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FREQUENCY OF GAMMA ACTIVITY IS MODULATED BY MOTIVATION IN THE AUDITORY CORTEX OF CAT*

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Repetitive acoustic stimuli elicit steady-state response (SSR) in the gamma-band both in humans and in mammals. Our aim was to investigate changes of the spontaneous gamma activity and the SSR in the auditory cortex of cats in the background of an instrumental conditioning situation.

Epidural electrodes were chronically implanted above the auditory neocortex. The presentation rate of the clicks varied between 20 and 65/s. Spontaneous EEG and SSR were collected in three behavioral states: in an indifferent environment, in the instrumental cage while the cat was waiting for the light CS, and when she stepped on the pedal and was waiting for the meat reward. Using different repetition rate clicks we determined which stimulus rate elicited the largest SSR in these three situations.

In quiet animal the highest SSR appeared at 28–30/s. Before and during the CS the optimal stimulus rate shifted to 32–38/s. The frequency of the spontaneous gamma activity changed in parallel way depending on the situation. We conclude that both the SSR and the spontaneous gamma activity reflect resonant activity of the same neuronal circuit of the auditory cortex, and it is modulated by the motivational state of the animal.

Keywords: Gamma activity – auditory steady-state response – instrumental conditioning – motivation – cat

INTRODUCTION

One of the most intensively studied questions of perception is the mechanism by which neocortex groups distributed data into coherent object representation. Since the pioneering work of Hubel and Wiesel [12] neurophysiologists mapped the sensory cortical areas where neurons are sensitive to different attributes of the sensory stimuli. Features belonging to the same object, like contrast, color and luminance, are coded by separate neurons located in different areas of the visual cortex [16]. The organization is similar in the auditory areas, too [30]. The question is how these neurons are bound together to form a single perceptual entity.

Gray and Singer [10] reported that neurons in the visual cortex of cats showed stimulus-dependent oscillatory responses in 40–60 Hz frequency range and these

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[*] Dedicated to Professor György Ádám on the occasion of his 80th birthday.

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responses were tightly correlated with oscillatory field potentials. This rhythm corresponded to the gamma band of EEG therefore it was called “gamma oscillation”. According to Singer [36] the synchronous gamma oscillation of spatially distributed sensory cortical neurons with zero phase-lag represents the bioelectrical correlate of the “binding mechanism”. This hypothesis attracted great attention since it gave an answer, how the neurons sensitive to the different features of a complex stimulus are bound together to form a coherent (gestalt) object representation. In the last decade both human and animal studies provided supportive evidence for the relevance of gamma oscillation in perceptual integration and cognitive processes.

Attended stimuli induce enhanced auditory gamma response [2, 23, 44]. Increased gamma oscillation appears at self-paced movement above the corresponding cortical motor area [26]. Increased gamma activity was related to perceptual processing [29].

The binding theory throws a new light upon older 40 Hz EEG data. In human studies increase of spontaneous gamma band activity was found in cognitive task situations [19, 34]. In animal studies Freeman [6] already carried out experiments in the late sixties in which he recorded gamma activity in the olfactory structures of cats and found correlation between the amplitude and phase of the gamma waves and the motivational and learning processes. Enhanced neocortical gamma activity was related to increased attention and to performance in a conditional reflex [3, 38].

Recently Tallon-Baudry et al. [42, 43] studied in detail the changes of gamma activity in visual tasks in humans. They reported that the gamma activity increased not only as an effect of an imperative visual stimulus but also in a visual search task, if the subject had to activate the visual representation of the searched object. Similarly, the gamma activity increased in a delayed task if the visual stimulus had to be stored in the recent memory. The increased gamma activity appeared above the occipital area during the coding of the stimulus while during the recall of the memory it increased above the occipito-temporal and frontal areas. According to them these data provide strong evidence that gamma activity is related to cognitive processes since it increased in all cases when – either to external or internal cues – the central representation of the visual object had to be activated.

Repetitive stimuli also elicit gamma rhythm in the human EEG. The 40 Hz auditory “steady state response” (SSR) was first described by Galambos et al. [8]. If the repetition rate of short auditory stimuli was increased to about 40 Hz a high amplitude sinusoid evoked rhythm appeared in the frontal and central leads. Since then the SSR has been widely applied in audiology and for monitoring anesthesia since its amplitude is intensity dependent and it disappears in general anesthesia [9, 13, 15]. The SSR is absent or greatly reduced in slow wave sleep but in REM sleep its amplitude is similar to that in active wakefulness [22].

The changes of SSR in task situation were studied by Rohrbaugh et al. [31, 32]. They reported that if the gamma oscillation was induced by 40 Hz click stimuli in the background of an instrumental reaction time task, the imperative stimuli induced a latency shortening of SSR, which means that the gamma waves displayed phase-shortening. They concluded that the latency shortening was elicited by orientation related sensory facilitation.

Our knowledge on the neural mechanisms of the different type gamma activities – in spite of the growing amount of data – is still limited. The Singer group studied the neuronal activity of the visual cortex in detail, still the model on the gamma activity made by them is still relatively simple [27]. In slice studies pyramidal and stellate neurons were isolated which displayed spontaneous gamma rhythm [21].

Neurons in the superficial layers of the visual cortex intrinsically generate repetitive burst firing in the gamma range, in response to depolarizing current injection or to visual stimulation [11]. Cholinergic-, GABAergic and NMDA-mediated processes are involved in the generation of the gamma oscillation [4, 45].

Steriade and his research group studied the thalamocortical processes that may contribute to the generation of the gamma activity both by extra and intracellular recording techniques. According to them the gamma oscillation represents not only cognitive processes but rather a general cortical activation pattern induced by the ascending activating system through the basal forebrain cholinergic system [39]. They reported that depolarization of neurons both in the superficial (II–III) and deep (V–VI) cortical layers induced rhythmic burst activity in the gamma band. They concluded that the gamma oscillation is a general property of the cortical neurons, it does not represent a specific sensory process but an increased excitatory state of the neocortex and widespread synchronization is organized by the thalamo-cortical loops [40]. However, the data described above still favor the cognitive binding theory of Singer.

We first described the characteristics of the auditory SSR in alert freely moving cats [24]. We found that the SSR is behavior dependent it did not appear in the auditory cortex in slow wave sleep and in surgical anesthesia while the repetitive evoked potentials remained unchanged in the relay nucleus of the medial geniculate body. Our data do not support the view that SSR is composed by the summation of the middle latency components of the auditory evoked potential [7]. Transient acoustic stimuli also elicit short gamma oscillations in cat which are intensity dependent [5]. Recording intracortical field potentials we reported that the SSR is generated by an oscillatory process in the superficial layers of the auditory cortex [18].

In the present experiments the spontaneous and stimulus driven gamma activity (SSR) was studied in the background of an instrumental conditioning task. We wanted to check whether the modulation of the SSR, described by Rohrbaugh et al. [31, 32] appears also in cats. We were also interested whether the changes of the spontaneous gamma oscillation and the SSR in the different motivational states are similar or not. In the earlier human and animal studies usually only the amplitude of the whole gamma band or a given frequency oscillation was followed. Here we focused our attention to follow the changes of the frequency of the gamma activity.

MATERIALS AND METHODS

The experiments were carried out in three adult cats in accordance with the international ethical norms of animal experimentation. Electrodes were made of 0.23 mm diameter stainless steel wire. They were implanted under pentobarbital anesthesia

(40 mg/kg i.p.) using aseptic technique. Small holes (1.5 mm in diameter) in a 6×5 matrix format were drilled into the skull bone over the auditory neocortex and small loops, formed from the 1 mm bare end of the electrode wires, were placed on the dura mater. The electrode matrix covered both the primary and secondary auditory fields [28]. A stainless steel screw in the bone of the frontal sinus served as reference. The leads were connected to a miniature multicontact connector and the whole implant was fixed to the skull by dental acrylic. An impression was formed for the bone conductor in the frontal part of the acrylic implant.

The brain electrical activity recording was carried out in experimental cages, which were in a sound attenuated (40 dB) room. The behavior of the animal was observed through a closed loop video system. One of the cages served as indifferent environment where the control recordings were made. In another cage instrumental alimentary conditioned reflex was elaborated. In one of the walls of the cage an automatic feeder served to deliver small pieces of meat to the cat. Above it the light of a small bulb served as conditioned stimulus (CS). If the light CS was switched on the animal had to step on the feeder and had to wait for the meat reward delivered after a 5–10 s delay. The spontaneous gamma activity and the auditory SSR were recorded in three experimental situations. In one of them the cat was sitting quietly in the cage representing indifferent situation (quiet). The second was the instrumental situation when the animal was waiting to the light CS (before CS); and the third, when the animal was waiting for the meat reward (during CS).

The brain electrical activity was fed to a multichannel preamplifier by a light multiconductor cable, which did not limit the movements of the animal. After amplification of the signal (bandpass 1 Hz–1 kHz) it was digitized at 2000 Hz sampling rate. The offline analysis of the data was made by Neuroscan® data processing software. We used FFT analysis to quantify the power of the stimulus driven and spontaneous gamma activity. To measure the phase shift the SSR was averaged and band pass filtered between 15 and 50 Hz.

The auditory stimuli were clicks generated by 0.1 ms square waves with an intensity of 80 dB peSPL. They were delivered as background probes through a bone conductor fixed to acrylic implant for the time of the experiments [17]. The repetition rate of the clicks varied between 20 and 65/s. At the beginning of the experiments we mapped which electrode of the matrix produced the highest amplitude SSR. In the behavioral experiments spontaneous gamma activity and SSR recorded from that electrode was analyzed in detail.

RESULTS

Changes of the auditory steady state response

Increasing the repetition rate of the clicks the amplitude of the evoked response gradually decreased. If the power at frequencies corresponding to the stimulus rate was measured, at 25–35 Hz the slope of power changed to an increase [24]. This is the

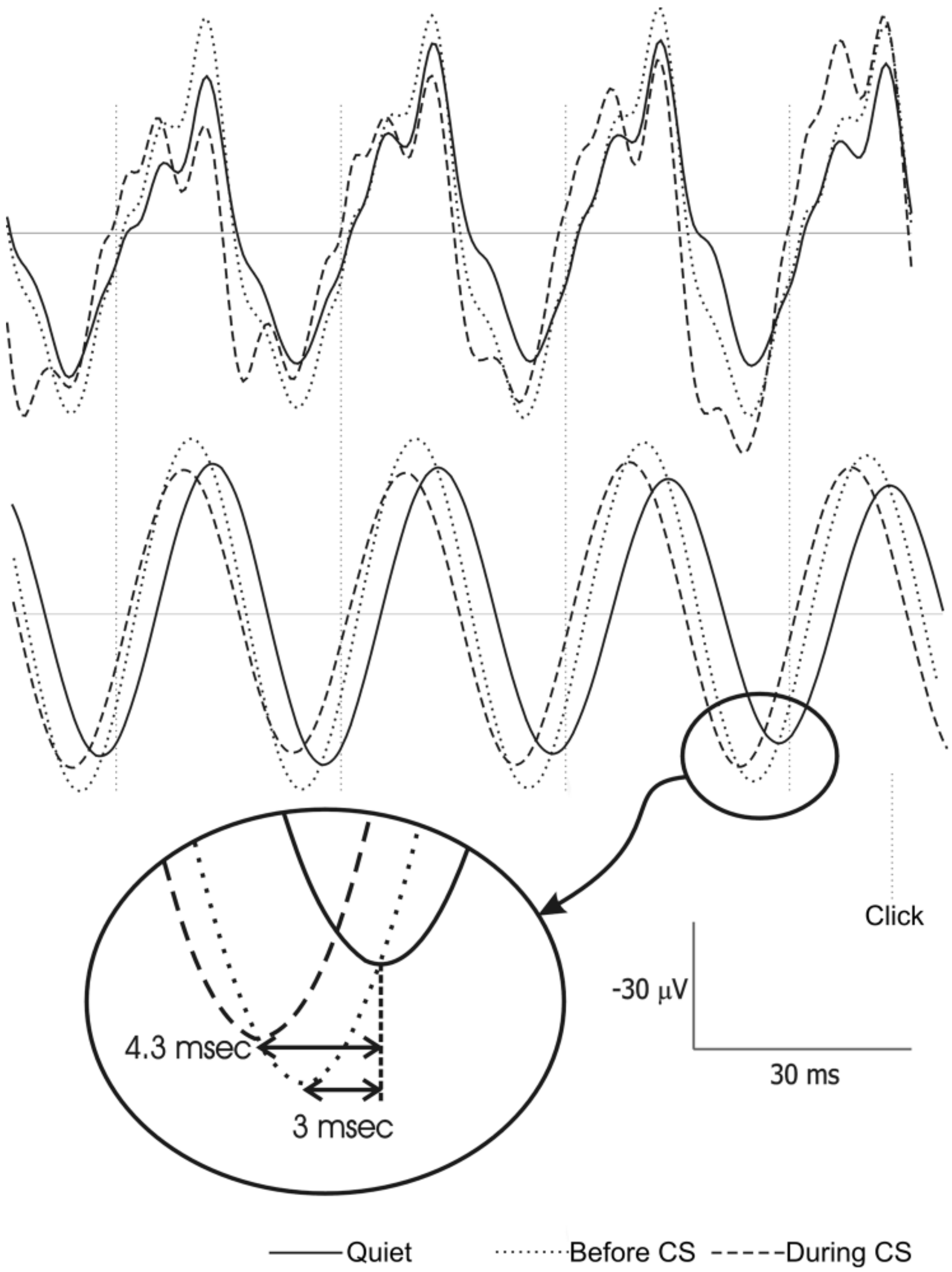

Fig. 1. Stimulus-driven gamma activity (SSR) elicited by 32/s click stimuli in the three experimental situations. Dotted vertical lines mark the time of the clicks. Upper curves: unfiltered SSR. Lower curves: band pass filtered SSR (15–50 Hz). The enlarged picks show the phase shifts in the conditioning situation

frequency range of the stimulus driven gamma activity (SSR). The SSR, recorded from the surface of the auditory cortex of the cat, was a rhythmic oscillation similar to a sine wave, however additional small subcomponents – in form of notches – appeared superimposed on the main wave, in the first 8–10 ms after the clicks (Fig. 1). These correspond to the auditory brainstem responses, which also can be seen on the transient auditory evoked potentials. In the present experiments we did

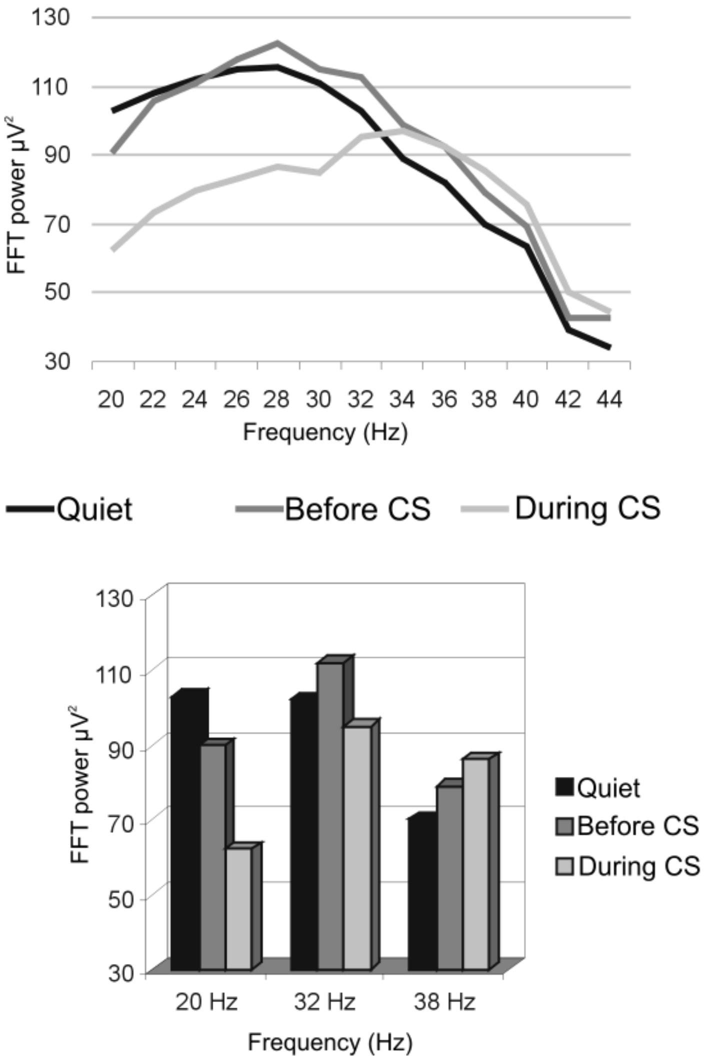

Fig. 2. The changes of the SSR, elicited by different repetition rate clicks in the three experimental situations. Above: SSR power values measured at frequencies corresponding to the stimulus rates. Below: Columns show power values in the three experimental situations at different stimulus repetition rates

not study these subcomponents. In each experimental situation an “optimal stimulus rate” could be observed, eliciting highest power SSR. This was different in individual animals but the tendency of its changes in different behavioral states was found similar [20].

The phase-shift of the SSR, observed in the three experimental situations is depicted in Fig. 1. The stimulus repetition rate was 32/s. The latency of the SSR in the con-

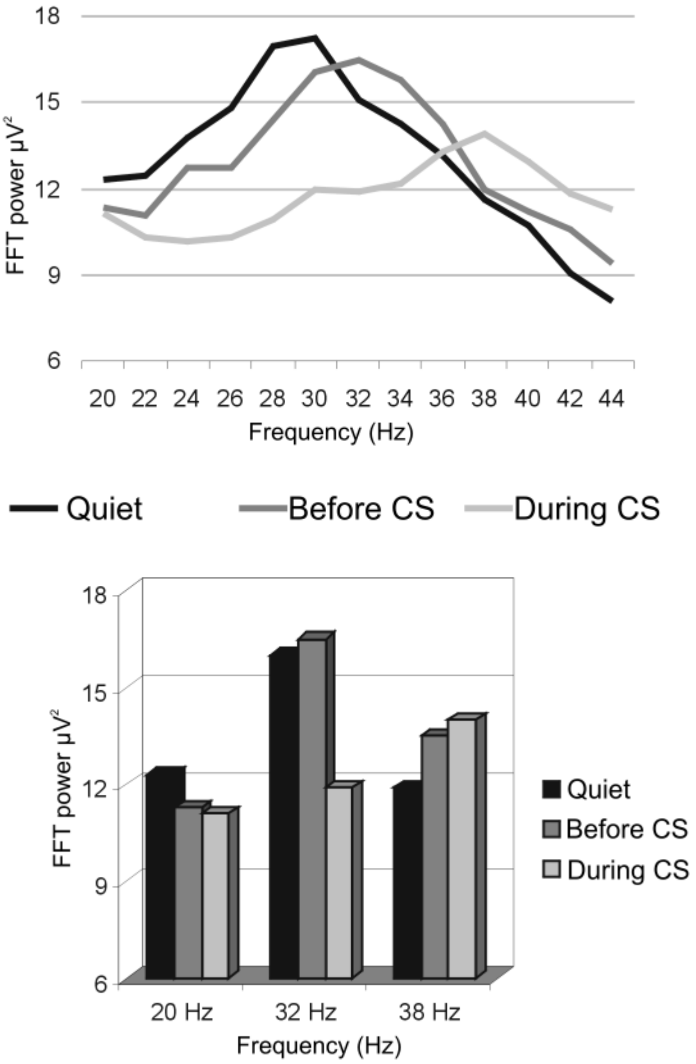

Fig. 3. Above: FFT power spectrums of the spontaneous gamma activity in the three experimental situations. Below: Columns show the changes of power values at given frequencies in the three experimental situations

ditioning situation decreased compared to that recorded in the control situation. The latency decreased with 3 ms (35°) while the animal was waiting for the CS, during the CS, when the animal was waiting for the meat reward, the latency shortening was even greater: 4.3 ms (50°).

In Fig. 2 the change of the optimal stimulus rate in the three situations are demonstrated. The stimulus repetition rate was changed from trial to trial and the FFT power values corresponding to the stimulus rates form the graphs in the left side of the figure. The maximal power value was elicited in the control situation by 28/s click rate. In the instrumental conditioning situation the graphs shifted toward higher values. The highest power value before the CS was again 28 Hz, but the powers were more enhanced at higher values than in the quiet state. During CS the lower frequency components greatly decreased and the optimal repetition rate shifted to 34 Hz. The columns at the right side of the figure clearly show that the lower frequency values (20 Hz) were greatly attenuated in the conditioning situation. Contrary to this at frequencies around 40 Hz (38 Hz indicated in the figure) the power increased while the cat was waiting for the light CS and further during the CS while she was waiting for the meat reward.

Changes in the spontaneous gamma activity

We recorded the spontaneous EEG in the same three experimental situations as in the case of SSR. The EEG activity was filtered by a 15 Hz high pass filter and the gamma band activity was analyzed by FFT. Figure 3 shows the frequency distribution of the gamma activity in the three experimental situations. In quiet state the highest power value appeared at 28–30 Hz. In the conditioning situation before CS the highest value got shifted to 32 Hz and during the CS to 38 Hz. In the right side of the figure the columns indicate that the amplitude and frequency changes of the spontaneous gamma activity were similar to that, which was observed when the optimal stimulus rate of the SSR was measured.

DISCUSSION

The three experimental situations in which we recorded the spontaneous gamma activity and the SSR represented different levels of motivation. In the conditioning cage the level of the motivational excitement of the animal was higher than in the quiet animal in the indifferent environment. During the incentive CS, while the animal was waiting for the food reward, the motivation further increased. These made possible the comparison of the spontaneous gamma activity and the SSR in three different levels of motivation.

The latency of the click evoked SSR became shorter – phase reduction appeared – as the level of the motivation increased. This observation corresponded to the earlier human data [31, 32]. The earlier human and animal studies dealt mainly with the amplitude changes of the gamma oscillations. The data of the present study indicate that both the spontaneous and the stimulus driven gamma activity display motivation dependent frequency changes. The question is whether there is any relevance of these frequency changes from the point of the feature binding. We do not know which frequency of the gamma oscillation is optimal for the binding process. It is possible that the frequency shift caused by increased motivation may set the optimal gamma frequency. Since the neuronal spikes occur at a given phase of the oscillation [37], the higher frequency oscillation may increase the synchronization of the population activity, consequently promote the processing of the incoming information [33].

The spontaneous and stimulus induced gamma activity displayed similar frequency shifts in our experiments. On the basis of this observation we may suppose that in case of the SSR the repetitive auditory stimuli drive the same local cortical circuits that are responsible for the generation of the spontaneous gamma oscillation.

In the recent years numerous new achievements were made regarding the intracortical mechanisms of the gamma activity. *In vivo* data indicate that interneurons in the II and III layers of the sensory cortex play essential role in the generation of the gamma oscillation [11]. These interneurons synchronize the activity of large neuron populations both by GABA-ergic synaptic processes and by gap junctional coupling [41]. The stimulation of the brainstem activating system increases the gamma response induced by sensory stimuli [25]. Motivational and interoceptive features are provided also by the nonspecific system [1]. The nonspecific afferents projecting to the superficial layers of the neocortex together with the specific input to layer IV may together produce that coherent oscillation which integrates the “top down” and “bottom up” effects in perception [14, 35].

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