Focal Stimulation of the Thalamic Reticular Nucleus Induces Focal Gamma Waves in Cortex

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MacDonald, Kurt D., Eva Fifkova, Michael S. Jones, and Daniel S. Barth. Focal stimulation of the thalamic reticular nucleus induces focal gamma waves in cortex. J. Neurophysiol. 79: 474–477, 1998. Electrical stimulation of the thalamic reticular nucleus (TRN; 0.5-s trains of 500-Hz 0.5-ms pulses at 5–10 μA) evokes focal oscillations of cortical electrical potentials in the gamma frequency band (~35–55 Hz). These evoked oscillations are specific to either the somatosensory or auditory cortex and to subregions of the cortical receptive map, depending on what part of the TRN is stimulated. Focal stimulation of the internal capsule, however, evokes focal slow potentials, without gamma activity. Our results suggest that the TRN’s role extends beyond that of general cortical arousal to include specific modality and submodality activation of the forebrain.

INTRODUCTION

Sensation requires that sensory information be relayed to the brain and that the brain be aroused to process this information. The thalamus is essential to both of these functions, serving as a major synaptic relay for cortical sensory input and as a central regulator of cortical arousal (Jones 1985; Minciacchi et al. 1993). However, in contrast to the well-established thalamic relay nuclei, thalamic centers responsible for modulating cortical arousal are poorly understood. The unique organization of the thalamic reticular nucleus (TRN) suggests that it may play a pivotal role (Crick 1984; Jones 1975; Scheibel and Scheibel 1966; Steriade et al. 1986; Steriade and Llinás 1988). The TRN comprises a shell encasing the dorsal thalamus, which is traversed by sensory fibers that make synaptic contact on their way to the neocortex (Jones 1975; Scheibel and Scheibel 1966). Recent evidence indicates that when the cortex is naturally aroused (Freeman and van Dijk 1987; Murthy and Fetz 1996) and processing sensory information (Basar and Bullock 1992; Eckhorn et al. 1988; Gray and Singer 1989), it produces electrocortical oscillations in the gamma frequency band (~35–55 Hz). To investigate the role that the TRN may play in cortical arousal, we developed a method of electrical thalamic stimulation accompanied by multielectrode, high spatial resolution cortical recording (Barth and MacDonald 1996). We applied this method to electrically stimulate the TRN and map gamma oscillations from the surface of auditory and somatosensory cortex.

METHODS

Potentials were mapped from the cortex of eight ketamine/xylazine anesthetized Sprague-Dawley rats (350–450 g) by using two placements of an 8 × 8 electrode array that covered a 3.5-mm² area of auditory cortex and the vibrissal and forepaw region of somatosensory cortex (Fig. 1A). Responses were amplified (band-pass cutoff = −6 dB at 0.01–100 Hz; roll-off = 5 dB/octave) and digitally sampled (500 Hz). Auditory and somatosensory potentials evoked by clicks and mechanical stimulation of the contralateral vibrissae and forepaw were used to consistently align the array across animals. In four additional animals, stereotaxic coordinates for TRN stimulation were determined by injecting horseradish peroxidase conjugated to wheat germ agglutinin (Fig. 1A; WGA-HRP; 0.02 μl) into either auditory cortex or the forepaw region of somatosensory cortex. All experimental animals were cared for in accordance with institutional guidelines and all methodology was approved before initial investigation.

TRN stimulation consisted of 500 ms trains of current pulses (5–10 μA; 0.5-ms duration; 500 Hz). Single trial evoked gamma oscillations were quantified for mapping by subtracting the prestimulus spectral power from that computed during stimulation, within a 35–55 Hz bandwidth (Fig. 2A, insert, shaded region) and the resultant difference, reflecting evoked gamma, was averaged across all trials for each animal. Evoked slow potentials were similarly quantified by averaging their amplitude from 100 to 400 ms post-stimulation (Fig. 2B, shaded region).

RESULTS

Auditory injections of WGA-HRP resulted in a band of retrogradely labeled fibers originating in the medial geniculate nucleus and coursing rostrally then laterally through the auditory sector of the TRN and internal capsule (TRNaud and ICaud) on their way to the cortex (Fig. 1B). Close examination of the TRNaud revealed labeling characteristic of axon terminals clustered about the large cell bodies in this region (Jones 1975). Injection into the forepaw region of somatosensory cortex labeled fibers that originated in the ventroposterior lateral nucleus of the thalamus and traversed the more rostral TRN and internal capsule (Fig. 1C: TRNSom and ICsom). In Fig. 1, B and C, the arrow points to the approximate sites of thalamic stimulation.

TRNaud stimulation consistently produced fast oscillations in auditory cortex for the duration of the stimulus (Fig. 2A; left). The power spectral density change (Fig. 2A; insert) revealed a large increase at ~40 Hz and a decrease in lower frequencies. Stimulation of TRNaud had no effect on surface potentials recorded from somatosensory cortex (Fig. 2A; right). Although electrical stimulation must have excited both local cells of the TRNaud and numerous thalamocortical and corticothalamic fibers traversing this zone, evoked oscillations required activation of local cells; stimulating fibers of passage in the adjacent ICaud at the same intensity always resulted in a positive slow potential lasting the duration of the stimulus without evoking any oscillations.
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along the rostrocaudal axis resulted in a shift in the focus of evoked gamma oscillations from auditory to somatosensory cortex. The spatial distribution of fast oscillations and slow potentials produced in somatosensory cortex by stimulation of the TRNsom and ICsom were analogous to results obtained in the auditory system. Stimulation of the TRNsom produced a focal region of evoked oscillations restricted to the forepaw region of somatosensory cortex and absent from other somatotopic representations including the prominent vibrissal area (Fig. 3C), whereas slow potentials produced by stimulation of the ICsom were more widespread, but still centered on the forepaw region (Fig. 3D). To further investigate the organization of the TRNsom, WGA-HRP was injected into the rostral vibrissal area. It labeled a distinct TRN sector ~0.5 mm caudal to that identified for the forepaw region. Stimulation of this sector in two additional animals resulted in an evoked gamma focus in the rostral barrel field with no activation of the forepaw region or auditory cortex (Fig. 3, E and F).

DISCUSSION

Both the TRN and the thalamic intralaminar nuclei (ILN) receive input from areas of the brainstem reticular formation (Fig. 2 B; left). Again, no effect was recorded in somatosensory cortex (Fig. 2 B; right). Stimulation of the somatosensory TRNsom (Fig. 2C) and ICsom (Fig. 2D) produced modality specific fast oscillations and slow potentials (respectively) in somatosensory cortex that were quite similar to those recorded in auditory cortex during stimulation of the acoustic thalamic regions.

The focus of evoked gamma power resulting from stimulation of the TRNaud covered an ~1 mm² caudal area of auditory cortex (Fig. 3A). The slow potential produced by ICaud stimulation covered a wider area but remained constrained to auditory cortex (Fig. 3B). Evoked oscillatory responses demonstrated a remarkable degree of modality specificity. Movement of the stimulating electrode ~2 mm

FIG. 1. A: placements of electrode array (dots) above auditory cortex (Aud) and vibrissal and forepaw region of primary somatosensory cortex (Som). B: thalamic reticular nucleus (TRNaud) and internal capsule (ICaud) labeled by horseradish peroxidase conjugated to wheat germ agglutinin (WGA-HRP) injection into auditory cortex. C: thalamic reticular nucleus (TRNsom) and internal capsule (ICsom) labeled by WGA-HRP injection into forepaw region of somatosensory cortex. Inserts: mm caudal to Bregma.

FIG. 2. A: typical gamma oscillations evoked on a single trial in auditory cortex by stimulation of TRNaud (left) persist for duration of stimulus (darkened portions). Changes in spectral power evoked by stimulus (insert) were consistently largest in the gamma frequency band (shaded region), depicted here for 4 single trials (light traces) and for the average of 20 trials (dark trace). TRNaud stimulation had no effect in somatosensory cortex (right). B: slow potentials resulting from stimulation of ICaud were quite consistent on single trials (light traces) and for the average of 20 trials (dark trace). No effect was recorded in somatosensory cortex. C and D: similar to A and B but depicting single trial results from TRNsom and ICsom stimulation respectively. Gamma oscillations and slow potentials were in somatosensory and not auditory cortex.
Our results demonstrate a surprising specificity of evoked oscillations within a given sensory modality. Stimulation of discrete sectors of the TRNsom, labeled by WGA-HRP injections into the forepaw or vibrissal regions of somatosensory cortex, evokes oscillations tightly linked to corresponding parts of the somatotopic map. The possibility that the TRNsom may be somatotopically organized is supported by recent tracing studies (Crabtree 1996) and similar results also suggest a receptotopic organization for auditory (Conley et al. 1991) and visual (Montero et al. 1977) sectors of the TRN. The highly focal oscillations reported here reflect a capacity of the TRN to activate subpopulations of cells within a cortical receptotopic map. Because the TRN has no direct cortical projections, the fast oscillations evoked in the cortex by TRN stimulation must be generated indirectly, by way of inhibitory projections from the TRN to the sensory relay nuclei.

The fact that evoked oscillations are in the gamma frequency band is consistent with recent evidence indicating a relationship between these higher frequency oscillations and a spatiotemporal synchronization of neuronal networks during brain activation (Munk et al. 1996; Steriade et al. 1996a) and sensory information processing (Basar and Bullock 1992; Eckhorn et al. 1988; Gray and Singer 1989). Intrinsic synchronized gamma oscillations appear to be a general property of brain regions as they have been recorded not only in the phylogenetically newer regions like the thalamus (TRN) (Pinault and Deschenes 1992; Steriade et al. 1996b) and cortex (Gray and McCormick 1996; Llinás et al. 1991; Nuñez et al. 1992; Silva et al. 1991), but also in the phylogenetically older regions like the basal forebrain and hippocampus (Freund and Buzsaki 1996). The remarkable sensory specificity demonstrated here for extrinsic gamma oscillations evoked in the cortex by TRN stimulation suggests that they may be viewed as a separate category in the oscillatory capacity of the brain, one that is designed to encode specific behavioral events.

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