40 Hz. Thereafter, dominant frequencies moved to higher values of 60–90 Hz. During the period 98–909 ms after stimulus onset, the amplitude of dominant frequencies in the band >40 Hz was increased by factors of 1.31–7.80 over the corresponding amplitude of ongoing field potentials with a median increase of 1.95. Figure 3 also shows that the time course of increased field potential amplitudes was largely similar to the time course of the response probability of the units that were recorded in parallel with the field potentials. The initial period of low-frequency increase of field potential amplitudes was associated with the transient part of the spike response of neurons, whereas γ oscillations coincided with the sustained part of their responses.

Acoustic stimulation with pure tones of 100-ms duration induced increased field potentials with frequency components >40 Hz in 321 of 422 (76.1%) recording sites in AI and CM in at least one time window ≥98 ms after stimulus onset (Table 1). Results were not much different when tones with a duration of 300 or 500 ms instead of 100 ms were tested; they were similar to those shown in Figs. 2 and 3 except that, at some recording sites, epochs with increased field potential amplitudes occurred for a slightly longer duration. This suggests that γ oscillations were induced by the onset or by the steady state part of acoustic stimulation.

Despite some differences in the prevalence, amplitudes, and frequencies of γ oscillations between subjects (Table 1), the stimulus dependence of γ oscillations and the relation between receptive field properties and γ oscillations were similar in all
increase in power.

Field potentials were combined for all group results and figures (Figs. 2, 4–7, and 9) given in this report.

To examine the phase-locking to stimulus onset of different frequency components, we analyzed the spectrotemporal composition of the average field potential complex. Like in the previous analysis, we used the 70 trials in which we presented the six tones closest to the greatest middle-latency-evoked potential and the tone that elicited the greatest middle-latency-evoked potential (Fig. 4). This analysis revealed that there were phase-locked field potential components up to a period of maximally 246 ms after stimulus onset. Most of them were in the frequency range between 20 and 41 Hz, which corresponded to the temporal structure of the middle-latency-evoked potential (Fig. 1C shows the evoked potential at a single recording site). This indicated that most of the γ oscillations that were observed during the period 98–909 ms after stimulus onset were not phase-locked to stimulus onset. Thus they can be identified as induced γ oscillations (see INTRODUCTION).

Correlation of γ oscillations at different cortical sites

The linear seven-electrode array with an interelectrode spacing of 330 μm allowed us to analyze the synchronization of neural signals that were simultaneously recorded at different sites within AI or CM. Because we were interested in the synchronization in specific frequency bands and time periods, we used short-term coherence spectra instead of the cross-correlation. This analysis was performed on the responses to the seven tones close to the mean of the tones that evoked the greatest amplitude of the middle-latency-evoked potential at the two recordings sites (see METHODS).

Figure 6A depicts median coherence spectra for the time window 100–400 ms after stimulus onset for 215 recordings pairs in which amplitudes of γ oscillations in field potentials were increased by a factor ≥2. In this time window, most γ oscillations were observed, as shown in Fig. 3. The coherence spectra demonstrate that γ oscillations at different sites of AI or CM could be synchronized. Synchronization was strongest for cortical sites separated by 330 μm and decreased monotonically with increasing separation of sites (Fig. 6B). A linear regression analysis of the frequency bin centered at 45.8 Hz indicated that γ oscillations at different sites could be synchronized up to a distance of 2.9 mm, at which coherence attained nonsignificant values (not shown). The synchronization of field

| Table 1. Numbers of stimulus-induced and synchronized γ oscillations |
|----------------|----------------|----------------|
| Subject | Field Potential Oscillations | Unit Oscillations | Unit Synchrony |
| M | 55 (60) | 107 (149) | 33 (175) |
| R | 93 (98) | 43 (72) | 111 (457) |
| B | 38 (44) | 58 (66) | 76 (372) |
| A | 60 (71) | 101 (122) | 48 (204) |
| S | 44 (65) | 77 (109) | 78 (309) |
| E | 31 (84) | 79 (98) | 71 (286) |
| All | 321 (422) | 465 (616) | 417 (1803) |

Number of recording sites with stimulus-induced γ oscillations (>40 Hz) and number of pairs of units with synchronized γ oscillations (numbers are given in parenthesis). For field potentials, the period 98–909 ms after stimulus onset was analyzed. For units, the period 100–400 ms after stimulus onset was analyzed.
potentials, however, was not restricted to the γ range but also occurred at lower frequencies. Generally, coherence of field potentials was highest at the lowest frequency and decreased monotonically with increasing frequency to nonsignificant values between 76 and 158 Hz, depending on the spatial separation of recording pairs. When the γ oscillations at two sites were correlated, they had, on average, zero phase lag [mean = 0.3 ± 1.4 (SD) ms; Fig. 6C]. This was found by computing the phase relation of the 215 pairs at the frequency >40 Hz at which the maximal coherence was found.

During the period 100–400 ms after stimulus onset, coherence of field potentials was selectively enhanced in the γ range over spontaneous coherence. Figure 7 compares the coherence spectrum 100–400 ms after stimulus onset with the spontaneous coherence spectrum (calculated from the period 0–300 ms before stimulus onset), pooled over all 215 recording pairs shown in Fig. 6A. During the time window of 100–400 ms after stimulus onset, significant (P < 0.0001) increases in coherence over values of ongoing activity were restricted to frequency bins between 56 and 87 Hz, as revealed by performing separate t-tests (P < 0.0001) for individual frequency bins between the distribution of coherence spectra of the two time windows. Enhanced coherence of field potentials was also found in the time window shortly after stimulus onset (0–100 ms). In contrast to the 100- to 400-ms period, however, coherence in the early time window was also increased over spontaneous coherence in frequency bins below the γ range.

The periodic discharge of units simultaneously recorded at different sites of AI or CM could be synchronized. This is illustrated in Fig. 8, which shows a typical cross-correlation of the discharges of two units in CM during the time window 100–400 ms after stimulus onset. The cross-correlogram had an oscillatory structure with a central and several satellite peaks, which suggested that the periodic discharges of the two units were phase-locked to the stimulus onset.
units were synchronized. This was verified by calculating the spectrum of the cross-correlation and by finding that the spectral peak in the $\gamma$ range was significantly above the corresponding peak of chance correlation.

The synchronization of the spike trains of pairs of units could be examined for 1,803 recording pairs from the response to a tone equal to the mean BF of the two units under investigation. Of them 417 (23.1%) exhibited significantly synchronized $\gamma$ activity ($>40$ Hz) during the time window 100–400 ms after stimulus onset. Generally, $\gamma$ synchronization was related to the similarity of the receptive fields of two units. The probability of two units to discharge synchronously was highest for pairs with the same BF and decreased with increasing difference of their BFs ($\chi^2$-test, $P < 0.001$; Fig. 9). This relation was found for units with small and large cortical separations. Results were similar when synchrony was analyzed for tones of different frequency.

**DISCUSSION**

Acoustic stimulation with pure tones could augment amplitudes of field potentials in auditory cortex for a period of $\pm 900$ ms. In this period, increases of amplitudes of field potentials occurred in a frequency-specific manner. During the initial 100 ms, low-frequency components between 20 and 40 Hz were increased at most recordings sites. These components were mostly phase-locked to stimulus onset and corresponded to the
temporal structure of the stimulus-evoked potential complex. At some sites, the low-frequency components were associated with increased frequency components >40 Hz that sometimes were phase-locked to the stimulus. The early increase of power in the γ band by acoustic stimulation could be interpreted as evidence for the existence of stimulus-evoked γ oscillations in auditory cortex. However, it could also be due merely to a broadband increase of stimulus-evoked field potential power. The early response period differed from the late response period in which most sites exhibited increases of high-frequency components between 40 and 100 Hz that rarely were associated with increases in lower-frequency bands. Therefore the high-frequency oscillations commencing ~100 ms after stimulus onset were probably not an artifact of a broadband increase of field potential power but rather because of their latency and their lack of phase-locking to stimulus onset, represent γ oscillations induced by sensory stimulation.

The stimulus-induced γ oscillations seen in the present study resemble in many respects γ oscillations observed previously in different types of neural signals recorded in auditory cortex of rodents (Barth and MacDonald 1996; Franowicz and Barth 1995; MacDonald et al. 1996,1998; Metherate and Cruikshank 1999) that demonstrated that γ oscillations never occurred in the absence of a slow potential, evoked by electric stimulation of the thalamic radiation. The absence of late responses might be a reason why acoustically induced firing patterns in the γ range have not been observed in most previous studies of auditory cortex. The emergence of late responses and, thus γ oscillations, appears to depend, at least

acoustic click stimuli or by electric stimulation of unspecific thalamic nuclei were observed over all regions of AI and AII with amplitudes being largest at the border of AI and AII. In monkey auditory cortex, γ oscillations could be induced by pure tone stimuli at many sites of AI and CM. In contrast to rat auditory cortex, the present study found no indication that amplitudes of γ oscillations were largest at any site of the fields AI and CM in monkeys.

The frequency and stimulus dependence of γ oscillations seen in this and other animal studies (Barth and MacDonald 1996; Franowicz and Barth 1995; MacDonald et al. 1996,1998; Metherate and Cruikshank 1999) are comparable to γ oscillations observed in humans after acoustic stimulation (Bertrand et al. 1998; Crone et al. 2001; Joliot et al. 1994; Knief et al. 2000; Llinas and Ribary 1993; Marshall et al. 1996; May et al. 1994; Pantev 1995; Pantev et al. 1991; Tiitinen et al. 1993). The findings in animals that γ oscillations can be induced over wide regions of auditory cortex and that γ oscillations at different sites can be synchronized suggest that the signals of a large number of local oscillators can superimpose to yield a macroscopic signal of a size that can be measured outside the skull. This corroborates recent findings in the human electrocorticogram (Crone et al. 2001) that evoked and induced γ signals seen in human EEG and MEG recordings originate, at least in part, from neural activity emanating in the auditory cortex.

A prerequisite for the observation of oscillatory neural activity appears to be the existence of late sustained responses to sensory stimulation (Fig. 3). This is corroborated by experiments in a slice preparation of the auditory forebrain (Metherate and Cruikshank 1999) that demonstrated that γ oscillations never occurred in the absence of a slow potential, evoked by electric stimulation of the thalamic radiation. The absence of late responses might be a reason why acoustically induced firing patterns in the γ range have not been observed in most previous studies of auditory cortex. The emergence of late responses and, thus γ oscillations, appears to depend, at least

FIG. 8. Typical example of the correlation of 2 spike trains recorded simultaneously from the caudomedial auditory field. Separation of recording sites was 1.330 μm. A: cross-correlation calculated from a 300-ms long period commencing immediately after the cessation of a 600-Hz tone of 100-ms duration. B: amplitude spectrum of the cross-correlogram shown in A. Dashed line, the amplitude spectrum of the chance correlation of 2 spike trains, each with the same rate as the spike trains under investigation but with independent Poissonian interspike interval distributions. The thin line represents 4 SDs above the chance amplitude spectrum.

FIG. 9. Relation between the ratio of BFs of pairs of units and correlation of γ oscillations in auditory cortex. The distribution of BF ratio was divided into 8 classes such that all classes, except the 1st class, consisted of the same number of units (n = 201; 1st class: n = 246). The ordinate shows the percentage of units with significantly correlated spike trains in the γ range. Correlation between units was analyzed for the tone whose frequency was equal to the mean BF of 2 units during the time window 100–400 ms after stimulus onset.
partly, on the sensory stimulus. After stimulation with acoustic clicks, power of field potentials in the γ band was suppressed for a period of ~300–350 ms that was followed by a rebound of γ power (Franowicz and Barth 1995). Pure tones, by contrast, elicited γ activity at markedly shorter latencies (Fig. 3). The proper selection of the acoustic stimuli for the induction of γ oscillations is further stressed by the finding that, in visual cortex, γ oscillations occurred at highest amplitudes in response to smooth visual stimuli, whereas transient-rich visual stimulation evoked fewer γ oscillations (Kruse and Eckhorn 1996; but see Friedman-Hill et al. 2000).

Generally, there are striking similarities between induced γ oscillations observed in auditory cortex (Barth and MacDonald 1996; Franowicz and Barth 1995; MacDonald et al. 1996, 1998; Metherate and Cruikshank 1999; Sukov and Barth 2001; present study) and in visual cortex (Eckhorn 1999; Gray 1999; Singer 1999). This includes the frequency range, the temporal relation to the evoked potential, their lack of phase-locking to stimulus onset, the prevalence, the stimulus selectivity, and the finding that oscillatory activity recorded within the same or in different cortical fields could be synchronized with each other at near-zero phase lag. This suggests that different parts of the sensory cortex utilize similar discharge patterns to code stimulus information.

Most of the differences between visual and auditory cortex were seen with respect to amplitudes and synchrony of γ oscillations. In monkey auditory cortex, acoustic stimulation increased amplitudes of stimulus-induced γ oscillations in field potentials, on average, by a factor of 1.95 over respective amplitudes of ongoing activity. The increase was smaller than in the visual cortex of the cat (2.2) (Bauer et al. 1995) and of the monkey (2.8) (Eckhorn 1999). Figure 7 shows that in auditory cortex, synchrony of γ oscillations was restricted to a range <3 mm. This range is larger than one would expect from passive volume conduction for which the decay constant in the range was estimated to be maximally 200 μm in visual cortex (Engel et al. 1990). Nevertheless, the range is smaller than in the visual cortex of cats where coherence of γ oscillations extended over wider regions (Brosch et al. 1995; Engel et al. 1990). It was still ~0.5 at a separation of 2 mm and synchronous oscillations were found up to separations of ≥6 mm.

The differences with regard to amplitudes and synchrony of γ oscillations in field potentials might simply result from differences in the effect of sensory stimulation. In most of the studies in visual cortex, amplitudes and synchrony of γ oscillations were measured with stimuli extending over wide regions of the visual field and, hence, excited a large fraction of visual neurons (Eckhorn 1999; Gray 1999; Singer 1999). Reduction of stimulus size decreased amplitudes of induced γ oscillations considerably (Bauer et al. 1995). Therefore it is possible that γ oscillations with larger amplitudes and at more sites of auditory cortex can be observed with acoustic stimuli more complex than pure tones, which excite only a limited part of the auditory system (Crone et al. 2001). In addition it could be that stationary stimuli evoke more γ oscillations than transient-rich stimuli (Kruse and Eckhorn 1996; but see Friedman-Hill et al. 2000). The differences in oscillation amplitudes and synchrony in the auditory and visual cortex could also arise from dissimilarities in animal preparation or from physiologically dissimilarities of the cortical tissue serving the visual and auditory modality. In visual cortex, oscillation amplitudes were considerably greater in awake monkeys (Eckhorn 1999) than in anesthetized cats (Bauer et al. 1995). In the current study, we used ketamine, whereas studies in visual cortex preferentially used gas anesthesia. Although ketamine is known to alter neurotransmission (e.g., Zurita et al. 1994), the effects on γ oscillations seem to be different in auditory and visual cortex. In cat visual cortex, ketamine has been reported to induce spontaneous γ oscillations at high amplitudes (R. Eckhorn, personal communication). In auditory cortex, neither the present study in monkeys nor previous studies in cats (e.g., Brosch and Schreiner 1999; Eggermont 1994) has found bursts of spontaneous γ oscillations with ketamine.

The occurrence of γ oscillations was related to the frequency specificity of neurons in auditory cortex. γ activity was most often found when neurons were stimulated with a BF tone. Comparable findings have recently been reported for the orientation tuning of neurons in visual cortex (Friedman-Hill et al. 2000; Frien et al. 2000). This indicates that γ activity is not only a simple arousal effect (Barth and MacDonald 1996) and occurs whenever neurons are activated but that it is related to the specific excitation of neurons. To our knowledge, the present finding provides the first evidence that, in addition to conventional rate and latency measures, high-frequency tones are represented by the temporal patterning of neural discharges in auditory cortex. It is interesting that the frequency of γ oscillations is above the highest frequency of modulated sounds to which most cortical neurons can phase-lock their response (Langner 1992). This offers additional coding capacity to cortical cells during the late part of the stimulus-evoked response when discharge rates are low.

It has been hypothesized that synchronized γ activity might be used for the definition of functional neuronal assemblies (Eckhorn 1999; Gray 1999; Singer 1999). Although our study was performed on anesthetized animals, present results are compatible with this hypothesis. Like in the visual cortex, the assembly formation in the auditory cortex by synchronizing the firing of neurons seems to be governed, in part, by the similarity of the receptive fields of neurons. Such assemblies might contribute to the cortical representation of auditory objects. This speculation does not exclude that assemblies might also be formed according to rules other than similarity of receptive fields. It neither excludes that assemblies might also be established by synchronization of stochastic activity or activity in other frequency ranges (von der Malsburg 1983; Reitböck 1983). In the present study, there was also an increase of synchrony of neural signals during the initial 100 ms after stimulus onset, which was most pronounced in the low-frequency range, consistent with recent findings of correlated activity in auditory cortex (Brosch and Schreiner 1999). These results suggest that different neuronal assemblies, dynamically formed by synchronization of neural discharges, contribute to the processing of acoustic signals in auditory cortex.

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REFERENCES

GAMMA OSCILLATIONS IN AUDITORY CORTEX


