Differential Distribution of Burst and Single-Spike Responses in Auditory Thalamus

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He, Jufang, and Bin Hu. Differential distribution of burst and single-spike responses in auditory thalamus. J Neurophysiol 88: 2152–2156, 2002; 10.1152/jn.00091.2002. The medial geniculate body (MGB) of the auditory thalamus comprises lemniscal and nonlemniscal neurons that project to the primary auditory cortex and limbic structures, respectively. Here we show that in anesthetized guinea pigs, MGB responses to a noise-burst stimulus exhibit distinct and synaptic pathway-specific firing patterns. The majority of nonlemniscal MGB cells exhibited bursting responses, whereas lemniscal neurons discharged mainly single or spike doublets. The burst firing is delayed in nonlemniscal neurons and exhibited several features that are characteristics of those mediated by low-threshold Ca2+ spikes. Such a synaptic pathway-specific allocation of bursting and single-spike firing patterns is consistent with the notion of parallel processing of auditory information in thalamocortical system.

INTRODUCTION

Parallel organization of synaptic signaling pathways is a prominent feature of mammalian auditory thalamus where acoustic relay is carried out by segregated lemniscal and nonlemniscal relay neurons (Imig and Morel 1983; Winer 1992). The former is located ventrally (MGv) in the medial geniculate body (MGB). They receive ascending input from the central nucleus of the inferior colliculus (IC) and project to the primary auditory cortex. The nonlemniscal neurons are situated in the dorsal (MGd), medial (MGm) and shell nuclei of the MGB. They receive input from the IC as well as other brain regions (Winer 1992) and provide a substantial and direct projection to the lateral amygdala nuclei (Doron and LeDoux 2000). Nonlemniscal pathway is critically involved in auditory associative learning and memory (Komura et al. 2001; LeDoux 2000). Previous in vitro studies have shown that MGd neurons tend to discharge in bursts in responding to sensory afferent stimulation, whereas MGv neurons fire mostly single or double spikes (Hu 1995). Such a pathway-specific allocation of burst neurons observed in vitro is not a trivial epiphenomenon. Burst or high-frequency firing not only enhances sensory event detection but also can modulate synaptic plasticity in their target neurons (Huang et al. 2000; Mooney and Hu 2002; Sherman 2001). In this study, we examined whether burst firing can be evoked by physiological acoustic stimuli in vivo and whether bursting neurons are preferentially associated with nonlemniscal nuclei.

METHODS

Preparations

The methodology used in this paper has been previously described in detail (He 2001) and approved by the Animal Subjects Ethics Committee of the Hong Kong Polytechnic University. Briefly, guinea pigs (400–627 g) were anesthetized with ketamine/xylazine (initially 40 and 10 mg/kg im, supplemented at 10 and 2.5 mg·kg−1·h−1 im). After mounted to a stereotaxic frame with the right ear freed from the ear bar, a craniotomy was performed to allow vertical access to the left MGB.

Acoustic stimuli, generated by a MALab system (Kaiser Instruments, Irvine, CA), were delivered via a dynamic earphone (Bayer DT-48) mounted in a probe in a double-walled sound-proof room (NAP, Clayton, Australia). The sound pressure level (SPL) was calibrated over a frequency range of 100 Hz to 35 kHz via a condenser microphone (Bruel and Kjær 1/4-in). Repeated noise bursts (100-ms duration) with 1 s or longer interstimulus intervals and a 5-ms rise/fall time were used. Repeated pure tones were used to characterize the best frequencies of the recorded neurons.

Recording

Platinum or tungsten microelectrodes with impedance of 9–12 MΩ (Frederick Haer & Co.) were advanced by a stepping-motor microdrive according to atlas (Rapisarda and Bacchelli 1977). A single electrode was used for each experiment so that the depth coordinates could be kept consistent for different penetrations and used for physiological map reconstruction based on a single lesion at the last penetration (He 2001). Single units were isolated via high-impedance recording electrodes and further confirmed on-line by means of their waveforms displayed on a digital oscilloscope. Only those units that exhibited stable waveforms throughout a trial session (typically <7 min) were recorded using an amplitude and time window-discriminator (He 2001) and displayed as raster or rate meter graphs for on-line monitoring and off-line analysis.

Histology

The animals were deeply anesthetized and transcardially perfused with conventional fixative. The brains were removed and stored in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
FIG. 1. Distribution of burst and nonburst neurons in the medial geniculate body (MGB). The recording sites (A–C) and pattern of spike activities (D) from 9 representative neurons from a single animal are shown. The penetrations coordinates are rostrocaudal (RC) and mediolateral (ML). A frontal map indicating on-off responding neurons is superimposed on the Nissl section at the same level. Note the “sudden” response transition from burst to single spike between dorsal and ventral MG (MGd and MGv; f and g). R: response. L: long latency (>50 ms). W: weak response. N: no response. Numbers indicate the best frequencies. The scale bar is in mm.
Lemniscal and nonlemniscal MGB neurons exhibited varying degrees of spontaneous activity, some of which appeared as rhythmic high-frequency bursts resembling spindle oscillations (Steriade and Llinás 1988). The following criteria were then adopted in the selection of responsive neurons. 1) The average spike counts (20 trials) within the first 100 ms of a peristimulus histogram must be three times higher than that in the rest of the histogram (900 ms). 2) An evoked burst response must have multiple spikes (2–6) occurring within a 15-ms time period, and a bursting neuron must show burst responses in ≥50% of the trials. 3) A single spike neuron must show no more than two spikes during a 15-ms poststimulus window in ≥75% trials. A lower ratio was adopted for bursting cells because they tended to have a higher rate of response failures (see following text) than single-spike neurons. Furthermore, we found that <2% of neurons in our study showed frequent two-spike responses and none of which could be classified as burst neuron because they did not appear in >50% trials together with high-frequency bursts. Hence, neurons with frequent two-spike responses were all in the single or nonbursting cell category. Based on the preceding criteria, our database included 63 bursting neurons and 60 single-spike cells.

Figure 1 illustrates typical bursting versus single-spike neurons recorded from the MGv and several subregions of the nonlemniscal shell (He 2001). Data pooled from two animals showed that ~77% or 33 of 43 nonlemniscal neurons were bursting cells (Fig. 1D, a–d); in contrast, only 17% or 5 of 29 lemniscal neurons were found to discharge high-frequency bursts (P < 0.001). An inverse distribution was, however, observed for single spike cells (Fig. 1D, h and i), which were observed in 83% MGv cells and 23% nonlemniscal neurons (P < 0.001). Bursting neurons often co-localized with off-respoding cells (He 2001) and exhibited longer on-response latencies (see following text).

Our study also uncovered a significant population (~35%) of lemniscal and nonlemniscal MGB cells that cannot be confidently classified as either single or burst cell type based on above-mentioned criteria. However, the poststimulus time histograms (PSTHs) constructed from “nonbursting” (i.e., single, double, and multiple spike) cells clearly exhibited a different temporal pattern of spike activities from bursting neurons. The latter, as a population, showed a more sustained pattern of excitation (Figs. 1 and 2A) and a more diverse and delayed first spike latencies that lagged nonbursting response by ~7 ms (Fig. 2B). Furthermore, the failure of bursting responses during individual trials often took place in an all-or-none fashion (n = 6; Fig. 3A).

Quantitative analysis of the intra-burst structure in a subpopulation of neurons revealed that the evoked burst response had a mean interspike interval of 3–4 ms (Fig. 3B; n = 22). Interspike interval increased progressively within a burst (Fig. 3B). The underlying trend of this increase can be clearly seen by fitting the data with an arbitrary bi-exponential curve. Interestingly, spontaneous and evoked bursts recorded from the same neuron often exhibited similar features (data not shown).

**DISCUSSION**

The present study examined the firing pattern of lemniscal and nonlemniscal MGB neurons responding to acoustic stimulation. Our data show that many neurons located within the nonlemniscal MGB discharged high-frequency bursts. The burst is, however, not a common feature of lemniscal neurons where the acoustic responses are dominated by single spikes or spike doublets of significantly shorter latency.

To our knowledge, the phenomenon of differential distribution of bursting neurons in vivo has not been documented before. Previous studies, however, show that lemniscal and nonlemniscal auditory neurons have distinctive physiological features (Bordi and LeDoux 1994; Calford 1983; Edeline et al. 1999). In contrast to MGv cells, the synaptic responses evoked in many nonlemniscal neurons, particularly those located in the caudodorsal part of the MGB, are characterized by delayed spike firing, widely fluctuating latency, a broad frequency tuning, and an absence of tonotopic organization (Bordi and LeDoux 1994; Calford 1983).

The differential anatomical distribution of single-spike and bursting responses cannot be readily ascribed to the antagonistic effect of ketamine anesthesia on N-methyl-D-aspartate (NMDA) receptors. Previous study has shown that the fast or early excitatory postsynaptic potentials (EPSPs) that mediate single-spike response in MGv neurons are largely mediated by non-NMDA receptors whereas burst firing in MGd requires...
NMDA receptor activation (Hu et al. 1994). In this context, we may have underestimated the proportion of bursting neurons in the nonlemniscal auditory thalamus. The persistence of bursting responses in the MGd may result from an incomplete blockade of NMDA receptor synaptic potentials (Deschenes and Hu 1990) and/or a relatively low sensitivity of NMDA receptors comprising NR2D subunits to uncompetitive NMDA receptor antagonists e.g., MK-801, (Bresink et al. 1996). In receptors comprising NR2D subunits to uncompetitive NMDA and/or a relatively low sensitivity of NMDA receptors expressed in HEK 293 cells. Br J Pharmacol 119: 195–204, 1996.


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REFERENCES


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