Subcortical Modulation of High-Frequency (Gamma Band) Oscillating Potentials in Auditory Cortex

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Brett, Barbara and Daniel S. Barth. Subcortical modulation of high-frequency (gamma band) oscillating potentials in auditory cortex. J. Neurophysiol. 78: 573 ± 581, 1997. The purpose of this study was to use depth electrical stimulation and retrograde horseradish peroxidase (HRP) labeling to determine what role certain subcortical nuclei play in the neurogenesis of high-frequency gamma (40 Hz) oscillations in rat auditory cortex. Evoked and spontaneous electrocortical oscillations were recorded with the use of a high-spatial-resolution multichannel epipial electrode array while electrical stimulation was delivered to the posterior intralaminar (PIL) region of the ventral acoustic thalamus and to the centrolateral nucleus (CL) and the nucleus basalis (NB), which have been previously implicated in the production of cortical gamma oscillations. PIL stimulation consistently evoked gamma oscillations confined to a location between primary and secondary auditory cortex, corresponding to the region where spontaneous gamma oscillations were also recorded. Stimulation of the CL and NB did not evoke gamma oscillations in auditory cortex. HRP placed in the cortical focus of evoked gamma oscillations labeled cell bodies in the PIL, and in more lateral regions of the ventral acoustic thalamus, which on subsequent stimulation also evoked gamma oscillations in auditory cortex. No cells were labeled in either the CL or NB. These results indicate that the PIL and the lateral regions of ventral acoustic thalamus provide anatomically distinct input to auditory cortex and may play an exclusive and modality-specific role in modulating gamma oscillations in the auditory system.

INTRODUCTION

High-frequency electrocortical oscillations in the gamma band (30–50 Hz) have been widely observed in animal (Bressler and Freeman 1980; Eckhorn et al. 1988; Engel et al. 1991a,b; Gray et al. 1990) and human cerebral cortex (Joliot et al. 1994; Llinás and Ribary 1992, 1993), and have received recent attention because of their association with focused arousal (Bouyer et al. 1981; Bressler 1990; Murthy and Fetz 1992; Sheer 1984; Tiitinen et al. 1993) and because of their possible role in transiently synchronizing activity in distributed populations of sensory cortical neurons during perception (see Singer 1994 for a review). However, the functional significance of cortical gamma oscillations is poorly understood and depends in large part on establishing the mechanisms of their neurogenesis.

Our laboratory has been investigating the neurogenesis of gamma oscillations with the use of high-spatial-resolution multichannel electrode arrays to determine spatial and temporal characteristics of the oscillations at the cortical surface (Brett and Barth 1996; Franowicz and Barth 1995; MacDon-ald and Barth 1995; MacDonald et al. 1996). This work has demonstrated that in the region of auditory and somatosen-sory cortex, neither evoked nor spontaneous gamma oscillations are spread equally throughout the cerebral hemispheres, but instead share a spatial distribution similar to that of the sensory evoked potential complex. In these studies limited to the auditory and somatosensory cortical regions, gamma oscillations are constrained to sensory cortex of the auditory and somatosensory modalities and are markedly attenuated or absent from interposed cortex. These findings are of interest because sensory cortex receives dense afferent input from specific and nonspecific thalamic nuclei. Thus, like sensory evoked potentials, gamma oscillations appear to be a characteristic of cortical networks in primary and secondary auditory and somatosensory cortex receiving thalamocortical projections. Furthermore, evoked and spontaneous gamma oscillations averaged within a given modality (somatosensory or auditory) reveal a systematic phase shift between primary and secondary sensory cortex, suggesting that they may serve to synchronize activity between these zones via intracortical connections (MacDonald and Barth 1993; Mac-Donald et al. 1996).

These results suggest that gamma oscillations are closely associated with sensory information processing in both the somatosensory and auditory cortex, and may rely on intra-cortical neurocircuitry for their generation and synchronization with sufficient spatial and temporal coherence to be observed in local field potentials, a hypothesis supported by recent observations that large lesions of the acoustic thalamus, anterior intralaminar nuclei, and basal forebrain have no effect on the frequency or spatial distribution of spontaneous gamma oscillations in auditory cortex (Barth and MacDonald 1996; Brett and Barth 1996). This hypothesis is also in agreement with recent in vitro and in vivo experiments demonstrating that cortical pyramidal cells and interneurons have the inherent capacity to produce subthreshold, high-frequency oscillations in smaller neural circuits with the absence of subcortical input (Amitai 1994; Gutfreund et al. 1995; Llinás 1992; Llinás et al. 1991; Nuñez et al. 1992; Silva et al. 1991; Whittington et al. 1995).

Yet, there is recent evidence that the centrolateral nucleus (CL) of the thalamus (Canu et al. 1994; Steriade 1993; Steriade et al. 1990, 1991, 1993a,b, 1996a,b) and the nucleus basalis (NB) of the basal forebrain (Metherate et al. 1992) may participate in the generation of cortical gamma oscillations in the intact nervous system. Particularly interesting is recent evidence reported by Steriade et al. (1996a,b) that in the somatosensory system, the synchronization of gamma oscillations between reciprocally connected areas of thalamus and cortex may serve as a fundamental mechanism for coordinating thalamocortical interactions. Furthermore, in...
the auditory system, electrical stimulation of acoustic thalamus reveals a strong modulatory influence on cortical oscillations (Barth and MacDonald 1996). Electrical stimulation of the medial geniculate nucleus (MG) inhibits, and similar stimulation of the posterior intralaminar nucleus (PIL) activates cortical gamma oscillations. Thus, although the cortex is capable of generating gamma oscillations in isolation, the presence of a strong and modality-specific modulation from the thalamus may be of direct importance to sensory information processing in intact preparations. The purpose of the present study was to systematically investigate possible modulation of gamma oscillations in auditory cortex effected by the PIL, CL, and NB with the use of both subcortical electrical stimulation and retrograde horseradish peroxidase (HRP) tracing.

**METHODS**

**Surgical preparation**

Thirty-five Sprague-Dawley rats (300–500 g) were anesthetized for surgery with intramuscular injections of ketamine (66 mg/kg) and xylazine (26 mg/kg) and secured in a stereotaxic frame equipped with hollow ear bars. The eyes were coated with ophthalmic ointment and normal body temperature was maintained with a regulated heating pad (37.5°C). A unilateral craniotomy extending from bregma to lambda and lateral to the temporal bone exposed auditory cortex in the right hemisphere. The dura was reflected and the pial surface was frequently bathed with physiological saline. Light anesthetic levels were maintained for the duration of the experiment with halothane. Although most of the experiments performed were acute, a semichronic preparation was required for animals in HRP studies to permit a 48-h survival period. In these animals, the muscle attached to the temporal bone was sutured to the dorsal fascia to provide protection for the exposed cortex, and the skin around the original midline cut was sutured and coated with lidocaine.

**Stimulation**

Bilateral auditory click stimuli were presented with high-frequency ribbon speakers placed ~15 cm lateral to each ear. The clicks were generated by computer-controlled monophasic square-wave pulses (0.3 ms, 0.5 mV). Subcortical electrical stimulation consisted of 500-ms trains of current pulses (15 μA, duration 0.5 ms, 500 Hz) delivered with a stainless steel bipolar electrode positioned in 100-μm increments along a dorsoventral tract passing through select subcortical structures in the acoustic thalamus, anterior intralaminar nuclei, and basal forebrain, according to the stereotaxic coordinates of Paxinos and Watson (1986).

**Recording**

Evoked and spontaneous field potentials were mapped from the pial surface of primary and secondary auditory cortex with an 8 × 8 array of 64 silver electrodes (tip diameter 100 μm) covering a 3.5 × 3.5 mm² area in a single placement. Recordings from the 64 epipial electrodes were referred to a silver ball electrode mounted in a burr hole drilled in the left frontal bone and simultaneously amplified and filtered (band-pass cutoff = –6 dB at 1–100 Hz, rolloff = 5 dB/octave). The array was initially positioned according to stereotaxic coordinates and then adjusted to similarly align the spatial distribution of midlatency auditory evoked potentials (MAEPs) across animals. MAEPs were digitally sampled (1,000 Hz, 225 ms) and averaged (n = 100). The characteristic spatiotemporal pattern of the MAEP complex (Barth and Di 1990, 1991; Di and Barth 1992, 1993) was also used to identify the locations of primary (area 41) and secondary (areas 36 and 20) auditory cortex.

Data were collected for six different stimulation/recording conditions. In condition 1, 2 min of ongoing spontaneous field potentials were digitally sampled (500 Hz) from six animals and stored for subsequent analysis. In condition 2, potentials were evoked by electrical stimulation of the PIL [4.8 mm posterior to bregma (B −4.8), 3.0 mm lateral to midline (M +3.0), 6.4 mm ventral to the cortical surface (CS 6.4)] in six animals. In conditions 3 and 4, potentials evoked by electrical stimulation of the NB (B −1.4, M +2.0, CS +6.0) and CL (B −2.4, M +1.2, CS +5.0) were recorded in four animals for each condition. Ten to 20 single trials of electrically evoked potentials were stored for each animal. Six animals in condition 5 underwent a histological procedure in which a solid pellet of HRP was implanted in the middle cortical layers. The site of HRP pellet placement was based on the spatiotemporal distribution of the MAEP complex. In condition 6, potentials were electrically evoked in eight animals from regions of ventral acoustic thalamus lateral to the PIL on the basis of the distribution of cell bodies labeled by HRP in condition 5.

**Data analysis**

Two-second blocks of spontaneous potentials recorded in condition 1 were displayed on a computer graphics screen and accepted for analysis or rejected on the basis of the presence of visually identified artifacts produced by respiration movement or occasional sharp waves produced by ketamine anesthesia. Bursts of gamma oscillations evident in accepted 2-s blocks of data were visually identified, marked with a cursor, and resampled in 128-ms blocks. In a typical 1-min sample of spontaneous data, ~20 bursts were selected. These were analyzed for frequency content with the use of a fast Fourier transform, and power spectral density (PSD) estimations were computed for each burst and averaged across all bursts for a given animal and across all animals. PSD estimations were also computed for 2-s subcortical stimulation trials in conditions 2, 3, 4, and 6. For each 2-s trial, the period between 100 and 400 ms after stimulus onset was studied to avoid including the fast wave on response in the analysis. PSDs for 10–20 stimulation trials were averaged for a given animal and a grand average was computed across all animals.

**Histology**

HRP was implanted into the region of cortex found to exhibit evoked gamma oscillations. Although the optimal procedure would have been to implant HRP pellets in animals receiving subcortical stimulation, this was not possible because of damage caused by the depth electrode, which interfered with the retrograde transport of HRP. However, in condition 2, it was determined that the cortical focus of evoked gamma oscillations was consistently 1 mm posterior and 0.25 mm lateral to the focus of maximum potential of the MAEP’s earliest negative amplitude peak. Therefore the MAEP complex was used to estimate the location of the gamma focus and HRP implant in a separate group of six animals. This was done by placing a frame made out of suture thread on the cortex to mark the borders of the electrode array where MAEPs were recorded. The location of maximum potential within this frame during the early negative amplitude peak of the MAEP was determined on the basis of bicubic spline-interpolated topographic maps, providing a relative reference point for the application of HRP. At the estimated site of the cortical gamma focus, a 25-gauge needle was stereotaxically lowered to a depth of 2 mm, removed, and replaced by an 0.5 mg pellet of HRP [25 mg HRP (Sigma type VI)/20 μl saline] inserted into the middle cortical layers along the tract made by the needle.
After a 48-h survival period, these animals were reanesthetized and perfused. Transcardial perfusion facilitated by gravity began with an initial perfusate followed by a 1.25% gluteraldehyde/1.0% paraformaldehyde buffered fixative solution and a cold buffered sucrose solution. The brains were removed from the skull and stored at 4°C in 30% buffered sucrose solution. The tissue was frozen, sectioned coronally at 40 μm on a cryocut microtome, and processed with the tetramethylbenzidine reaction for visualizing HRP (Mesulam 1978). The sections were then mounted onto gelatinized slides, counterstained with neutral red, coverslipped, and examined for the accumulation of HRP-stained cell bodies. To replicate earlier HRP results (Brett et al. 1994), in one additional animal, a pellet of HRP was placed directly in area 41 and identical histological procedures were performed.

The brains of animals in conditions 2, 3, 4, and 6 were also examined histologically. Transcardial perfusion was performed with the use of just the initial perfusate. The brains were removed and stored at 4°C in a Formalin/buffered sucrose solution. The tissue was frozen and sectioned coronally at 40 μm on a cryocut microtome. Sections were mounted onto gelatinized slides, counterstained with neutral red, coverslipped, and examined to verify the stereotaxic coordinates of bipolar electrode tracts.

RESULTS

Figure 1A shows the position of the 8×8 channel electrode array in relation to primary (area 41; dark shaded region) and secondary (areas 36 and 20; light shaded region) auditory cortex in the right hemisphere. The MAEP complex (Fig. 1B) recorded from this position was similar to those recorded in previous investigations (Barth and Di 1990, 1991; Brett et al. 1994; Di and Barth 1992, 1993) and was quite consistent across all animals used in the six experimental conditions of this study (Fig. 1B, superimposed traces). The MAEP complex was characterized by an early positive/negative biphasic response in area 41 (Fig. 1B, frame a; Fig. 1C, ---) that preceded a similar positive/negative biphasic response in area 36 (Fig. 1B, frame b; Fig. 1C, ——) by 4–5 ms. The highly stereotyped spatiotemporal characteristics of the MAEP complex permitted consistent alignment of the electrode array across animals and experimental conditions. Furthermore, the systematic latency shift between the rostrolateral and caudomedial region of the electrode array is typical of responses in areas 41 and 36, respectively, and permitted alignment of a template representing these regions in relation to the recording sites. However, the exact location and borders of areas 41, 36, and 20 indicated by this template must be considered approximate because no cytoarchitectural analyses of auditory cortex were performed in this study. The template was derived from previous histological studies of the areal distributions of these regions (Barth and Di 1991; Krieg 1946; Patterson 1977; Zilles 1990).

In the six animals in which spontaneous potentials were collected, bursts of gamma oscillations were evident, typically lasting for 100–500 ms and followed by a period of relatively low-amplitude activity of similar duration (Fig. 2A, shaded strips). The gamma bursts were not of equal amplitude at all electrodes of the array, but were instead largest in areas 41, 36, and 20, at electrode numbers 11–46. A burst at electrode 21 (Fig. 2A, darkened trace) has been enlarged in Fig. 2B to help illustrate the analysis procedure. Here it may be seen that in a typical 128-ms epoch of oscillatory activity resampled from the ongoing spontaneous record there are approximately five oscillations or ~40 Hz. PSD estimates for this single burst peaked, as expected, near 40 Hz (Fig. 2C). To quantify gamma power at each electrode, PSD coefficients between 30 and 40 Hz (Fig. 2C, shaded region) were summed. Normalized gray-scale maps were then computed to visualize the relative amplitude of gamma power across the electrode array. For the single burst of this example, the focus of maximum gamma power was near the border between areas 41 and 36 (Fig. 2D, white region). A similar location and spatial distribution of gamma power was evident when the PSD of all bursts for this animal was averaged (Fig. 2E). Here the location of maximum power is indicated with a small circle just within the caudal border of area 41. Although the foci of maximum gamma power for spontaneous bursts varied by ~1 mm across the six animals studied (Fig. 2F, small circles), the grand average PSD remained centered on the border between areas 41 and 36 (Fig. 2F).
Electrical stimulation of the PIL evoked a characteristic cortical response consisting of a monophasic negative sharp wave followed by gamma oscillations lasting for the stimulus duration and often continuing for several hundred milliseconds after the stimulus was terminated (Fig. 3, A and B). Evoked gamma oscillations were quite sensitive to the location of the thalamic stimulating electrode, and required placement in the PIL at stereotaxic coordinates (B ≈ 4.8, M ≈ 3.0, CS ≈ 6.0–6.5). Stimulation of regions 200–300 μm above or below these coordinates on the dorsoventral axis in a given animal failed to evoke gamma oscillations. PSD estimates for evoked gamma were computed at latencies of 100–400 ms after stimulus onset and averaged between 30 and 40 Hz (Fig. 3C, shaded area) for mapping. Similar to the results for spontaneous gamma bursts, evoked gamma averaged across animals formed a small focus near the border of areas 41 and 36 (Fig. 3D), with little variability in the locations of maximum gamma power in the individual animals (Fig. 3D, solid circles). Although electrical stimulation of the PIL (Fig. 4A) consistently evoked gamma oscillations in auditory cortex (Fig. 4B), similar stimulation of the NB (Fig. 4C) and CL (Fig. 4E) did not evoke gamma oscillations in any regions of the epipial recording array (Fig. 4, D–F).

To examine the location of cell bodies projecting axons into the region of auditory cortex found to exhibit evoked...
gamma oscillations, solid pellets of HRP were implanted into the middle cortical layers of this region. As noted in the METHODS section, it was not possible to perform this procedure directly on animals receiving PIL stimulation because of damage created by the electrode tract. Therefore a separate set of animals was studied with the use of the MAEP complex as a reference to determine the relative location of the gamma focus and subsequent HRP implant site. When the earliest negative fast wave of the MAEP complex was averaged across the six animals of this group and topographically mapped, it revealed a consistent focus of maximum amplitude in area 41 (Fig. 5A), with very little variability across animals (Fig. 5A, open circles). Figure 5D is a reproduction of the evoked gamma focus averaged across the six animals who received PIL stimulation (Figs. 3D and 4B). Here it can be seen that there was a displacement of the evoked gamma focus ~0.25 mm lateral and 1.0 mm caudal to the MAEP peak. This displacement was used to compute the locations of HRP implant (Fig. 5D) in the present group of animals. In one animal with HRP implanted directly in area 41, at the locus of maximum MAEP amplitude, results replicated those of a previous study (Brett et al. 1994), labeling cell bodies in the ventral division of the MG (MGv) in both anterior (Fig. 5B) and posterior (Fig. 5C) sections. When HRP was implanted into the estimated locus of evoked gamma oscillations, staining was evident in cell bodies of the PIL (Fig. 5, E and F), but was also concentrated in the lateral MGv, the marginal zone of the MG (MGmz), and the peripeduncular nucleus (PP).

Because HRP labeled cell bodies in locations lateral to the PIL over a region extending from 4.8 to 5.8 mm posterior to bregma, from 2.9 to 3.5 mm lateral to midline, and ventral to the MGv (the ventral MGmz and PP), electrical stimula-
tion was delivered to these regions in an additional set of eight animals (Fig. 6A, × mark stimulation sites). This stimulation was equally effective in evoking gamma oscillations in auditory cortex (Fig. 6B). Similar to stimulation of the PIL, the locus of evoked gamma was located near the border between areas 41, 36, and 20.

**DISCUSSION**

These results indicate that thalamocortical projections from a small region of the ventral acoustic thalamus are uniquely capable of modulating gamma oscillations in auditory cortex. Electrical stimulation of the PIL, and a zone just lateral to it, consistently evokes gamma oscillations centered on the border between primary and secondary auditory cortex in the location where similar spontaneous gamma oscillations are recorded. Electrical stimulation of subcortical nuclei in each of the two main ascending cholinergic pathways thought to be involved in cortical activation, the CL and the NB, did not evoke gamma oscillations in auditory cortex. Retrograde transport of HRP from the evoked gamma focus in auditory cortex complements the results of electrical stimulation, labeling cell bodies only in the PIL and more lateral regions, with no evidence for labeling in the CL or NB.

The PIL is located below the MGv in a region of the acoustic thalamus that anatomically overlaps the peripeduncular area (Arnault and Roger 1987, 1990; Moster 1964) and the ventrolateral shell nucleus of the MG (Patterson 1977; Scheel 1988). This region is known to share connections with auditory, motor, and limbic systems as well as nonspecific diencephalic and mesencephalic centers. Although little is known about the function of the PIL, it may be considered part of the ascending auditory system. Anatomic studies indicate that the PIL receives afferent input from the inferior colliculus (Arnault and Roger 1987; Ledoux et al. 1987) and shares reciprocal connections with the ventrocaudal auditory cortex in the rat (Arnault and Roger 1987, 1990). In the present study, HRP histochemistry provides evidence that the region of auditory cortex that produces gamma oscillations in response to electrical stimulation of the PIL receives afferent input from cell bodies in this structure. HRP also labeled cell bodies in the PP, the MGmz, and the MGv, indicating that there are additional direct connections between these more lateral thalamic regions and the cortical gamma focus. The labeling of cell bodies in ventrolateral acoustic thalamus could be due to placing the HRP near the ventrocaudal border of area 41, which has been shown to receive tonotopically organized projections from the ventrolateral MGv (Arnault and Roger 1990; Patterson 1977; Scheel 1988). However, electrical stimulation of the lateral HRP-labeled regions also produces gamma oscillations in auditory cortex, suggesting a modulatory role similar to that of the PIL.

The possibility must be considered that gamma oscilla-
tions in auditory cortex may be evoked, in part, by the stimulation of fibers of passage in the ventral acoustic thalamus. The MGv is located lateral to the brachium of the inferior colliculus, a fiber pathway carrying ascending auditory input that traverses the MG complex, whereas the medial division of the MG, which extends toward the MGv, is located medial to the brachium (Jones 1985). The PIL is positioned directly below these nuclei in the approximate location of the brachium, and in the opossum, colliculogeniculate fibers actually course laterally through the PIL (Winer et al. 1988). Electrical stimulation used here could have activated these fibers of passage terminating in the MG and by this means activated gamma oscillations in the cortex. Additional studies in which chemical instead of electrical stimulation of the PIL is used will be required to shed light on the relative contributions of cell bodies versus fibers to the evoked gamma response recorded here.

There is evidence that brain stem cholinergic systems may also be involved in the modulation of cortical gamma oscillations via either of two parallel pathways through the thalamus and the basal forebrain. Oscillations have been recorded intracellularly in thalamocortical intralaminar cells, including the ventroanterior-ventrolateral complex and the CL, and have been potentiated in the primate and anterior suprasylvian gyri of anesthetized cats by stimulation of the cholinergic brain stem pedunculopontine nucleus (Steriade et al. 1991, 1996b). Because mesopontine cholinergic nuclei are thought to maintain activation in thalamocortical systems, and the anterior intralaminar nuclei receive afferent input from these nuclei and exhibit gamma oscillations, it has been suggested that the brain stem–thalamic cholinergic system may facilitate the neurogenesis of gamma oscillations recorded in somatosensory and motor cortex by acting on the intralaminar nuclei, which are known to innervate widespread cortical regions (Steriade et al. 1991). Additionally, there is evidence that the mesopontine cholinergic pedunculopontine nucleus may be involved in the synchronization of gamma oscillations in reciprocally connected regions of the CL and the cortex (Steriade et al. 1996b).

In no animals of the present study did electrical stimulation of the CL evoke gamma oscillations in auditory cortex. Nor were cells in the CL labeled on placement of an HRP pellet into the evoked gamma focus. This suggests a marked modality specificity to the projections and modulatory function of the intralaminar nuclear complex, with the PIL projecting exclusively to auditory cortex and the anterior intralaminar nuclei projecting to visual and somatosensory cortex (Minciacci et al. 1993). Cytoarchitectural studies in the opossum demonstrate that the intralaminar nuclei extend beyond the intramedullary lamina farther than previously appreciated, forming shells around the MGs and main sensory nuclei (Morest and Winer 1986; Winer et al. 1988).

These newly recognized posterior and lateral intralaminar nuclei include the PIL and MGmz, two regions whose cell bodies were labeled in this study by placement of an HRP pellet into the evoked gamma focus in auditory cortex. Our results therefore support the hypothesis that the PIL and the more lateral HRP-labeled regions of the ventral acoustic thalamus may represent a posterior extension of the intralaminar nuclei, supplying thalamocortical input to auditory cortex and providing modality specific modulation of gamma oscillations in this region.

A parallel cholinergic system involving the NB, which is thought to be the primary source of cholinergic input to the cortex, has also been implicated in the generation of cortical gamma oscillations (Metherate et al. 1992). It has been reported that in vivo stimulation of the NB elicits EEG activation in auditory cortex via cortical muscarinic receptors, depolarizes cortical neurons, and produces a change in subthreshold membrane potential fluctuations from slow (1–5 Hz) to fast (20–40 Hz) frequencies. However, electrical stimulation of the NB in the present study did not evoke gamma band oscillations in auditory cortex, nor were cells in this nucleus labeled on placement of an HRP pellet in the evoked gamma focus. There are two possible explanations for this discrepancy. First, lower current levels (15 μA) were used for stimulation in the present experiment compared with the current levels (100–500 μA) used in the aforementioned study. It is possible that stimulation of the NB with higher current levels would have been effective in eliciting gamma oscillations; however, this was not tested. Second, the NB was not systematically explored for effective stimulation sites. This nucleus exhibits a highly topographical organization with only the caudal cholinergic portion projecting to auditory cortex (Metherate et al. 1992; Morizumi and Hattori 1992; Saper 1984). Because cholinergic activity at the stimulation sites of the present study was not verified, it is possible that stimulation was delivered outside of the area thought to be capable of eliciting gamma oscillations in auditory cortex.

In the absence of electrical stimulation of the PIL or more lateral regions, auditory cortex exhibits spontaneous gamma oscillations with a spatial distribution and frequency quite similar to those evoked by PIL stimulation. However, lesions of the PIL (Barth and MacDonald 1996) or the entire acoustic thalamus (Brett and Barth 1996) have no detectable effect on spontaneous gamma oscillations, suggesting that large intracortical networks are capable of generating and coherently synchronizing gamma oscillations independent of subcortical input, similar to mechanisms proposed by others to explain the neurogenesis of induced gamma oscillations in cat visual cortex (Eckhorn et al. 1988, 1992; Engel et al. 1991a; Gray and Singer 1989; Gray et al. 1992). It is unlikely that the failure of lesions in acoustic thalamus to alter spontaneous gamma oscillations in auditory cortex is due to parallel cholinergic input from either the CL or NB, because complete ablation of these regions also has no effect (Brett and Barth 1996), and electrical stimulation of these regions in the present study was equally ineffective in modulating gamma oscillations in auditory cortex. Cellular mechanisms for the production of oscillations in the gamma frequency range have been demonstrated in cortex (Connors and Gutnick 1990; Llinás et al. 1991; Silva et al. 1991; Whittington et al. 1995), indicating that cortical cells are at least capable of producing gamma oscillations in small neural circuits in the absence of subcortical input. These data suggest the presence of cellular networks in auditory cortex endowed with an intrinsic capacity to produce gamma oscillations independent of main sensory or cholinergic input, whose oscillatory activity is modulated and possibly synchronized over larger neural networks by the PIL complex.
The intralaminar system, of which the PIL and more lateral regions of the ventral acoustic thalamus may be part, has been regarded as an anterior extension of the midbrain reticular formation, mediating cortical activation through its widespread projections. Stimulation of the reticular formation is known to produce cortical arousal (desynchronization, fast oscillations) and to alter the activity of intralaminar neurons (Steriade and Buzsaki 1990). Low-frequency stimulation of the intralaminar nuclei themselves produces cortical activity characteristic of sleep, and high-frequency stimulation produces cortical arousal (Wainer and Mesulam 1990). Although the existence of reticular formation projections to specific thalamic nuclei has been demonstrated, this has not been widely explored (Wainer and Mesulam 1990). It is plausible that as part of the intralaminar system, the PIL may receive input from cholinergic nuclei of the reticular formation, such as the pedunculopontine nucleus. This would provide a pathway by which the reticular activating system could exert a modality specific role in auditory cortical activation, a role that could be essential for such behavioral processes as focused attention. Activation of the PIL may effect a transition in primary and secondary auditory cortex to an aroused state, reflected in the appearance of high-frequency gamma oscillations, that is optimal for the processing of auditory information.

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