

Fundamental Differences Between the Thalamocortical Recipient Layers of the Cat Auditory and Visual Cortices

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ABSTRACT

In visual and somatosensory cortices of several species, spiny stellate cells in layer 4 are the first elements in signal processing where thalamic information is integrated and emergent receptive field properties are generated and sent on to more superficial cortical layers. In vivo and in vitro experiments have provided important information about how the anatomy and physiology of these cells and this layer fit into the functional cortical circuitry. No such data exist for the auditory cortex but are requisite if we are to understand whether ideas about information processing in one sensory cortical area can be generalized to another. Accordingly, we used in vitro slices from which to record and labeled cells in the middle layers of the cat auditory and visual cortices to compare basic anatomical and physiological features of cells recovered in similar layers using the same methods. Our results demonstrate a striking difference in a basic characteristic of two primary sensory cortical areas. In the visual cortex, spiny stellate cells predominate, receive short-latency synaptic inputs, and project to supergranular layers. No such spiny stellate population is encountered in the middle layers of the auditory cortex. Spiny cells that are not stellate or pyramidal are occasionally encountered but, as a group, do not display consistent anatomical or physiological features that might allow them to function as auditory cortical versions of the visual spiny stellates. Rather, pyramidal cells in the lower half of layer 3 and layer 4 appear to have assumed this role. *J. Comp. Neurol.* 436:508–519, 2001. © 2001 Wiley-Liss, Inc.

Indexing terms: auditory cortex; visual cortex; layer 4; thalamocortical cell; spiny stellate cell; pyramidal cell

The spiny stellate cell populates layer 4 of primary visual and somatosensory cortices (O'Leary, 1941; Lund, 1973, 1984; Jones, 1975; Braak, 1978; Feldman and Peters, 1978; Simons and Woolsey, 1984), replacing pyramidal cells as the dominant excitatory neuron. As the major recipient of thalamocortical terminals in layer 4, spiny stellate neurons form an important link between thalamus and cortex (see, e.g., LeVay, 1973; LeVay and Gilbert, 1976; White, 1978, 1979; White and Rock, 1980). Evidence also suggests that one of their main functions is to integrate this thalamic information and convey it primarily to superficial cortical layers (Gilbert and Wiesel, 1983).

The small profile of the spiny stellate cell body in layer 4 is one of the features that led to early descriptions of primary cortical cytoarchitecture as "granulous" or "koniocortical" (von Economo, 1929), including primary auditory cortex in human (von Economo and Koskinas, 1925), monkey (Walker, 1937), and cat (Bremer and Dow, 1939). However, Rose (1949) questioned its granular nature, not-

ing that layer 4 was not heavily granular and concluded that, by strict definition, cat auditory cortex was not koniocortical. Rose's observation may have foreshadowed observations of fundamental differences between layer 4 in auditory and other sensory cortices. Golgi studies in rabbit (McMullen and Glaser, 1982), cat (Winer, 1984), mustached bat (Fitzpatrick and Henson, 1994), and human (Meyer and Ferres-Torres, 1984; Meyer et al., 1989) showed that spiny stellates are rare in layer 4. In contrast to the symmetric dendritic trees of visual and somatosensory spiny stellates that are confined to layer 4, a great

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variety occurs in the dendritic arborization patterns of these infrequently encountered cells purported to be spiny stellate homologues. If spiny stellate cells are not the primary excitatory cell type, what is? Several reports (McMullen and Glaser, 1982; Meyer et al., 1989; Fitzpatrick and Henson, 1994) indicate that pyramidal cells populate layer 4 in several species, although they are reported to be absent in cat primary auditory cortex (Winer, 1984).

In vivo and in vitro experiments in visual and somatosensory cortex of nonrodent mammals have verified that the spiny stellate is the major excitatory cell type in layer 4 and have provided important information about how their anatomy and physiology fit into the functional circuitry of their respective regions (Gilbert and Wiesel, 1983; Martin and Whitteridge, 1984; Katz et al., 1989; Anderson et al., 1994; Hirsch, 1995; Woolsey, 1996; Callaway, 1998; Fleidervish et al., 1998; Hirsch et al., 1998; Somogyi et al., 1998). The same cannot be said for auditory cortical layer 4, about which, beyond the initial Golgi studies, little is known.

Documenting structural and physiological differences between these layers in auditory and visual cortices may shed further light on how sensory information from different modalities is processed in cerebral cortex. Accordingly, our goal was to determine the composition of the spiny cell population of the middle layers of the cat auditory cortex. We performed additional experiments in cat primary visual cortex to compare basic anatomical and physiological features of cells recovered in similar layers using the same methods. We also wanted to make sure that we could successfully record from and recover spiny stellates such as those found in primary visual cortex, where they are abundant.

MATERIALS AND METHODS

Healthy adult cats, aged one year or older, with no signs of external or middle ear infections, were initially anesthetized with an intramuscular injection of a combination of ketamine (20 mg/kg) and acepromazine (0.4 ml). Anesthesia was maintained with intravenous injections of sodium pentobarbital (35 mg/kg). Body temperature was stabilized at 37°C. A tracheotomy was performed, with all wound areas swabbed liberally with lidocaine. All methods were approved by the University of Wisconsin Institutional Animal Care and Use committee. Animals were maintained in an American Association for Accreditation of Laboratory Animals Care-approved facility.

Slices of auditory and visual cortex

To harvest auditory cortical slices, the following steps were taken. The temporal and occipital bones overlying the temporal cortex were removed on one side, and the anterior ectosylvian sulcus (AES), posterior ectosylvian sulcus (PES), and suprasylvian sulcus (SSS) were identified (Fig. 1A). The amount of time and the numerous penetrations required to define physiologically the exact boundaries of the primary auditory cortex and map the frequency organization would compromise the integrity of the slices subsequently taken from this region, so this was not done. Instead, we used the surface maps illustrated in the figures of Rose (1949), Reale and Imig (1980), and Brugge and Reale (1985) as indicators of the boundaries of primary auditory cortex and harvested our slices from these areas. Thus, although we are con-

fident that we recorded from cells in primary auditory cortex, we cannot be certain where the cells were within the frequency map because the boundaries of primary auditory cortex and the frequency map within those boundaries varies somewhat from animal to animal. Cold oxygenated saline (see below) was perfused onto the exposed cortical surface, and scalpel cuts were made to remove a wedge of brain containing auditory cortex. Two coronal cuts were made, one approximately 1 mm rostral to the AES and the other approximately 2 mm caudal to the PES. A horizontal cut was made between the bottom points of the two coronal cuts at a level just dorsal to the pseudosylvian sulcus. A final sagittal cut was then made between the SSS and the midline of the brain, between the two coronal cuts. The isolated cortical wedge was then removed and placed in cold oxygenated saline. For horizontal slices, the wedge was glued ventral side down, and 500 μm sections were taken using the AES, PES, and SSS as landmarks defining the location of A1. For coronal slices, the wedge was glued caudal side down, and 500 μm sections were taken using the three sulci as landmarks.

To generate visual cortical slices, the following steps were taken. The locations of the primary visual cortex and its boundaries were based on the figures of Tusa et al. (1978). The occipital bone was removed to expose the entire occipital cortex on one side and the top of the occipital cortex on the other in order to yield a good view of the midline where area 17 is located (Fig. 1A). Cold oxygenated saline was perfused onto the cortical surface, and scalpel cuts were made to remove a wedge of brain containing visual cortical area 17 on one side. Two coronal cuts were made from the top of the cortex down to about 5 mm below the suprasylvian sulcus, one about 6 mm from the caudalmost tip of the occipital cortex and the other about 1.5 cm rostrally, both extending across the midline. A cut was then made in the horizontal plane at the bottom of the two coronal cuts. A final cut was next made in the sagittal plane, in the occipital cortex just across the midline from the side to be sliced, that ran rostrocaudally between the two coronal cuts. The isolated cortical wedge was removed and immediately immersed in cold oxygenated saline. The block was glued rostral end down, and 500 μm coronal sections of visual cortex were taken, trimmed, and stored in oxygenated saline.

The cortical slices were placed in a holding chamber containing normal, oxygenated artificial cerebrospinal fluid (ACSF) at room temperature. After equilibrating in the holding chamber for at least 30 minutes, one slice was transferred to the recording chamber, placed between two sets of nylon mesh, and perfused with normal, oxygenated ACSF at 33–35°C containing the following (in mM): NaCl, 124; KCl, 5; KH_2HPO_4 , 1.2; CaCl_2 , 2.4; MgSO_4 , 1.3; NaHCO_3 , 26; and glucose, 10.

Recording and stimulation

Electrical activation of synaptic inputs was accomplished using bipolar stimulating electrodes (A and M Systems, Everett, WA), with tips separated by about 500 μm that were placed in the white matter below layer 6. Shock duration was either 100 or 200 μsec . The white matter consists of thalamocortical axons as well as other axons heading to and from the cortex. Thalamic axons have been shown to be the thickest, and both in vivo and

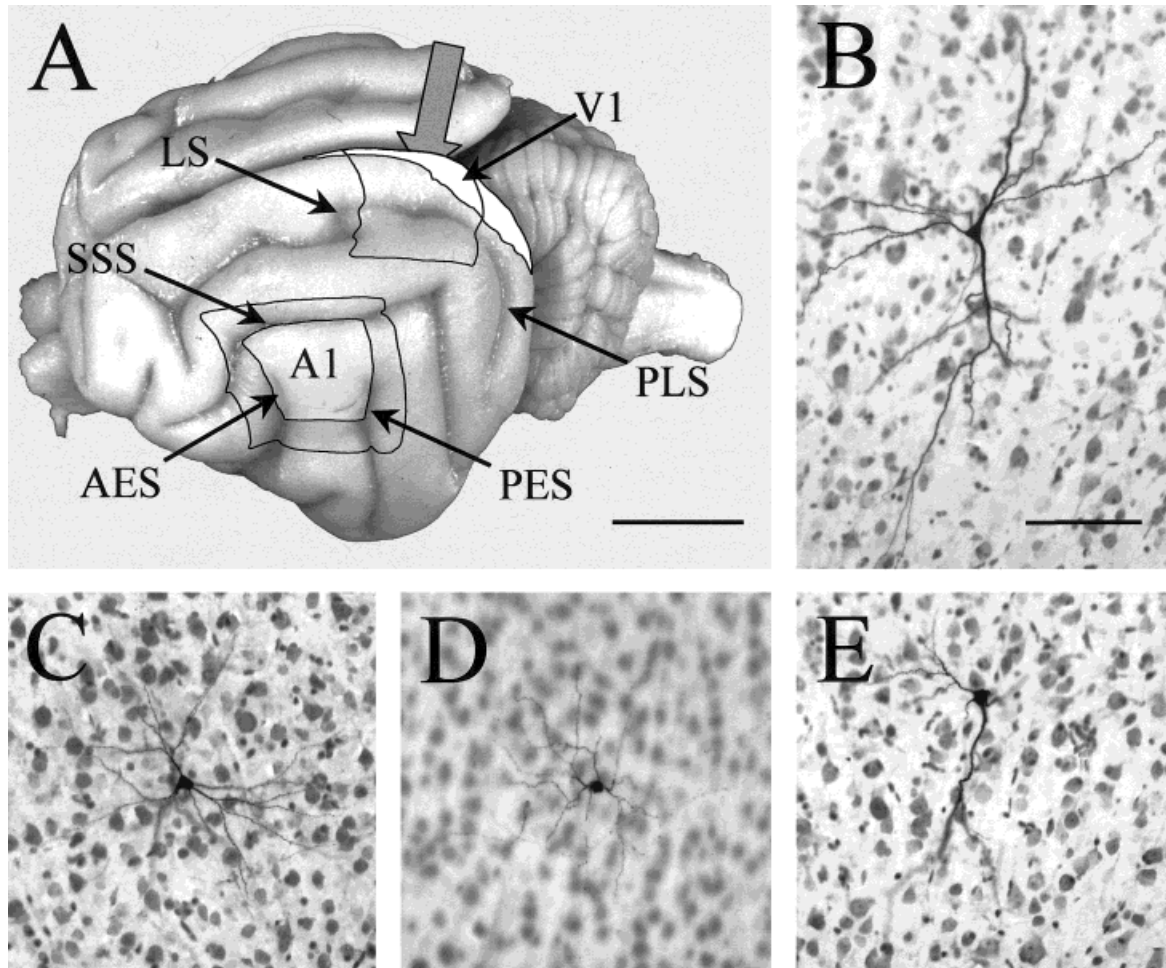


Fig. 1. **A:** Lateral view of a cat brain with the left side tilted down so that the dorsal midline is visible. The typical location of the primary auditory cortex (A1) is outlined. The block of cortex that was removed for taking auditory cortical slices is the larger outline surrounding A1. The white area labeled V1 represents the typical location of the portion of the primary visual cortex that can be seen from this viewpoint. Most of the primary visual cortex is located on the medial surface of the temporal lobe (large gray arrow). The block of cortex that was removed for taking visual cortical slices is outlined.

Several of the sulci used as landmarks have been labeled. **B-E:** Photomicrographs of four cells that were labeled with Neurobiotin in layer 4 of the auditory (B,E) and visual (C,D) cortices. Camera lucida drawings of the cells in B and E are cells 1 and 3, respectively, in Figure 3. Camera lucida drawings of the cells in C and D are cells 5 and 1, respectively, in Figure 4. AES, anterior ectosylvian sulcus; PES, posterior ectosylvian sulcus; PLS, posterior lateral sulcus; LS, lateral sulcus; SSS, suprasylvian sulcus. Scale bar in A = 1 cm; scale bar in B = 100 μm for B-E.

in vitro studies have indicated that they have the lowest activation threshold (Bullier and Henry, 1979; Ferster and Lindstrom, 1983, 1985; McGuire et al., 1984; Katz, 1987; Ferster, 1990; Hirsch, 1995). We used shock strengths of moderate intensity, so we are confident that much of the excitatory synaptic activity we elicited was from the activation of thalamocortical axons. We have some direct evidence for this. We recorded from and labeled many cells whose axons could be followed into the white matter. It was unusual to drive antidromically these or any cells from which we recorded with shock stimulation of the white matter, and when this did occur it was usually at the highest shock strengths used. The excitatory postsynaptic potentials (epsp) and inhibitory postsynaptic potential (ipsp) latencies on which we report were elicited at lower shock strengths, so it is very unlikely that these were generated by the axon collaterals of backfired cortical cells.

Intracellular recordings were made with sharp glass microelectrodes, which, when filled with 2% Neurobiotin (Vector, Burlingame, CA) in 2 M potassium acetate, had resistances of 90–140 M Ω . Physiological data were collected with custom software developed at the University of Wisconsin. The difference between the voltage measured extracellularly in saline and intracellularly during recording was taken as the resting membrane potential. Epsp and short-latency ipsp latencies were measured from stimulus artifact onset to where the psp consistently changed the membrane potential. To dissociate epsp and ipsp latencies when both were present, responses were recorded while the cell was polarized around the resting membrane potential. Epsp latencies were calculated near the ipsp reversal potential. Spike widths were measured at the base of the spike defined by the point at which the upswing of the spike became all or none.

Histology

Slices were removed from the recording chamber and immediately fixed in fresh 4% paraformaldehyde. The slice was then cryoprotected, and frozen 60 μm sections were collected. The sections containing the Neurobiotin-labeled cells were then processed using methods describe previously (Smith, 1992), mounted, counterstained with cresyl violet, and coverslipped. Examples of labeled cells from the auditory and visual cortices are illustrated in Figure 1B–E.

Cells and their axons were drawn either at 630 \times or 1,000 \times using a camera lucida attached to a Nikon Biophot microscope. The depths that corresponded to a particular cortical layer for auditory cortex were taken from Winer (1992) and for visual cortex were taken from Gilbert and Wiesel (1979). We also expressed the location of cells as a percentage of the total depth of the cortex. For this, the distance between the surface of the cortex and the layer 6/white matter border was measured at the location of the labeled cell body and the cell's location expressed as a percentage of the total depth of the cortex at that point. In the visual cortex the distinction between the bottom of layer 6 and the white matter was well defined. In auditory cortex, this distinction was not as apparent, so the bottom of layer 6 was defined as the point where the cell concentration changed from dense to sparse. Independent judgments made by two observers were typically within 50 μm of one another. The areas of cell bodies of auditory and visual cortical neurons were measured from scanned camera lucida drawings using NIH Image software from Scion Corporation.

RESULTS

General features

We recorded from and labeled 110 cells located within the confines of layers 3–5 of auditory cortex. One hundred of these cells were pyramidal and five cells were classified, based on their dendritic profiles, as “nonpyramidal with spines” (referred to below as “nonpyramidal cells”). The remaining five were aspiny interneurons and are not discussed further here. Figure 2A illustrates the depth of the pyramidal cells (squares) and nonpyramidal cells (circles) from the surface and their layer locations based on the values for the cat auditory cortex described by Winer (1984, 1992). Measurements of the cell body size of the pyramidal and nonpyramidal population revealed that (1) virtually all the pyramidal cells in layer 5, and at the boundary between layers 4 and 5, could be grouped into two size categories, those with cell bodies larger than 300 μm^2 (designated “large”) and those with cell bodies smaller than 220 μm^2 (designated “small”); the large cells, including those at the 4/5 boundary, all had large, thick apical dendrites that extended to layer 1; the members of the small cell population had much thinner, less profusely branching apical dendrites that only extended into layer 3; the axonal projection patterns and the synaptic and intrinsic physiology of these two populations differed as well, but the details are not discussed in this report; (2) small, medium-sized, and large pyramidal cells were found in layer 3, but the medium-sized and large cells were confined to the deeper half of the layer; and (3) the large majority of the pyramidal cells at depths corresponding to layer 4 were in the small category, as were four of

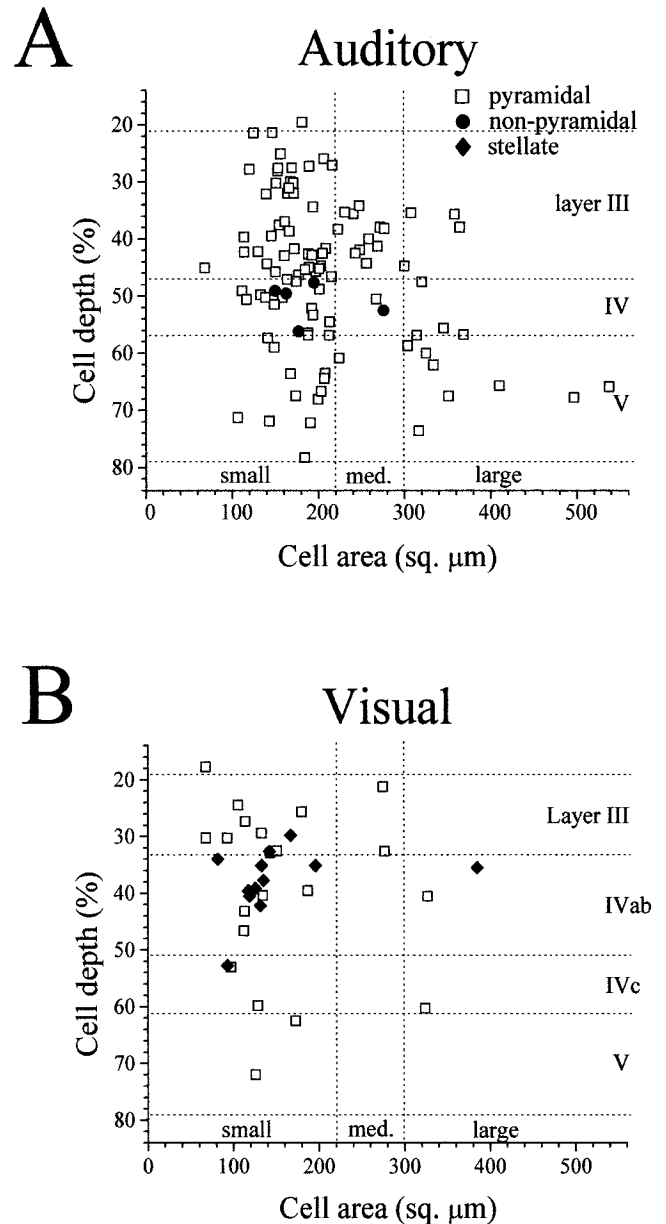


Fig. 2. Depth and soma size of labeled spiny cells in the auditory (A) and visual (B) cortices. Horizontal dotted lines distinguish between layer boundaries; vertical dotted lines distinguish between cell size categories.

the five nonpyramidal cells in this layer. Two other features of auditory cortical layer 4, relative to the surrounding layers, are apparent from Figure 2A. First, there is no obvious break in the distribution of pyramidal cells at layer 4. Second, the infrequently encountered and labeled nonpyramidal cells were located in, or at the boundary of, layer 4.

Comparison to layer 4 of visual cortex

In the visual cortex pyramidal cells also populate layer 4, but, in cats and higher primates, the most abundant excitatory cell type in this layer is the spiny stellate (see,

e.g., O'Leary, 1941; Lund et al., 1979; Gilbert and Wiesel, 1979; Martin and Whitteridge, 1984; Dudek and Friedlander, 1996). We were curious to know (1) why we had not encountered any true spiny stellates in auditory cortex, (2) whether the infrequently encountered nonpyramidal cells in auditory layer 4 might be the homologue of the spiny stellate cell in layer 4 of the visual cortex, and (3) were that the case, why had we not encountered them more frequently?

To rule out a possible recording bias for our lack of labeled stellate cells in layer 4 of the auditory cortex, and, as a means of comparison, we also recorded from and labeled 32 cells in primary visual cortical slices. Thirty-one were located in layers 3–5 as defined by Gilbert (1977). Figure 2B illustrates the depth of both pyramidal and stellate cells in visual cortex. Twenty of these cells were pyramidal, and 12 were nonpyramidal. All of the nonpyramidal cells had stellate dendritic configurations. Eleven of 12 were considered spiny stellate and not local inhibitory interneurons based on the following: (1) Eight of 12 were labeled darkly enough to distinguish dendritic spines, and (2) three of the remaining 4 had an axon that headed into the white matter, a common feature of the spiny stellates of layer 4ab (Gilbert and Wiesel, 1979), where most of our sample was located. As Figure 2B illustrates, the majority of the spiny cells labeled in layer 4 were spiny stellates. This is consistent with the reports, cited above, that pyramidal cells are replaced by stellates as the major excitatory cell type in layer 4 of the cat visual cortex. It is also consistent with the notion that we were reliably sampling the excitatory cell types in this layer of the visual cortex and presumably the auditory cortex as well.

In comparison to the labeled population from the auditory cortex, Figure 2 illustrates that, as with the spiny stellate cells labeled in the visual cortex, our small population of labeled nonpyramidal cells in auditory cortex was located in layer 4 and the majority (4/5) of these had small cell bodies. This, however, was the only clear similarity between the two populations. Other parameters would indicate that these auditory nonpyramidal cells are not the homologue of the visual spiny stellates. First, the number of these auditory nonpyramidal cells in layer 4, as a percentage of spiny neurons there, is quite low compared to that of the visual spiny stellates (11/21, or about 52% in visual vs. 5/31 or about 16% in auditory). Second, the members of the nonpyramidal population in the visual cortex are stellate, whereas those in the auditory cortex are not. Examination of the dendritic tree of these nonpyramidal cells (Fig. 3) shows that they are not consistently oriented, nor are they symmetric or confined to layer 4, two characteristics of spiny stellate cells in the visual and somatosensory cortices. As Figure 3 illustrates, at least one dendrite on each of the five auditory nonpyramidal cells extended a considerable distance from the soma, often out of layer 4 to more superficial or deeper adjacent layers. A closer view of dendritic branches (insets in Fig. 3) also reveals that the spines decorating the dendrites are not of a consistent shape or length. Several of these nonpyramidal spiny cells resemble cells defined as "inverted pyramids" that have been described for the auditory cortex of several species, including cats (Tunturi, 1971; McMullen and Glaser, 1982; Winer, 1992). Figure 4 illustrates five examples of the visual, layer 4 stellate cells. In contrast to those of the auditory nonpyramidal cells, their

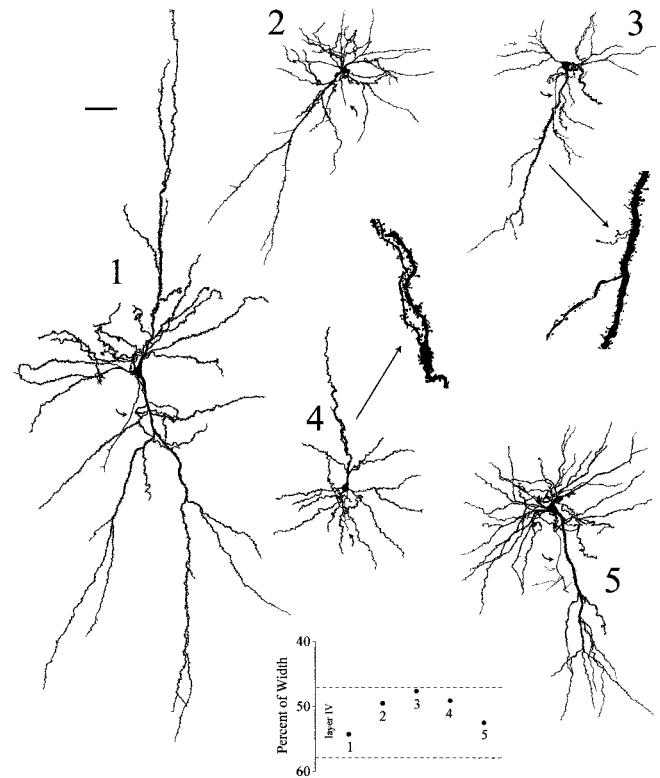


Fig. 3. Camera lucida drawings of the five nonpyramidal spiny cells in or at the border of layer 4 of the cat auditory cortex. Portions of the dendritic trees (highlighted in gray) of two cells are enlarged to illustrate spines. **Inset** below cell 4 illustrates the depth of each cell and the layer 4 boundaries (dashed lines). Curved arrows indicate axons. Cells are oriented so that the top edge of the figure would be parallel to the cortical surface. Scale bar = 50 μ m.

dendritic trees are relatively symmetric about the cell body and remain confined primarily to layer IV, typical of the spiny stellate cell classification. A closer view of dendritic branches (insets in Fig. 4) indicates that their spines tend to be more uniform in size and shape.

In addition to their fairly consistent cell body size and dendritic configuration, visual spiny stellates tend to share another important anatomical feature, namely, their axon collateral branching pattern, which is not seen in the auditory nonpyramidal cells. Several reports (Gilbert and Wiesel, 1979; Martin and Whitteridge, 1984; Anderson et al., 1993) have shown that visual spiny stellate cells primarily innervate the same and more superficial cortical layers. Figure 5 illustrates the axons of four spiny stellate cells in visual cortex. It is clear that much of the collateral system for these cells concentrates in layer 4 and more superficially. Reconstructions of the axons of the nonpyramidal population from the auditory cortex show no such consistency (Fig. 6). Although some collaterals of all of these cells remain within the same layer or head superficially, this does not appear to be their primary target.

We also examined physiological properties of these cells that might indicate whether they represent the auditory cortical version of the visual cortical spiny stellate cell. One important feature is epsp latency. Several studies of

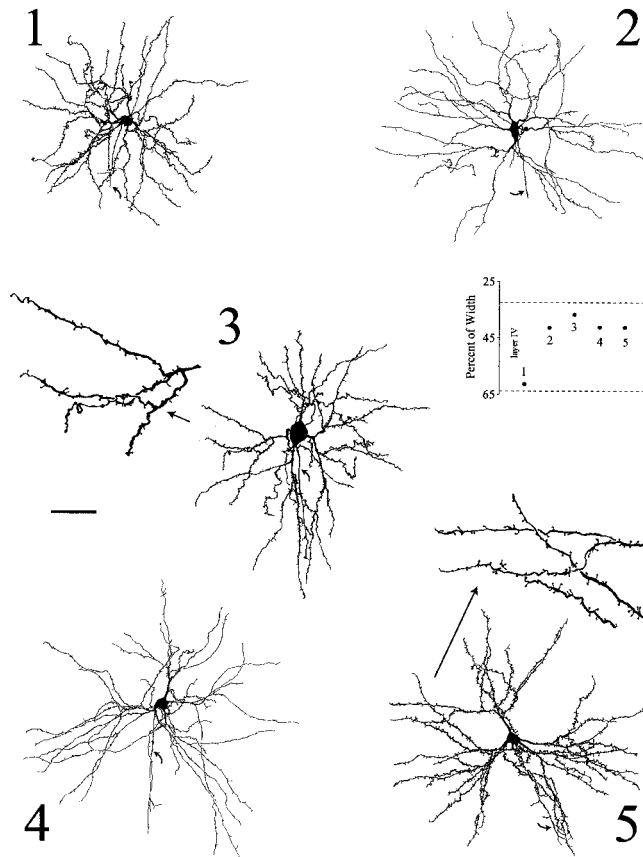


Fig. 4. Camera lucida drawings of five spiny stellate cells in or at the borders of layer 4 of the cat visual cortex. Portions of the dendritic trees (highlighted in gray) of two cells are enlarged to illustrate the spines. **Inset** to the right of cell 3 illustrates the depth of each cell and the layer 4 boundaries (dashed lines). Curved arrows indicate axons. Cells are oriented so that the top edge of the figure would be parallel to the cortical surface. Scale bar = 50 μ m.

the visual cortex have indicated that spiny stellates receive a monosynaptic input from the thalamocortical axons (Gilbert, 1983; Martin and Whitteridge, 1984; Ferster, 1992; Hirsch, 1995; Stratford et al., 1996). These axons are the thickest, most rapidly conducting axons entering the gray matter; are activated at the lowest threshold; and generate epsp in spiny stellate cells with the shortest latencies (Hirsch, 1995; Stratford et al., 1996; Hill et al., 1997). Similar short-latency epsp have been reported in the auditory system, where stimulation of the auditory thalamus consistently elicited monosynaptic events in cortical layer 4 (Mitani and Shimokouchi, 1985; Mitani et al., 1985). Based on the epsp latency values reported by Stratford et al. (1996) for thalamocortical epsp latencies in visual spiny stellates located in sublayer 4ab and by Mitani in the auditory cortex, we set a minimum latency of 1.5 msec as the criterion for whether a cell was receiving a direct input from thalamocortical axons. For reasons described in Materials and Methods, we are reasonably confident that our short-latency excitatory synaptic events arose from axons that were thalamocortical. As the top panel of Figure 7B illustrates, all of our spiny stellate cells located in this sublayer had latencies below this level. A

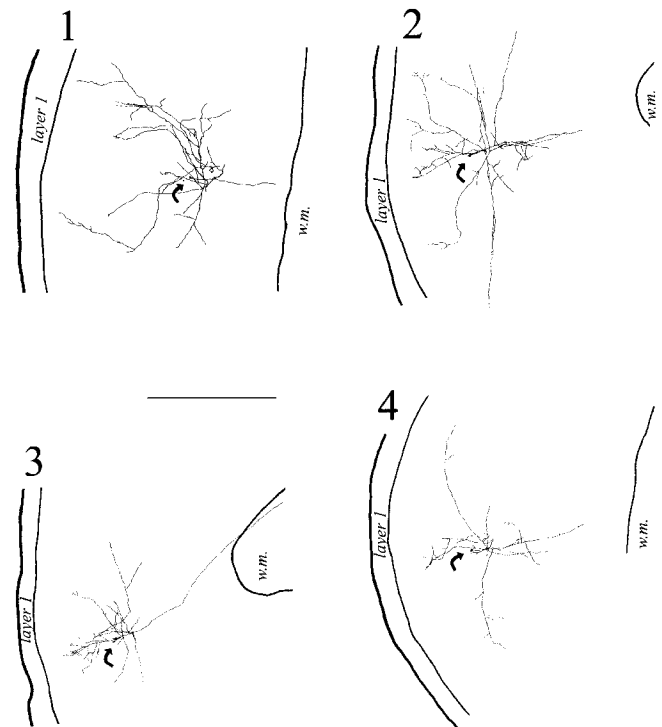


Fig. 5. Camera lucida drawings of the cell bodies and axons of four of the spiny stellate cells in the visual cortex, shown in Figure 4, drawn in the section of the cortex containing the cell body (curved arrows). Thick lines represent the cortical surface. Thin lines immediately below represent the boundary of layers 1 and 2. Thin lines between the label w.m. and the cell represent the boundary between the white matter and layer 6. Scale bar = 1 mm.

comparison of the same feature for the nonpyramidal cells in layer 4 of the auditory cortex (Fig. 7A, top panel) shows that the epsp of only one of these four cells that received an excitatory input was below 1.5 msec. The lower two panels in Figure 7B show that criteria can also be set for the layer 4ab spiny stellate ipsp latency (3.0 msec or less for those receiving an ipsp) and spike width (0.9 msec or less). A comparison of the same features for the nonpyramidal cells in layer 4 of the auditory cortex (Fig. 7A, bottom and center panels) shows that they are inconsistent and can fall on either side of these boundaries.

Another feature that several visual spiny stellate cells displayed and that has been reported elsewhere (Hirsch, 1995; Stratford et al., 1996; Fleidervish et al., 1998; Feldmeyer et al., 1999) was the spike response to depolarizing current pulses (Fig. 8). At depolarizing current level close to threshold, they would often (6/11) either fire a single-onset spike, then pause for some time, then resume spiking (Fig. 8A), or show a slow ramping and then start to fire some time considerably after current onset (Fig. 8B). At higher current levels they would all fire repetitively in what has been classified as a regular spiking (RS) response (Agmon and Connors, 1992). None of the nonpyramidal auditory cells would show such a pause or ramping response before becoming RS at some level above threshold (Fig. 9). In addition, one of them also showed very-high-frequency spike bursts during the RS responses (Fig. 9B, inset), a feature similar to the "chattering response"

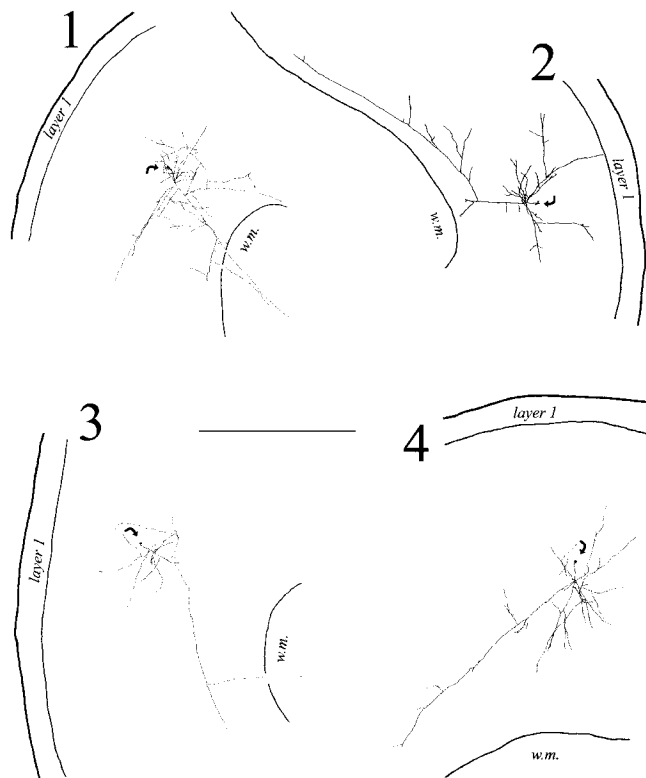


Fig. 6. Camera lucida drawings of the cell bodies and axons of four of the spiny nonpyramidal cells in the auditory cortex, shown in Figure 3, drawn in the section of the cortex containing the cell body (curved arrows). Thick lines represent the cortical surface. Thin lines immediately below represent the boundary of layers 1 and 2. Thin lines between the label w.m. and the cell represents the boundary between the white matter and layer 6. Scale bar = 1 mm.

previously described for some pyramidal cells in the superficial layers of cat visual cortex (Gray and McCormick, 1996; Brumberg et al., 2000) and for some of the layer 2/3 auditory pyramidal cells described below. Thus, the visual spiny stellates tend to show similarities in their general anatomical and physiological features, whereas the auditory layer 4 nonpyramidal cells do not seem to show either anatomical or physiological features similar to those of one another or to those of visual spiny stellates.

Redefinition of auditory cortical layer 4

In the visual system, the thalamocortical inputs from the major thalamic pathways (X and Y) terminate primarily in layer 4, with only a slight spillover into a narrow region at the bottom of layer 3 (LeVay and Gilbert, 1976; Ferster and LeVay, 1978; Gilbert and Wiesel, 1979; Freund et al., 1985a,b, 1989). This thalamic input extends over a depth of from about 35% to about 60% from the surface. The primary or lemniscal auditory thalamic input to the middle layers of cat auditory cortex extends for a considerable distance beyond the upper limits of the very narrowly defined layer 4 into the lower half of layer 3, where they are as dense as or more dense than in layer 4 (Winer, 1992; Huang and Winer, 2000). When measured in terms of depth, this thalamic input to the middle layers of auditory cortex also extends from about 35% to 60% of the depth from the cortical surface.

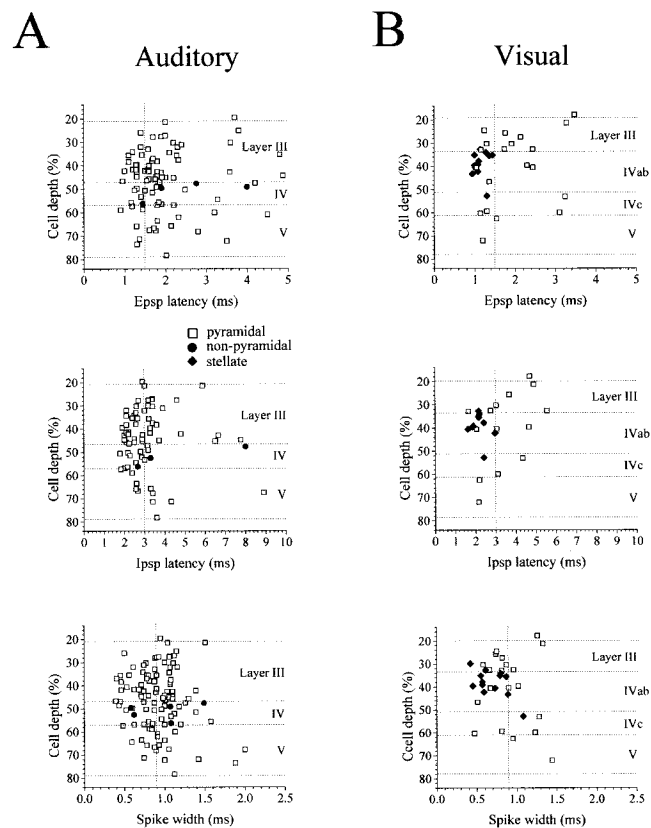


Fig. 7. Plots of epsp latency (**top**), ipsp latency (**middle**), and spike width (**bottom**) for cells in the middle layers of the auditory (**A**) and visual (**B**) cortices. Vertical dotted lines in each plot represent the upper limits of these parameters for our labeled spiny stellate cells in layer 4ab of the visual cortex.

Given the apparent lack of true spiny stellates in layer 4 of auditory cortex and the failure of the rare nonpyramidal cells there to display consistently several of the important spiny stellate features, we reasoned that perhaps the pyramidal cells in the more broadly defined “thalamocortical recipient region” of auditory cortex might be providing a functional “service” similarly to the visual spiny stellates. Such a service would entail receiving a short-latency input from thalamocortical axons and the capability of transferring that information, via axon collaterals, to the same and more superficial cortical layers. Thus, given the extensive auditory thalamocortical innervation of both layer 4 and the lower half of layer 3 (Winer, 1992; Huang and Winer, 2000), we extended our observations to look for these features in cells of lower layer 3 as well. We found that several pyramidal cells in this “thalamocortical recipient zone” of auditory cortex did, in fact, have both short synaptic latencies and collaterals that innervated granular and supragranular layers. Figure 10 (same plot as in the top panel of Fig. 5A, with the nonpyramidal cells removed) shows the depths of pyramidal cells in the auditory cortex and their epsp latencies. The area enclosed by the box formed by the dotted line represents the approximate location of layer 4 of the visual cortex but is also the thalamocortical recipient zones of both visual and auditory cortex. A large majority of the

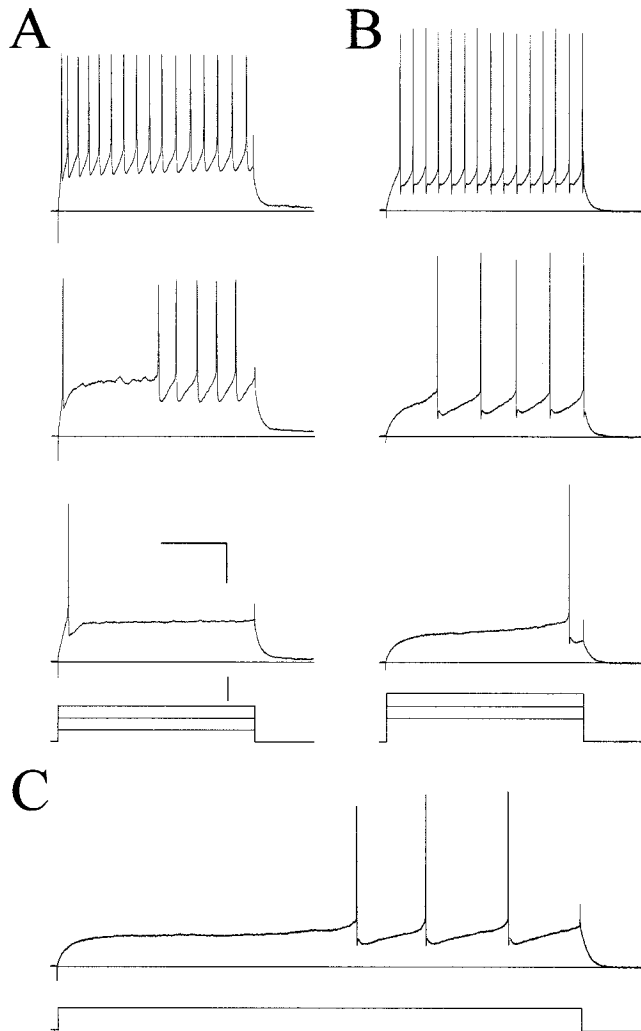


Fig. 8. **A,B:** Spike outputs of two spiny stellate cells, in layer 4 of the visual cortex, in response to 300 msec current pulses (bottom trace) at increasing current strengths (lower to higher traces) illustrating the onset/pause (A) and buildup (B) responses often seen close to threshold for this cell type. **C:** Response of the same cell as in B to a long current pulse (lower trace) close to threshold. Upper scale bars = 100 msec and 20 mV and are for all traces; lower scale bar = 0.2 nA and applies to all current traces.

pyramidal cells whose epsp latencies fall below the latency criteria set by spiny stellates in the visual cortex (1.5 msec, vertical dotted line) are located near the edges or within the boundaries of this thalamocortical recipient zone. Another interesting feature of several of these pyramidal cells in lower layer 3 and layer 4 of auditory cortex was their spike duration. Many of them had the shortest spike duration seen in the pyramidal cell population [Figs. 10A (open symbols), 11C]. At low current strengths, they would all fire in the RS mode, but, at high current strengths, several would fire spike doublets, triplets, or bursts at high frequency (Figs. 9B,C, 10A, open triangles). In fact, all but one of the pyramidal cells encountered, which had short-duration spikes (defined as less than 0.7 msec at the spike base), also had epsp latencies less than 1.5 msec (Fig. 10B), and the one exception had an epsp

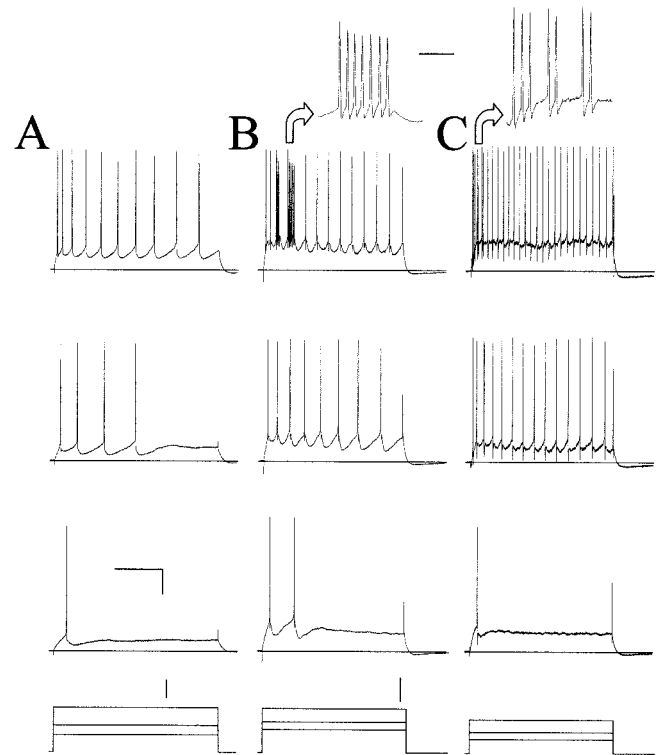


Fig. 9. **A,B:** Spike output of two spiny nonpyramidal cells, in layer 4 of the auditory cortex, in response to 300 msec current pulses (bottom traces) at increasing current strengths (lower to higher traces) illustrating the regular spiking (RS) responses seen for this cell type. **Inset** above B illustrates one of the spike bursts generated during the response. **C:** Spike output of a pyramidal cell in deep layer 3 of auditory cortex in response to 300 msec current pulses (bottom trace) at increasing current strengths (lower to higher traces) illustrating the RS responses seen for this cell type at lower current strengths and doublet and triplet firing at higher current strengths. **Inset** above C illustrates the three multispike responses generated early in the trace. Upper scale bars in A = 100 msec and 20 mV and are for all voltage traces except the insets. Lower scale bar in A = 0.2 nA and applies to the current traces in A; scale bar in B = 1 nA and applies to current traces in B and C; scale bar in inset = 10 msec and applies to both insets.

latency of 1.6 msec. Two of these fast spike/short epsp latency pyramidal cells were well labeled, and both had collaterals heading superficially (Fig. 11C). Unfortunately, these pyramidal cells were unusually difficult to label with Neurobiotin. Despite several minutes of current injection, which in other penetrations would almost always darkly label pyramidal cells with longer duration spikes, these cells would usually be moderately or lightly labeled. Thus, although the dendritic tree filled darkly enough to distinguish them as pyramidal cells, the axon collateral branching of most could not be followed for more than a short distance from their origin off the main axon.

Those pyramidal cells that had short-duration spikes and short-latency epsp were not the only cells to send collaterals to the same or more superficial layers. For example, some of them did not have short-latency epsp (Fig. 11A,D) or short-duration spikes (Fig. 11A,B,D), and, although all of the cells showed RS responses to depolarizing current pulses, none of them showed the buildup or pause response pattern at threshold levels.

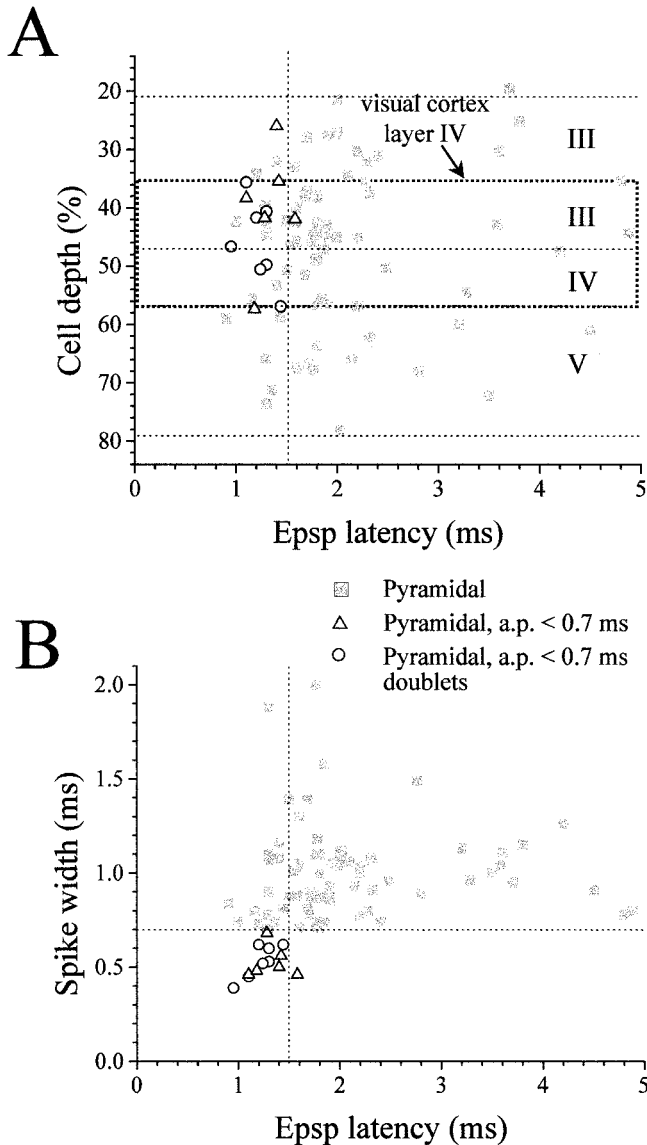


Fig. 10. **A:** Plot of the depth of labeled pyramidal cells in the auditory cortex vs. epsp latency. Open symbols represent pyramidal cells with short spike durations (triangles) some of which could fire multiple action potentials (doublets) with very short interspike intervals (circles). Areas enclosed by darker dotted lines represent the thalamocortical recipient zone of the auditory cortex as determined from Winer (1992), which also closely resembles the area encompassed by layer 4 (the thalamocortical recipient zone) of the visual cortex. Roman numerals to the right and lighter horizontal lines represent the typically defined auditory cortical layers. **B:** Plot of the spike width vs. epsp latency for all pyramidal cells illustrating that those with narrow spike widths also showed short-latency epsp.

DISCUSSION

We recorded from and labeled cells in the middle layers of the cat auditory and visual cortices, paying particular attention to cells in the thalamocortical recipient zone. Our results demonstrate that, in a given species, a difference exists in a fundamental feature of two primary sensory cortical areas. In visual cortex, spiny stellate cells predominate in layer 4. As several studies previously

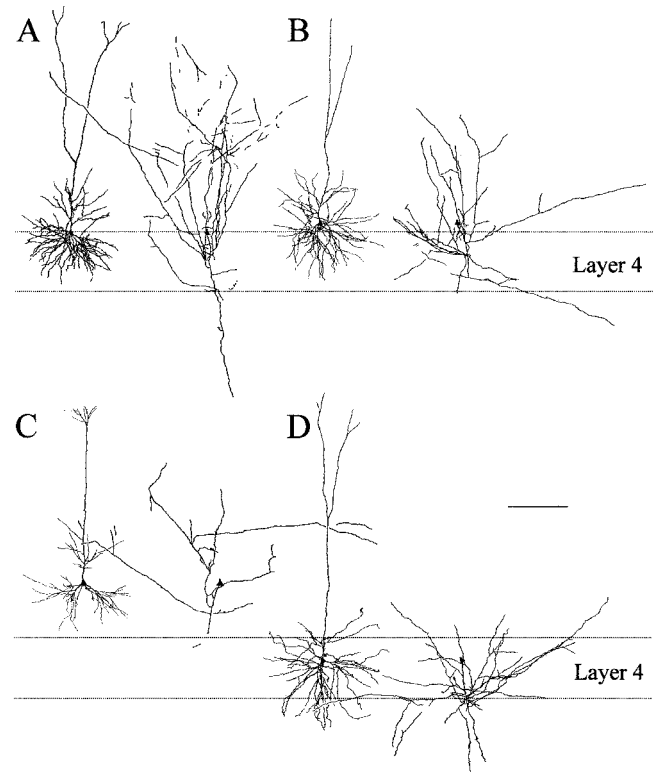


Fig. 11. **A–D:** Camera lucida drawing of four pyramidal cells in the thalamocortical recipient zone of the auditory cortex. Left figure in **A–D** represents the cell body and dendritic tree; right figure represents the cell body and axon collaterals. The cell in **A** had an action potential (AP) duration of 0.74 and an epsp latency of 1.86 msec, the cell in **B** an AP duration of 1.1 and epsp latency of 1.3 msec, the cell in **C** an AP duration 0.45 msec and epsp latency of 1.1 msec, and the cell in **D** an AP duration of 1 msec and epsp latency of 1.8 msec. Shaded areas represent the thalamocortical recipient zone of the auditory cortex as determined from Winer et al. (1992, 2000), which also closely resembles the area encompassed by layer 4 (the thalamocortical recipient zone) of the visual cortex. Dotted lines represent the boundaries of layer 4 in the auditory cortex as defined by Winer (1992). Scale bar = 200 μ m.

pointed out, these cells act as the first elements in intracortical signal processing. It is here, at the thalamocortex interface, where several emergent properties arise (Hubel and Wiesel, 1962, 1968; Gilbert, 1977; Blasdel et al., 1985; Douglas et al., 1991). In contrast, spiny stellates are rarely encountered in the middle layers of the auditory cortex, whereas pyramidal cells predominate. Spiny cells that are not stellate or pyramidal are occasionally encountered here but, as a group, do not display consistent anatomical or physiological features that might allow them to function as auditory cortical versions of the visual spiny stellates. Our data, combined with anatomical evidence from previous Golgi studies in several species, indicate that the spiny stellate is not the predominant or even a major cell type in any auditory thalamocortical recipient zone studied (McMullen and Glaser, 1982; Meyer and Ferres-Torres, 1984; Winer, 1984; Fitzpatrick and Henson, 1994).

In rabbit, human, and bat, but not cat, pyramidal cells were named as the major layer 4 spiny cell type. For the

cat, Winer (1984) indicates that layer 4 is a 250 μm stratum starting at a depth of about 800 μm that has few commissurally projecting neurons and is devoid of pyramidal cells. Our data show no break in the pyramidal cell population here, but, given the variable thickness of the cortex, plots like the one in Figure 2 might not distinguish such a small break. However, even if this narrow region of primary auditory cortex is devoid of pyramidal cells, inputs from primary auditory thalamus span a larger region not confined to this definition of layer 4. We show that several of the auditory pyramidal cells in this thalamocortical recipient zone send collaterals to more superficial layers, have short-latency epsp, and could potentially represent the auditory version of the spiny stellate. Many of those with short-latency epsp also showed very narrow spike widths. Thus, pyramidal cells are likely to be the major excitatory cell type receiving thalamic input and could serve to transfer this information to more superficial layers.

No data are available to suggest why, in many species, the visual and somatosensory systems utilize the spiny stellate cell as their receiver/distributor of thalamic information; but the auditory system does not, nor is there conclusive evidence that the spiny stellate cell is either a developmentally distinct cell type (e.g., derived from a unique type of neural stem cell) or a form of pyramidal cell modified during development by interactions with the cortical environment. One study in monkey visual cortex reported the presence of the stellate form early in development (Lund et al., 1977), but a preliminary report on rat somatosensory cortex (Peinado and Katz, 1990) and a study of cat visual cortex (Vercelli et al., 1992) suggested that stellate cells are initially pyramidal cells that lose their apical dendrites during development. Another confounding variable is that, although spiny stellates are common in primary visual and somatosensory cortices of most terrestrial vertebrates, including cat, monkey, man, and ferret, some species lack them. Layer 4 of guinea pig visual cortex has mostly pyramidal cells (Dudek and Friedlander, 1996), as does rat, in which most were classified as star pyramidal cells (Peters and Kara, 1985), a cell class originally described by Lorente de No (1949). These cells resemble the spiny stellate cell with its radiate apical dendritic bush but mimic pyramidal cells with an apical dendrite, although it is reduced in size and complexity. Such cells often populate layer 4 along with the more numerous spiny stellates or, as in rat, may be the major cell type. Some consider them to be intermediates in a continuum between the spiny stellate and pyramidal cell morphology. Likewise, in the somatosensory cortex, although several species, such as mouse, rat, and rabbit, have been shown to favor spiny stellates (Simons and Woolsey, 1984; Benshalom and White, 1986; Feldmeyer et al., 1999), monkey somatosensory cortex is reportedly populated by star pyramidal cells (Jones, 1975).

Considerable information is available on the transition occurring between the visual thalamic synapses and layer 4 spiny stellate cells. In contrast to the small, circular, on-and-off-center receptive fields of LGN cells, spiny stellate cells show predominantly "simple" receptive fields with new features, including larger rectangular receptive fields with adjacent on-and-off regions, orientation tuning, directional selectivity to motion, and end inhibition (Hubel and Wiesel, 1962; Gilbert, 1977; Gilbert and Wiesel, 1979; Martin and Whitteridge, 1984). These presum-

ably result from the converging direct thalamocortical inputs combined with secondary excitatory inputs primarily from layer 4 and layer 6 cells and local inhibitory inputs. The contribution of each input to these emergent properties is not completely understood, but thalamocortical inputs must certainly be vital. Emergent properties occurring at the thalamocortical-layer 3/4 interface of the auditory system have not been determined. Steinschneider et al. (1980, 1992) attempted to distinguish differences in speech-evoked activity between auditory thalamic axons and cortical cells of awake monkey using evoked potential/multiunit recordings. Although some sharpening of response differences between different syllables was noted in supragranular layers, in layers 3/4 no distinction could be made between the thalamocortical and cortical population responses, so the function of the thalamocortical zone in making this conversion could not be evaluated. Others (Clarey et al., 1995; Barone et al., 1996; Samson et al., 2000) compared spatial/directionality tuning of MGB cells and cortical layer 3/4 cells. The authors have noted that, although more cortical cells display such tuning, this was not a unique new feature of cortical responses. Similarly, more cells in the cat middle cortical layers were sensitive to interaural intensity differences (Ivarsson et al., 1988; Semple and Kitzes, 1993a,b), but this was not a new feature unique to the cortex.

Perhaps the difference we describe, between a basic feature of the auditory and visual cortices, should not be surprising. Certainly there are considerable differences at more peripheral levels. For example, a map of visual space is represented at the receptor level, where light from a point in space stimulates a set of sensory receptors while immediately adjacent receptors are stimulated by immediately adjacent areas of space. This retinotopic space map is transferred through LGN onto cortex, where it is precisely represented. In the auditory system, receptors are lined up in the cochlea, and no mapped representation of spatial location is provided. Which receptors are stimulated provides information about stimulus frequency but not spatial location. It is one of the primary tasks of auditory brainstem nuclei to extract such information. Despite this, although removal of cat auditory cortex eliminates the ability to localize (Kaas et al., 1967; Strominger, 1969; Cranford et al., 1971; Whitfield et al., 1972), and although some cells in primary auditory cortex have receptive fields specific to particular regions of auditory space (Masterton and Imig, 1984; Imig et al., 1990; Brugge et al., 1996; Irvine, 1998), no map of space is found there.

Another fundamental difference between auditory and visual systems may be in the functional output of cells in the thalamic recipient zone. In visual system, layer 4 is the most peripheral site for binocular convergence of synaptic input from two eyes. Segregated inputs from the two eyes make most cells in this layer primarily monocular. It is the convergence of outputs of spiny stellate cells onto cells in the same and more superficial layers that are likely to confer binocularity. In the auditory system, convergence of input from the two ears occurs in the brainstem, and binaurality is first seen here. Thus, one of the major functions of visual spiny stellates, namely, converging the inputs from receptors in both sensory apparatus onto upstream cells, has already been carried out far downstream in the auditory system.

Recent findings add an interesting twist to this speculation on the similarities and differences between auditory

and visual systems. It was noted that the fundamental representation of, and responses to, the visual world can be generated in and through the auditory cortex by diverting visual inputs to auditory thalamus (Sharma et al., 2000; von Melchner et al., 2000). Cells in ferret auditory cortex could be made to respond to visual stimuli, become organized into a retinotopic space map, and have receptive fields similar to that of normal visual cortex. In addition, visual stimuli received by auditory cortex were perceived as visual and could direct visually guided behavior. Do these findings imply that auditory cortical wiring, including the thalamocortical recipient zone, has enough structural homology to the visual system to perform visual tasks? The authors noted that the visual input, routed through auditory thalamus, caused changes in the horizontal connectivity of the auditory cortex. Perhaps structural changes had to take place in the middle cortical layers as well.

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LITERATURE CITED

- Agmon A, Connors BW. 1992. Correlations between intrinsic firing patterns and thalamocortical synaptic responses of neurons in mouse barrel cortex. *J Neurosci* 12:319–329.
- Anderson JC, Douglas RJ, Martin KA, Nelson JC. 1994. Synaptic output of physiologically identified spiny stellate neurons in cat visual cortex. *J Comp Neurol* 341:16–24.
- Anderson JC, Martin KA, Whitteridge D. 1993. Form, function, and intracortical projections of neurons in the striate cortex of the monkey *Macaca nemestrinus*. *Cereb Cortex* 3:412–420.
- Barone P, Clarey JC, Irons WA, Imig TJ. 1996. Cortical synthesis of azimuth-sensitive single-unit responses with nonmonotonic level tuning: a thalamocortical comparison in the cat. *J Neurophysiol* 75:1206–1220.
- Benshalom G, White EL. 1986. Quantification of thalamocortical synapses with spiny stellate neurons in layer IV of mouse somatosensory cortex. *J Comp Neurol* 253:303–314.
- Blasdel GG, Lund JS, Fitzpatrick D. 1985. Intrinsic connections of macaque striate cortex: axonal projections of cells outside lamina 4C. *J Neurosci* 5:3350–3369.
- Braak E. 1978. On the structure of the human striate area. *Lamina IV β* . *Cell Tissue Res* 188:217–234.
- Bremer F, Dow RS. 1939. The acoustic area of the cerebral cortex in the cat: a combined oscillographic and cytoarchitectonic study. *J Neurophysiol* 2:308–318.
- Brugge JF, Reale RA. 1985. Auditory cortex. In: Peters A, Jones EG, editors. *Cerebral cortex*. New York: Plenum. p 229–271.
- Brugge JF, Reale RA, Hind JE. 1996. The structure of spatial receptive fields of neurons in primary auditory cortex of the cat. *J Neurosci* 16:4420–4437.
- Brumberg JC, Nowak LG, McCormick DA. 2000. Ionic mechanisms underlying repetitive high-frequency burst firing in supragranular cortical neurons. *J Neurosci* 20:4829–4843.
- Bullier J, Henry GH. 1979. Laminar distribution of first-order neurons and afferent terminals in cat striate cortex. *J Neurophysiol* 42:1271–1281.
- Callaway EM. 1998. Local circuits in primary visual cortex of the macaque monkey. *Annu Rev Neurosci* 21:47–74.
- Clarey JC, Barone P, Irons WA, Samson FK, Imig TJ. 1995. Comparison of noise and tone azimuth tuning of neurons in cat primary auditory cortex and medial geniculate body. *J Neurophysiol* 74:961–980.
- Cranford J, Ravizza R, Diamond IT, Whitfield IC. 1971. Unilateral ablation of the auditory cortex in the cat impairs complex sound localization. *Science* 172:286–288.
- Douglas RJ, Martin KA, Whitteridge D. 1991. An intracellular analysis of the visual responses of neurones in cat visual cortex. *J Physiol (London)* 440:659–696.
- Dudek SM, Friedlander MJ. 1996. Developmental down-regulation of LTD in cortical layer IV and its independence of modulation by inhibition. *Neuron* 16:1097–1106.
- Feldman ML, Peters A. 1978. The forms of non-pyramidal neurons in the visual cortex of the rat. *J Comp Neurol* 179:761–793.
- Feldmeyer D, Egger V, Lubke J, Sakmann B. 1999. Reliable synaptic connections between pairs of excitatory layer 4 neurones within a single 'barrel' of developing rat somatosensory cortex. *J Physiol (London)* 521:169–190.
- Ferster D. 1990. Binocular convergence of excitatory and inhibitory synaptic pathways onto neurons of cat visual cortex. *Vis Neurosci* 4:625–629.
- Ferster D. 1992. The synaptic inputs to simple cells of the cat visual cortex. *Progr Brain Res* 90:423–441.
- Ferster D, LeVay S. 1978. The axonal arborizations of lateral geniculate neurons in the striate cortex of the cat. *J Comp Neurol* 182:923–944.
- Ferster D, Lindstrom S. 1983. An intracellular analysis of geniculocortical connectivity in area 17 of the cat. *J Physiol (London)* 342:181–215.
- Ferster D, Lindstrom S. 1985. Augmenting response evoked in area 17 of the cat by intracortical axon collaterals of corticogeniculate cells. *J Physiol (London)* 367:217–232.
- Fitzpatrick DC, Henson OW Jr. 1994. Cell types in the mustached bat auditory cortex. *Brain Behav Evol* 43:79–91.
- Fleiderovich IA, Binshtok AM, Gutnick MJ. 1998. Functionally distinct NMDA receptors mediate horizontal connectivity within layer 4 of mouse barrel cortex. *Neuron* 21:1055–1065.
- Freund TF, Martin KA, Somogyi P, Whitteridge D. 1985a. Innervation of cat visual areas 17 and 18 by physiologically identified X- and Y-type thalamic afferents. II. Identification of postsynaptic targets by GABA immunocytochemistry and Golgi impregnation. *J Comp Neurol* 242:275–291.
- Freund TF, Martin KA, Whitteridge D. 1985b. Innervation of cat visual areas 17 and 18 by physiologically identified X- and Y-type thalamic afferents. I. Arborization patterns and quantitative distribution of postsynaptic elements. *J Comp Neurol* 242:263–274.
- Freund TF, Martin KA, Soltesz I, Somogyi P, Whitteridge D. 1989. Arborization pattern and postsynaptic targets of physiologically identified thalamocortical afferents in striate cortex of the macaque monkey. *J Comp Neurol* 289:315–336.
- Gilbert CD. 1977. Laminar differences in receptive field properties of cells in cat primary visual cortex. *J Physiol (London)* 268:391–421.
- Gilbert CD. 1983. Microcircuitry of the visual cortex. *Annu Rev Neurosci* 6:217–247.
- Gilbert CD, Wiesel TN. 1979. Morphology and intracortical projections of functionally characterized neurones in the cat visual cortex. *Nature* 280:120–125.
- Gilbert CD, Wiesel TN. 1983. Functional organization of the visual cortex. *Progr Brain Res* 58:209–218.
- Gray CM, McCormick DA. 1996. Chattering cells: superficial pyramidal neurons contributing to the generation of synchronous oscillations in the visual cortex. *Science* 274:109–113.
- Hill JC, Prasher DK, Luxon LM. 1997. Evidence for efferent effects on auditory afferent activity, and their functional relevance. *Clin Otolaryngol Allied Sci* 22:394–402.
- Hirsch JA. 1995. Synaptic integration in layer IV of the ferret striate cortex. *J Physiol (London)* 483:183–199.
- Hirsch JA, Alonso JM, Reid RC, Martinez LM. 1998. Synaptic integration in striate cortical simple cells. *J Neurosci* 18:9517–9528.
- Huang CL, Winer JA. 2000. Auditory thalamocortical projections in the cat: Laminar and areal patterns of input. *J Comp Neurol* 427:302–331.
- Hubel DH, Wiesel TN. 1962. Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J Physiol (London)* 160:106–154.

- Hubel DH, Wiesel TN. 1968. Receptive fields and functional architecture of monkey striate cortex. *J Physiol (London)* 195:215–243.
- Imig TJ, Irons WA, Samson FR. 1990. Single-unit selectivity to azimuthal direction and sound pressure level of noise bursts in cat high-frequency primary auditory cortex. *J Neurophysiol* 63:1448–1466.
- Irvine DRF. 1998. The representation of auditory space in the cerebral cortex: possible implications for the formation of auditory objects. *Zool Anal Complex Syst* 101:260–272.
- Ivarsson C, de Ribaupierre Y, de Ribaupierre F. 1988. Influence of auditory localization cues on neuronal activity in the auditory thalamus of the cat. *J Neurophysiol* 59:586–606.
- Jones EG. 1975. Varieties and distribution of non-pyramidal cells in the somatic sensory cortex of the squirrel monkey. *J Comp Neurol* 160:205–267.
- Kaas J, Axelrod S, Diamond IT. 1967. An ablation study of the auditory cortex in the cat using binaural tonal patterns. *J Neurophysiol* 30:710–724.
- Katz LC. 1987. Local circuitry of identified projection neurons in cat visual cortex brain slices. *J Neurosci* 7:1223–1249.
- Katz LC, Gilbert CD, Wiesel TN. 1989. Local circuits and ocular dominance columns in monkey striate cortex. *J Neurosci* 9:1389–1399.
- LeVay S. 1973. Synaptic pattern in the visual cortex of the cat and monkey. Electron microscopy of Golgi preparations. *J Comp Neurol* 150:53–85.
- LeVay S, Gilbert CD. 1976. Laminar patterns of geniculocortical projection in the cat. *Brain Res* 113:1–19.
- Lorente de No R. 1949. Cerebral cortex: architecture, intracortical connections, motor projections. In: Fulton JH, editor. *Physiology of the nervous system*. London: Oxford University Press. p 288–313.
- Lund JS. 1973. Organization of neurons in the visual cortex, area 17, of the monkey (*Macaca mulatta*). *J Comp Neurol* 147:455–496.
- Lund JS. 1984. Spiny stellate neurons. In: Peters A, editor. *The cerebral cortex*. New York: Plenum Press. p 255–308.
- Lund JS, Boothe RG, Lund RD. 1977. Development of neurons in the visual cortex (area 17) of the monkey (*Macaca nemestrina*): a Golgi study from fetal day 127 to postnatal maturity. *J Comp Neurol* 176:149–188.
- Lund JS, Henry GH, MacQueen CL, Harvey AR. 1979. Anatomical organization of the primary visual cortex (area 17) of the cat. A comparison with area 17 of the macaque monkey. *J Comp Neurol* 184:599–618.
- Martin KA, Whitteridge D. 1984. Form, function and intracortical projections of spiny neurones in the striate visual cortex of the cat. *J Physiol (London)* 353:463–504.
- Masterton RB, Imig TJ. 1984. Neural mechanisms for sound localization. *Annu Rev Physiol* 6:275–287.
- McGuire BA, Hornung JP, Gilbert CD, Wiesel TN. 1984. Patterns of synaptic input to layer 4 of cat striate cortex. *J Neurosci* 4:3021–3033.
- McMullen NT, Glaser EM. 1982. Morphology and laminar distribution of nonpyramidal neurons in the auditory cortex of the rabbit. *J Comp Neurol* 208:85–106.
- Meyer G, Ferres-Torres R. 1984. Postnatal maturation of nonpyramidal neurons in the visual cortex of the cat. *J Comp Neurol* 228:226–244.
- Meyer G, Gonzalez-Hernandez TH, Ferres-Torres R. 1989. The spiny stellate neurons in layer V of the human auditory cortex. A Golgi study. *Neuroscience* 33:489–498.
- Mitani A, Shimokouchi M. 1985. Neuronal connections in the primary auditory cortex: an electrophysiological study in the cat. *J Comp Neurol* 235:417–429.
- Mitani A, Shimokouchi M, Itoh K, Nomura S, Kudo M, Mizuno N. 1985. Morphology and laminar organization of electrophysiologically identified neurons in the primary auditory cortex of the cat. *J Comp Neurol* 235:430–447.
- O'Leary JL. 1941. Structure of the area striata of the cat. *J Comp Neurol* 75:131–164.
- Peinado A, Katz LC. 1990. Development of cortical spiny stellate cells: Retraction of transient apical dendrite. *Soc Neurosci Abstr* 16:1127.
- Peters A, Kara DA. 1985. The neuronal composition of area 17 of rat visual cortex. I. The pyramidal cells. *J Comp Neurol* 234:218–241.
- Reale RA, Imig TJ. 1980. Tonotopic organization in auditory cortex of the cat. *J Comp Neurol* 192:265–291.
- Rose JE. 1949. The cellular structure of the auditory region of the cat. *J Comp Neurol* 91:409–440.
- Sampson FK, Barone WP, Irons WA, Clarey JC, Poirier P, Imig TJ. 2000. Directionality derived from differential sensitivity to monaural and binaural cues in cat's medial geniculate body. *J Neurophysiol* 84:1330–1345.
- Semple MN, Kitzes LM. 1993a. Binaural processing of sound pressure level in cat primary auditory cortex: evidence for a representation based on absolute levels rather than interaural level differences. *J Neurophysiol* 69:449–461.
- Semple MN, Kitzes LM. 1993b. Focal selectivity for binaural sound pressure level in cat primary auditory cortex: two-way intensity network tuning. *J Neurophysiol* 69:462–473.
- Sharma J, Angelucci A, Sur M. 2000. Induction of visual orientation modules in auditory cortex. *Nature* 404:841–847.
- Simons DJ, Woolsey TA. 1984. Morphology of Golgi-Cox-impregnated barrel neurons in rat Sml cortex. *J Comp Neurol* 230:119–132.
- Smith PH. 1992. Anatomy and physiology of multipolar cells in the rat inferior collicular cortex using the in vitro brain slice technique. *J Neurosci* 12:3700–3715.
- Somogyi P, Tamas G, Lujan R, Buhl EH. 1998. Salient features of synaptic organisation in the cerebral cortex. *Brain Res Rev* 26:113–135.
- Steinschneider M, Arezzo J, Vaughan HG Jr. 1980. Phase-locked cortical responses to a human speech sound and low-frequency tones in the monkey. *Brain Res* 198:75–84.
- Steinschneider M, Tenke CE, Schroeder CE, Javitt DC, Simpson GV, Arezzo JC, Vaughan HG Jr. 1992. Cellular generators of the cortical auditory evoked potential initial component. *Electroencephalogr Clin Neurophysiol* 84:196–200.
- Stratford KJ, Tarczyhornocho K, Martin KAC, Bannister NJ, Jack JJB. 1996. Excitatory synaptic inputs to spiny stellate cells in cat visual cortex. *Nature* 382:258–261.
- Strominger NL. 1969. Localization of sound in space after unilateral and bilateral ablation of auditory cortex. *Exp Neurol* 25:521–533.
- Tusa RJ, Palmer LA, Rosenquist AC. 1978. The retinotopic organization of area 17 (striate cortex) in the cat. *J Comp Neurol* 177:213–235.
- Vercelli A, Assal F, Innocenti GM. 1992. Emergence of callosally projecting neurons with stellate morphology in the visual cortex of the kitten. *Exp Brain Res* 90:346–358.
- von Economo C. 1929. *The cytoarchitecture of the human cerebral cortex*. London: Oxford University Press.
- von Economo C, Koskinas GN. 1925. *Die cytoarchitektonik der hirnrinde des erwachsenen menchen*. Berlin: Springer.
- von Melchner L, Pallas SL, Sur M. 2000. Visual behaviour mediated by retinal projections directed to the auditory pathway. *Nature* 404:871–876.
- Walker AE. 1937. The projection of the medial geniculate body to the cerebral cortex in the macaque monkey. *J Anat* 71:319–331.
- White EL. 1978. Identified neurons in mouse SM1 cortex which are postsynaptic to thalamocortical axon terminals: a combination Golgi-electron microscopic and degeneration study. *J Comp Neurol* 181:627–661.
- White EL. 1979. Thalamocortical synaptic relations: a review with emphasis on the projections of specific thalamic nuclei to the primary sensory areas of the neocortex. *Brain Res* 180:275–311.
- White EL, Rock MP. 1980. Three-dimensional aspects and synaptic relationships of a Golgi-impregnated spiny stellate cell reconstructed from serial thin sections. *J Neurocytol* 9:615–636.
- Whitfield IC, Cranford J, Ravizza R, Diamond IT. 1972. Effects of unilateral ablation of auditory cortex in cat on complex sound localization. *J Neurophysiol* 35:718–731.
- Winer JA. 1984. Anatomy of layer IV in cat primary auditory cortex (AI). *J Comp Neurol* 224:535–567.
- Winer EL. 1992. Thalamus and cortex. In: Webster DB, Popper AN, Fay RF, editors. *The mammalian auditory pathway: neuroanatomy*. New York: Springer-Verlag. p 222–409.
- Woolsey TA. 1996. Barrels: 25 years later. *Somatosens Motor Res* 13:181–186.