OFF Responses in the Auditory Thalamus of the Guinea Pig

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He, Jufang. OFF responses in the auditory thalamus of the guinea pig. J Neurophysiol 88: 2377–2386, 2002; 10.1152/jn.00083.2002. ON and OFF auditory responses were examined in the medial geniculate body (MGB) of the guinea pig. Single- and multunit recordings were carried out on 12 anesthetized animals, and noise-burst or pure-tone stimuli were applied to the ear contralateral to the recording hemisphere. One hundred and thirty-five OFF or ON-OFF neurons and 160 ON neurons were studied, and the tuning curves of 21 ON-OFF or OFF neurons were examined from various nuclei of the MGB. The mean minimum threshold of the OFF responses (40.8 ± 20.0 dB SPL, mean ± SD; range: 0–80 dB SPL) was significantly higher than that of the ON responses (28.5 ± 17.6 dB SPL, range: 0–60 dB SPL; n = 17, P < 0.001). Of 10 ON-OFF neurons that showed identifiable tuning frequencies for both ON and OFF responses, 7 showed a higher OFF than ON best frequency (BF), 2 showed the same BF for both ON and OFF, and only 1 showed a slightly lower OFF than ON BF. Most OFF responses sampled from the borders of the ventral (MGv) and rostromedial (MGrm) nuclei of the MGB showed single-peaked tuning curves, similar to those of the ON responses in the MGv. The neurons located in the shell (MGs) and dorsal (MGd) nuclei of the MGB showed complicated—either multi-peaked or broad—tuning curves. All OFF responses showed long-duration-selectivity for acoustic stimuli: the mean half-maximum duration was 116.5 ± 114.8 ms (n = 19, range: 27–411 ms). The latencies of 135 OFF responses were studied in various divisions of the MGB. The ventral border region of MGv showed the shortest latency, followed by the dorsal border region of the MGv, the MGrm, and the caudomedial nucleus (MGcm) of the MGB. The posterior nucleus of the thalamus (Po), the MGd, and the MGs showed much longer mean latencies of >30 ms (P < 0.05 compared with the border regions of the MGv, ANOVA), with Po showing the greatest mean latency of 60.3 ms and the greatest deviation of 25.5 ms. The latency of the OFF response (29.0 ± 14.0 ms, n = 135) was significantly greater than that of the ON response (15.6 ± 9.6 ms, n = 160, P < 0.001). The present results provide valuable information about the threshold, frequency tuning characteristics, minimal response latency, and duration selectivity of OFF neurons in the auditory thalamus.

METHODS

Animal preparation

In a recent study, we found that many OFF neurons in the cat dorsal auditory cortex, which is connected to the dorsal division of the MGB and the posterior nucleus of the thalamus (Po), are stimulus-duration selective (He and Hashikawa 1998; He et al. 1997). Many of the duration-tuned neurons in the IC of the bat and the mouse were OFF response neurons (Brand et al. 2000; Casseday et al. 1994, 2000; Ehrlich et al. 1997). It has been proposed that OFF neurons are involved in the encoding of the amplitude change of the envelope of a sound signal (Kuwada and Batra 2000) and of sound source movement (Toronchuk et al. 1992).

Recently, we reported that OFF response neurons are spatially segregated from ON response neurons in the MGB (He 2001). The segregation of ON and OFF neurons suggests that their different functions might require separate processing in the thalamus.

Despite their potential functional significance, OFF response neurons have received relatively little attention compared with ON neurons, partially due to their small numbers. In the present study, we examined the response properties of OFF neurons, including duration selectivity, intensity dependence, tuning curves, and response latency, in various locations of the auditory thalamus.

INTRODUCTION

OFF response neurons in the auditory system were first reported in the bat and the cat (Kiang 1965; Suga 1964) and have been found in the cat cochlea (Grinnell 1973), the cat cochlear nucleus (Young and Brownell 1976), the superior olivary complex (Grothe et al. 1992), the bat inferior colliculus (IC) (Grinnell 1970; Lesser et al. 1990; Neuweller et al. 1971), the cat medial geniculate body (MGB) (Aitkin and Prain 1974), the human auditory cortex (Hari et al. 1987), and in the mouse auditory brain stem response (Henry 1985a; Hillyard and Picton 1978).

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Acoustic stimulus

Acoustic stimuli were generated digitally by a MALab system (Kaiser Instruments, Irvine, CA) that was controlled by a Macintosh computer (He 1997; Semple and Kitzes 1993). Acoustic stimuli were delivered to the subject via a dynamic earphone (Bayer DT-48) mounted in a pyramid-shaped container. A tube connecting with the container conducted the acoustic stimuli to the contralateral ear. The sound pressure level (SPL, expressed in dB re 20 mPa) of the earphone was calibrated over a frequency range of 100 Hz to 35 kHz under computer control by using a condenser microphone (Brüel and Kjær 1/4 in). The calibration data were stored in a computer file for use in controlling the attenuator to obtain the desired SPLs (Semple and Kitzes 1993). The animal was placed in a double-walled sound-proof room (NAP, Clayton, Australia). Repeated noise bursts and pure tones at rates of 1 Hz or lower were used to examine the ON and OFF responses. Pure tones of 50-ms duration and 5-ms rise/fall times in 400 ms or longer intervals were used to characterize the best frequencies (BFs) of the recorded neurons.

Recording

Platinum or tungsten microelectrodes with impedances of 9–12 MΩ (Frederick Haer) were advanced by a stepping-motor microdrive, which was controlled outside the sound-proof room. The time of spike occurrence relative to stimulus delivery was stored in the computer, which automatically created raster displays and peristimulus time histograms (PSTHs) of the responses, together with frequency response functions (responses to pure tones plotted as a function of frequency).

The MGB was accessed vertically from the top of the brain in the stereotactically positioned animal. The penetrations were made according to a guinea pig brain atlas (Rapisarda and Bacchelli 1977). The vertical coordinate of the electrode was determined at a point slightly above the cortical surface at the first penetration. A single electrode was used for each experiment so that the depth coordinates could be kept consistent for different penetrations during the experiment. For example, to obtain an ON-OFF map of a frontal plane, we fixed the rostrocaudal coordinate and moved the electrode only in the mediolateral direction after each penetration with its depth coordinate consistent for all penetrations. This technique enabled us to reconstruct a physiological map of a whole frontal or sagittal MGB plane containing many penetrations by applying only a single lesion at the last penetration and to superimpose it on the Nissl-stained histological sections.

We intended to isolate single units in the MGB during our recording by an amplitude and time window-discriminator. Multi-units of less than three were recorded in fewer than half of the cases and not specified in the present report.

Anatomical confirmation

After the recording session, the animals were deeply anesthetized with pentobarbital sodium and perfused transcardially with 0.9% saline followed by a mixture of 0.4% paraformaldehyde and 2.5% glutaraldehyde in 0.1 M phosphate buffer (pH 7.3). The brains were removed and stored overnight in 0.1 M phosphate buffer containing 30% sucrose. The thalami were cut transversally into 40-μm-thick sections using a freezing microtome. All sections were stained using the Nissl method. The Nissl sections were superimposed with the physiology map, using the electrode penetration tracks and lesions for guidance. Seven animals were used for the purpose of anatomical confirmation. The cyto-architecture of the thalamus, and the multiple electrode tracks, together with the lesion, enabled us to precisely locate the recording sites in the Nissl staining as in the examples shown in the previous reports (He 2001; He et al. 2002).

Data analysis

Unpaired Student’s t-tests were performed to examine the difference in response latency between the ON and OFF responses in every division of the auditory thalamus. Paired student t-tests were performed to compare BF thresholds between the ON and OFF responses of the ON-OFF neurons or neuron pairs. One-way ANOVA was performed to examine difference among the latency of the OFF responses in various divisions of the auditory thalamus. Results were considered significant at the 95% confidence level (P < 0.05).

Results

Guinea pig’s auditory thalamus

The data presented here are from 135 OFF or ON-OFF neurons and 160 ON neurons. The definitions of the ON and OFF responses were the same as previously reported (He 2001).

In the present study, we confirmed the gradient of the tonotopic organization of the MGv of the guinea pig MGB described by previous investigators (Redies and Brandner 1991; Redies et al. 1989): the BF increases mediolaterally and caudorotally. The neurons in the rostromedial nucleus (MGrm) showed similar characteristics of response latency and frequency tuning as those in the MGv and a rough tonotopic organization in some sections. Best-frequency mapping and neuronal response latency information, together with Nissl staining, permits the parcellation of the MGB, based on the criteria established by Redies and colleagues (He 2001; Redies and Brandner 1991; Redies et al. 1989). As shown in Fig. 1, two additional nuclei were distinguished: one was the MGd, which was located dorsal to the MGv and showed less dense cell packing than the MGv and the shell nucleus (MGs), and the other was the Po, an auditory responsive region, located dorsomedially to the MGrm near the rostral pole of the MGB, which is probably equivalent to the Po of the cat (He 2001; Imig and Morel 1985).

Figure 1 shows two examples for the parcellation of various nuclei of the MGB. OFF, ON, and ON-OFF neurons were sampled from the MGs, MGrm, MGd, Po, and MGv. Because OFF or ON-OFF neurons were only found in the border regions of the MGv (Fig. 1) (He 2001), we sampled these neurons from the ventral (vMGv) and dorsal (dMGd) borders of the MGv separately. The lateral border of the MGv with the MGs had many OFF or ON-OFF neurons, but they were mostly located in the MGs nucleus. No OFF or ON-OFF neurons were found in the core region (cMGv) of the MGv as shown in Fig. 1. For comparison, however, 20 ON neurons were sampled from the cMGv.

OFF or ON-OFF neuronal patches were found not only on the borders of the MGv but also in the MGrm, MGd, and Po (Fig. 1).

OFF neurons and duration tuning

The duration of the stimulus was changed to distinguish OFF neurons from long latency neurons and to distinguish ON-OFF neurons from ON neurons with a rebound response. Figure 2 shows two OFF neurons, which responded only to the OFF phases of stimuli of varied durations. Both neurons showed a phasic
OFF response to various durations from 50 to 400 ms, with a short latency of about 20 ms. Both neurons showed stronger responses to longer-duration stimuli. Using the same definition of duration-selective neurons as in the previous study (He et al. 1997), we classified neurons of this sort as long-duration-selective neurons.

Of 20 neurons examined with a change in the duration of the stimulus, 19 were long-duration selective neurons. The tuning curves of 11 examples are shown in Fig. 3. We defined the "half-maximum duration" (i.e., the duration at which response reached half its maximum level) as a measure of the duration sensitivity of these neurons. The half-maximum durations ranged from 27 to 411 ms \(\mu = 116.5 \pm 114.8 \) (SD) ms. We could find only one duration-tuned neuron, which showed a best duration of 200 ms as shown in Fig. 3 (open-diamond marked curve).

Intensity dependence of the off and on-off neurons

Figure 4 shows five examples of neuronal response patterns when the stimulus intensity is changed, in which three show no change in their response patterns (Fig. 4, A and B) and two show changes in their patterns (Fig. 4C).

The neuron in Fig. 4A was an off neuron. It did not respond to a noise stimulus of 0 dB SPL but showed a small response to 10 dB and its responses increased as intensity was increased.
to 40 and 60 dB. This neuron can be categorized as a monotonically OFF neuron.

The neurons in Fig. 4B were ON-OFF neurons. The neuron 36t146 started responding to the stimulus at 40 dB, showing a long-latency ON response and an OFF response. The characteristics of the response did not change when the intensity of the stimulus was changed from 40 to 80 dB SPL. Neuron 40t3 in Fig. 4B showed a weak OFF response to noise bursts of low intensity and increased response as the stimulus intensified, whereas its ON response did not change much.

Both neurons in Fig. 4C showed an ON response when the intensity of the stimulus was low at 20 dB SPL, showed both ON and OFF responses when the intensity increased to 40 dB SPL, and changed to an OFF response only as the intensity was increased to 80 dB SPL.

Of 10 OFF neurons, defined on the basis of responses to 60-dB noise-burst stimuli, 9 did not change their response patterns when we changed the stimulus to pure tones (see the example in Fig. 4A). Four of 18 ON-OFF response neurons did not change their response patterns (Fig. 4B). However, the remaining 14 ON-OFF response neurons changed their response patterns to either ON or OFF responses when we changed the stimulus to either a noise burst of a different intensity (Fig. 4C) or a pure-tone stimulus.

Frequency selectivity of ON and OFF neurons

Figure 5 shows the frequency-response function of a pair of ON and OFF neurons, where the OFF neuron was located on the ventral border of the MGv and 300 μm ventral to the ON neuron in the ventral portion of the MGv. Neuron 40t48, the ON neuron shown at the top, had a BF of 15–16 kHz, and OFF neuron 40t49 had a BF of ~21 kHz. The threshold for the OFF neuron was 10 dB, which was higher than that of the ON neuron, 0 dB SPL.

Converting the frequency-response functions to a frequency-tuning curve, we obtained the tuning curve of neuron 40t49, as shown in Fig. 6A. The frequency-tuning curves of 21 neurons including 19 ON-OFF and 2 OFF neurons in the MGB, were examined in the same way as neuron 40t49 and shown in Fig. 6.

Among these neurons, five were sampled from the borders of the MGv (Fig. 6A). The OFF tuning curves of three of these five neurons were relatively sharp, with a single peak. The other two (41t10 and 41t11) showed double peaks, with higher threshold. At the lower frequency peak, the OFF tuning characteristics were comparable with those of the ON tuning.

Seven neurons were sampled from the MGs (Fig. 6B) and showed complicated tuning characteristics: all but one (36t123) had multi-peaked or broad tuning curves for ON and/or OFF responses, which differed from the typical single-peaked frequency tuning characteristic of the MGv neurons.

Seven ON-OFF neurons were sampled from the MGcm (Fig. 6C). Of them, 5 OFF and 5 ON responses showed single-peaked frequency tuning curves, which were similar to the MGv neurons.

Two neurons (Fig. 6D) were from the MGd and showed either multipeaked or broad tuning curves.

Neurons 41t10 and 41t11 in Fig. 6A showed a similar pattern of ON and OFF tuning characteristics: a single BF for both ON and OFF tuning and the OFF BF slightly higher than the ON BF. Of 10 ON-OFF neurons (41t10, 32t10, 32t12, 41t11, 36t123, 37t117, 28t12, 27t127, 43t21, and 45t8) that showed identifiable tuning curves for both ON and OFF responses, 7 (41t10, 32t10, 32t12, 41t11, 36t123, 28t12, and 45t8) were found to have a higher OFF BF than the ON BF, 2 (37t117 and 27t127) to have the same BF, and only 1 (43t21) to have a slightly lower BF than the ON BF (Fig. 6).

As can be seen in the tuning curves of 41t10 and 32t10 in Fig. 6, OFF responses tended to have a higher threshold than ON responses. The ON and OFF thresholds of 17 neurons (3 excluded: 40t14, 18t3, and 41t34) in Fig. 6 were analyzed. Thirteen had higher OFF than ON thresholds, and 5 samples showed the same thresholds for ON and OFF tuning curves. On average, the OFF thresholds were significantly higher (40.8 ± 20.0 dB SPL, range: 0–80 dB SPL) than on thresholds (28.5 ± 17.6 dB SPL, range: 0–60 dB SPL; P < 0.001, t-test) as illustrated in Fig. 7.

Latency of OFF and ON neurons

The latency of the OFF responses was defined as the interval between stimulus offset and the response. Figure 8 shows two examples from each of seven different divisions of the auditory thalamus: the vMGv, the dMGv, the MGcm, the MGs, the MGd, and the Po. No differences in the firing patterns among the different nuclei can be identified. A trend of longer latencies in the Po and MGd, which are distant from the MGv, is apparent in Fig. 8, compared with those on the border of the MGv and nearby nuclei.

Figure 9 shows the means and SDs of the latencies of OFF responses in various divisions of the MGB. The vMGv showed the shortest latency (18.8 ± 6.3 ms), followed by the dMGv (20.5 ± 3.9 ms), MGcm (22.3 ± 7.2 ms), and MGs (27.4 ± 4.9 ms). The differences among these divisions were not statistically significant. However, mean latencies in the Po, MGd, and MGs were much longer (>30 ms) and were significantly different from those in the vMGv (P < 0.05, ANOVA). Of these divisions, the Po had the longest mean latency (60.3 ms), and the greatest SD (25.5 ms; n = 7), whereas the MGd and MGs had mean latencies of 38.6 ± 12.4 and 33.4 ± 10.9 ms, respectively.

In Fig. 9, the mean latency of 20 ON responses is also shown.
for every division. In addition to the preceding divisions, we also sampled 20 ON neurons from the core region (cMGv) of the MGv, where no OFF neurons were recorded. The latency of the OFF responses in every division was significantly greater than that of the ON responses \( (P < 0.01, \text{unpaired } t\text{-test; Fig. 9}) \). The overall mean latency of the OFF responses was 29.0 ± 14.0 ms \( (n = 135) \), which was again significantly greater than that of the ON responses \( (15.6 ± 9.6 \text{ ms}, n = 160, P < 0.001, \text{unpaired } t\text{-test}) \).

The ON neurons in the cMGv showed the shortest mean latency of 9 ± 1.5 ms, followed by the MGrm \( (11.5 ± 4.2 \text{ ms}) \), the dMGv \( (12.7 ± 4.4 \text{ ms}) \), and the vMGv \( (13.5 ± 4.7 \text{ ms}) \).

The MGs showed the longest mean latency \( (24.0 ± 12.4 \text{ ms}) \) and the MGd the second longest \( (20.4 ± 5.6 \text{ ms}) \). The Po and the MGcm showed similar mean latencies of 17.7 and 16.1 ms, while the Po showed the greatest deviation, of 17.2 ms, in the ON response latency.

**DISCUSSION**

The proportion of OFF or ON-OFF neurons relative to ON neurons in the visual system is much higher than in the auditory system, in which less than one-fifth of the responses (13% in the monkey thalamus: Allon et al. 1981; 20% in the guinea

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**FIG. 4.** Responses of OFF or ON-OFF neurons to acoustic stimuli of varied intensities. A and B: raster displays of 1 OFF (A) and 2 ON-OFF (B) neurons that did not show changes in their ON or OFF responsive characteristics, and those of 2 neurons (C) that showed changes in the ON and OFF responsive characteristics. Bars under the raster displays indicate the duration and intensity of the stimuli.
pig thalamus: He 2001; 13% in the bat IC: Lesser et al. 1990; 24% in the bat auditory cortex: Ostwald 1984) were estimated to be OFF or ON-OFF neurons. This could be a reason why OFF neurons have received very little attention in the auditory system.

OFF responses in the auditory system were reported as early as 1964 (Suga 1964). They have been found in the bat cochlea (Grinnell 1973), in frog auditory nerve fibers (Feng et al. 1994), in the cat cochlear nucleus (Young and Brownell 1976), and in the superior olivary complexes (Grothe et al. 1992; Kuwada and Batra 1999), the ICs (Brand et al. 2000; Cain and Jen 1999; Casseday et al. 1994, 2000; Grinnell 1970; Lesser et al. 1990; Neuweiler et al. 1971; O’Neill 1985; Pollak and Bodenhamer 1981; Pollak and Schuller 1981; Radionova 1988), the thalami (Atkin and Prain 1974; Calford 1983; Calford and Webster 1981; He 2001; Zurita et al. 1994), the auditory cortexes (Ahissar et al. 1992; Bieser and Muller-Preuss 1996; Hari et al. 1987; He et al. 1997; Heil and Scheich 1991; Heil et al. 1992; Ostwald 1984; Pellegrino-Toiba and Wollberg 1989; Toronchuk et al. 1992; Zurita et al. 1994), and the auditory brain stem responses (Henry 1985a,b, 1987a,b; Hilliard and Picton 1978; Laukli and Mair 1985) of various mammals. In the bat, it is believed that the OFF response is generated within the cochlea and the OFF tuning frequency is an indicative of the resonance frequency of the organ of Corti (Ko¨ssl and Vater 1985; Lesser et al. 1990; Suga et al. 1974, 1975).

In addition to the OFF sheets surrounding the MGv, which have been reported previously (He 2001), additional OFF patches were found in the Po, the MGd, and the MGcm in the present study. The OFF patches in the Po and MGd were more diffuse than those surrounding the MGv: they were mixed with the ON neurons and in most of the cases they showed up with an ON-OFF response (Fig. 1).

Using a multi-channel magnetoencephalograph device, Noda et al. (1998) could detect a spatial segregation of ON and OFF responses in the human auditory cortex. This might be explained by the fact that their origins of projection in the auditory thalamus are segregated (He 2001). In a recent study of the monkey auditory cortex, Recanzone (2000) found that the caudomedial auditory field, which receives projection mainly from the nonlemniscal MGB, has a greater percentage of OFF neurons than the primary auditory cortex to which the lemniscal MGB projects.

FIG. 5. The rate frequency functions of the ON and OFF responses. A pair of neighboring ON (40t08) and OFF (40t49) neurons are shown in A and B, respectively. A: rate frequency functions of the ON response neuron for the pure tone stimuli of 6 different intensities at 0, 10, 20, 40, 60, and 80 dB SPL. As shown in the raster display (inset in A), only the darkened spikes from 0 to 50 ms after stimulus onset were calculated as the ON responses. B: rate frequency functions for this OFF neuron were examined for pure-tone stimuli at 15, 20, 30, 40, 50, 60, and 80 dB SPL. As shown in the raster display (inset in B), only the darkened spikes from 0 to 100 ms after stimulus offset were calculated as the OFF responses. We used 400 ms as the duration of the stimulus, and this is shown below the raster displays.
Earlier studies on the bat showed that the segregation of the ON and OFF pathways could occur before the MGB: Suga et al. (1975) mentioned that the OFF neurons have a lower tuning frequency range than the ON neurons in the peripheral auditory neurons, hinting at site specificity of the OFF neurons, and Lesser et al. (1990) found that the ON-OFF neurons reside within the dorsoposterior division of the central nucleus (ICC) of the IC. The dorsoposterior division projects to the medial part of the MGv, the MGd, and the suprageniculate nucleus of the bat (Wenstrup et al. 1994). Because the functional implications of the OFF response for the bat could be different from those for other mammals, questions arise as to whether the OFF or ON-OFF neurons are segregated from the ON neurons before the thalamus (i.e., in the IC) in other mammals, and their locations in the IC.

A further question is whether OFF neurons’ segregation from ON neurons has anything to do with the inhibitory inputs in the thalamus. Giant GABAergic terminals have been found only in

**FIG. 6.** Threshold tuning curves sampled from different subdivisions of the MGB. A: 5 neurons were sampled from the MGv, mostly near the borders to other divisions. B: 7 neurons from the MGs. C: 7 neurons from the MGrm. D: 2 neurons from the MGd. —, tuning curves of ON responses; ••••, tuning curves of OFF responses.

**FIG. 7.** Minimal threshold of ON and OFF responses. The means and SDs were taken from 17 ON-OFF neurons. Threshold was obtained at the BF for ON or OFF response.
the non-MGv neurons in the cat thalamus (Winer et al. 1999). About 20% of the neurons in the IC are GABAergic (Oliver et al. 1994) and directly project to the thalamus (Peruzzi et al. 1997). There are long-duration-selective neurons and duration-tuned neurons in the cat auditory cortex as well as in the visual cortex (Duysen et al. 1996; He et al. 1997). Although it was not specifically stated in Casseday and colleagues’ reports, some of the duration-tuned neurons in the bat IC looked like OFF neurons (Cassaday et al. 1994; Ehrlich et al. 1997). In the midbrain of the mouse and the chinchilla, some duration-tuned neurons are OFF response neurons (Brand et al. 2000; Chen 1998). One neuron in Fig. 4 can be classified as a duration-tuned neuron, which responds best to a much longer duration of 150 ms than those in the bat midbrain.

**Duration selectivity of OFF neurons**

It was suggested in our previous report that the OFF neurons in the auditory cortex are involved in the temporal integration of auditory information, especially for duration selectivity (He et al. 1997). There are long-duration-selective neurons and duration-tuned neurons in the cat auditory cortex as well as in the visual cortex (Duysen et al. 1996; He et al. 1997). Although this parameter was not systematically examined, it is evident that the OFF tuning curves show higher thresholds than the ON tuning curves in primary auditory cortex neurons (Grinnell 1973; Pelleg-Toiba and Wollberg 1989) as well as in the auditory nerve (Suga et al. 1975).

**ON and OFF tuning characteristics**

Most of the OFF responses of the OFF or ON-OFF neurons located on the borders of the MGv and MGm showed single-peaked tuning curves, similar to those of the ON responses in the MGv. Those neurons located in the MGs and MGd showed complicated—either multi-peaked or broad—tuning curves. As OFF neurons are located mostly on the border of the MGv or other nuclei of the MGB, most OFF or ON-OFF neurons are not tuned to any specific frequency (partial data shown in Fig. 5).

Of 10 ON-OFF neurons that showed identifiable BFs for both ON and OFF responses, 7 were found to have a higher OFF than ON BF, 2 to have the same BF, and only 1 to have a slightly lower OFF than ON BF.

In three examples shown in an early study by Grinnell (Figs. 2 and 3) (Grinnell 1973), all OFF responses had BFs of ~110 kHz and a 20–40 dB higher threshold than the ON responses. Suga and colleagues showed that in the bat OFF neurons are tuned at 58–62 kHz, whereas ON neurons are tuned at 63–64 kHz (Suga and Manabe 1982; Suga et al. 1975). The results of Grinnell (1973) and Suga et al. (1975) were consistent with Lesser et al. (1990)’s finding that the ON-OFF neurons are located only within the dorsoposterior division of the ICC, where most neurons have a BF <63 kHz (Wenstrup et al. 1994). Using auditory brain stem response (ABR) tuning curves, Henry (1985b) has shown that the tuning curves of the OFF component are characterized by two peaks: one at a frequency below and the other at a frequency above the ON tuning frequency. For one auditory cortical neuron in Pelleg-Toiba and Wollberg’s report (1989), the OFF component was tuned to a higher frequency than the ON component; for another, ON and OFF components were tuned to the same frequency.

Our results show that the OFF responses have a significantly higher threshold (39.2 ± 20.7 dB) than the ON responses (26.9 ± 18.3 dB). The threshold of the OFF component of the ABR response is higher than that of the ON component (Henry 1985b). Although this parameter was not systematically examined, it is evident that the OFF tuning curves show higher thresholds than the ON tuning curves in primary auditory cortex neurons (Grinnell 1973; Pelleg-Toiba and Wollberg 1989) as well as in the auditory nerve (Suga et al. 1975).

**FIG. 8.** PSTHs of 14 OFF responses from varied locations of the MGB. Two OFF responses were sampled from each of the following locations: A, the cMGv; B, the dMGv; C, the MGcm; D, the caudomedial nucleus (MGcm); E, the MGs; F, the MGd; and G, the Po.

**FIG. 9.** Means and SDs of the 1st-spike latencies of the OFF and ON responses from varied locations. □, latencies of the OFF responses with their means indicated above the bars; □, latencies of the ON responses in white bars. The SDs are shown above the means. n, the numbers of samples used in the statistics. *p < 0.001, ANOVA, #, the difference between the OFF and ON response latencies within the same location was statistically significant (P < 0.01, unpaired t-test). As no OFF neurons were recorded in the central core of the MGv, the OFF latency of cMGv is not available.
Most off neurons in the present report were long-duration selective, although their minimal responsive, half-maximal responsive and saturation durations differ from neuron to neuron (Figs. 3 and 4). The duration-tuning curves (Fig. 3) of most off neurons had monotonic ascending slopes; these neurons might encode duration information in their spike numbers and provide the base for the duration-selective responses of both long-duration and duration-tuned off neurons in the auditory cortex (He et al. 1997). It is interesting to note that the off responses of the thalamic barrelloid neurons showed a similar long-duration selective property (Kyriazi et al. 1994).

Latency of off responses

The latency of the neuronal response has long been a parameter used to characterize the neurons in the MGB and the auditory cortical areas (Aitkin and Webster 1972; Calford 1983; He et al. 1997; Irvine 1980; Irvine and Huebner 1979). Neurons in the MGv showed very short latencies for on responses, whereas those in the MGd responded to auditory stimulus at long latencies (Calford 1983; Calford and Webster 1981; Hu 1995). Consistent with the previous results, we found that the MGv has the shortest mean latency, of 9.0 ms, in the core region, and a slightly longer one of 12.7 and 13.5 ms in the dorsal and ventral border regions. The MGs showed the longest mean latency of 24.0 ms with a large deviation of 12.4 ms. Together with the MGd, which also showed a long latency, the MGs of the guinea pig might be equivalent to the MGd of the cat.

The present report is the first time that latency information has been reported as a parameter for the off response. Interestingly it was revealed that the mean latency of the off response was significantly longer than the on latency in every region (Fig. 9). Although the physiological significance and the neuronal mechanism behind this result are to be investigated, the longer latency of the off neurons hints that the source of the input might be not from the primary nucleus of the IC.

The off neurons in the ventral and dorsal borders of the MGv showed the shortest mean latencies, followed by those in the MGvm and MGcm. The neurons in the Po and MGd showed the longest mean latencies, while those in the MGs showed a moderate mean latency. These results are consistent with those of the ON responses in various divisions of the MGB, for example, the neurons in the MGd showed longer latency than those in the MGv (Calford 1983; Hu 1995). There is a tendency for the off response latency of the Po and MGd neurons to show a much greater deviation than the latency of the MGv, MGvm, and MGcm neurons (Fig. 9).

Functional implications of the off neurons

Off neurons are thought to be involved in temporal information integration, as they respond at the end of the stimulus and show duration tuning characteristic (Brand et al. 2000; Casseday et al. 1994, 2000; Ehrlich et al. 1997; He et al. 1997). Off responses are correlated with the direction of movement of a sound source (Toronchuk et al. 1992), off neurons encode the decrement of the intensity with a wider range of sound levels (Kuwada and Batra 1999; Lesser et al. 1990). It will be interesting to see the relationship between the off responses and the binaural columns in the primary auditory field (I骂ig and Adrian 1977). Further investigation should be carried out to see the origin of the spatial segregation of the on and off pathways through physiological mapping down from the midbrain to the auditory nerve fibers. The anatomical organization of the on and off neurons is always associated with functional significances.

Although the functional implications of off neurons need to be further investigated, the present results provide solid information about their lowest responsive threshold, frequency tuning characteristics, minimal response latency, and duration selectivity of off neurons in the auditory thalamus.

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