Chandelier cells represent a unique type of cortical GABAergic interneuron whose axon terminals (Ch-terminals) form synapses exclusively with the axon initial segments of pyramidal cells. In this study, we have used immunocytochemistry for the high-affinity plasma membrane transporter-1 (GAT-1) to analyze the distribution and density of Ch-terminals in various cytoarchitectonic and functional areas of the human neocortex. The lowest density of GAT-1-immuoreactive (-ir) Ch-terminals was detected in the primary and secondary visual (areas 17 and 18) and in the somatosensory areas (areas 3b and 1). In contrast, an intermediate density was observed in the motor area 4 and the associative frontolateral areas 45 and 46, whereas the associative frontolateral areas 9 and 10, frontal orbital areas 11, 12, 13, 14, and 47, associative temporal areas 20, 21, 22, and 38, and cingulate areas 24 and 32 displayed the highest density of GAT-1-ir Ch-terminals. Despite these differences, the laminar distribution of GAT-1-ir Ch-terminals was similar in most cortical areas. Hence, the highest density of this transporter was observed in layer II, followed by layers III, V, VI, and IV. In most cortical areas, the density of GAT-1-ir Ch-terminals was positively correlated with the neuronal density, although a negative correlation was detected in layer III across all cortical areas. These results indicate that there are substantial differences in the distribution and density of GAT-1-ir Ch-terminals between areas and layers of the human neocortex. These differences might be related to the different functional attributes of the cortical regions examined.

**Keywords:** axon initial segment, cerebral cortex, GABA, inhibition, interneurons

**Introduction**

A large variety of gamma-aminobutyric acid (GABA)-ergic neurons with different morphological, molecular, and physiological characteristics has been described in the mammalian cerebral cortex. Chandelier cells are one of the best characterized cortical GABAergic interneurons because they are readily distinguished by their vertical rows of boutons in the terminal portion of their axons (Ch-terminals), which resemble candlesticks (Szentagothai and Arbib 1974; Jones 1975). Many interneurons establish synapses at different postsynaptic regions, both with pyramidal cells and interneurons. However, chandelier cells are unique because Ch-terminals only establish synapses with the axon initial segments (AIS) of pyramidal cells. Indeed, these cells represent the main source of the AIS synapses (Somogyi 1977; Fairen and Valverde 1980; Peters et al. 1982; Somogyi et al. 1982, 1985; Freund et al. 1983; DeFelipe et al. 1985, 1989; Williams and Lacaille 1992; Buhl et al. 1994; DeFelipe 1999). The AIS is a critical region in controlling cell excitability and the generation of axonal potentials, thereby determining the axonal output of principal cells (Stuart and Sakmann 1994; Colbert and Johnston 1996).

Thus, in contrast to interneurons that target membrane compartments of dendrites and somata, chandelier cells have traditionally been presumed to exert a strong influence on the output of pyramidal cells (Miles et al. 1996; DeFelipe 1999). Ch-terminals are found in different cortical areas and species, including rats (Somogyi 1977; Minelli et al. 1995; Tamas and Szabadics 2004), guinea pigs (Gulyas et al. 1993), cats (Fairen and Valverde 1980; Fariñas and DeFelipe 1991), rabbits (Muller-Paschinger et al. 1983), mice (Chiu et al. 2002), ferrets (Krimer and Goldman-Rakic 2001), monkeys (Somogyi et al. 1982, 1983; DeFelipe et al. 1985), and humans (Kisvarday et al. 1986; DeFelipe 1999; Lewis et al. 2005). However, it has become increasingly clear that inhibitory inputs to the AIS of pyramidal cells are not homogeneous across species, cortical regions, layers, or neuronal populations. In addition to occasional synapses from other types of interneurons (e.g., Gonchar et al. 2002), the single AIS of pyramidal cells may be innervated by one or a few chandelier cells (reviewed in DeFelipe 1999). Moreover, the number of synaptic inputs to the AIS differs as a function of age, location, and the projection target of the pyramidal cells (DeFelipe et al. 1985; Fariñas and DeFelipe 1991; Cruz et al. 2003). Chandelier cells are chemically heterogeneous and it has been shown that they express different combinations of substances in distinct layers and species, including the GABA transporter GAT-1; the calcium-binding proteins parvalbumin (PV) and calbindin D-28k; the peptide corticotrophin releasing factor; and the polysialylated form of the neural cell adhesion molecule (DeFelipe et al. 1989; Lewis et al. 1989; Lewis and Lund 1990; Schmidt et al. 1993; Conde et al. 1994; del Rio and DeFelipe 1994; Woo et al. 1998; DeFelipe 1999; Melchitzky et al. 1999; Arellano et al. 2004). Nevertheless, no systematic studies on the distribution and the density of Ch-terminals in the various cortical areas of the human neocortex have been performed.

In the present study, we have used GAT-1 immunocytochemistry to quantify the density of Ch-terminals because GAT-1-immuoreactive (-ir) Ch-terminals are easy to distinguish from other punctate terminal-like labeled structures in the neuropil (DeFelipe and Gonzalez-Albo 1998). We have examined the distribution of Ch-terminals as well as the density of GAT-1-ir Ch-terminals with respect to the total neuron density in each layer. The results reveal that there are significant differences in the distribution and density of GAT-1-ir Ch-terminals between the different areas and layers of the human neocortex.

**Materials and Methods**

In this study, we have used human autopsy brain tissue obtained 2-3 h post-mortem (kindly supplied by Dr R. Alcaraz, Forensic Pathology Service, Basque Institute of Legal Medicine, Bilbao, Spain), from 3 normal males who died in traffic accidents (M1, M7, and M8 aged 23, 49, and 69 years, respectively). The brain tissue was cut into 1.5-cm-thick coronal...
slices and initially fixed by immersion for 24 h in 4% paraformaldehyde diluted in 0.1 M pH 7.4 phosphate buffer (PB). Thereafter, small blocks of neocortical tissue were selected and postfixed for 1–2 days in the same fixative. The tissue was obtained from the somatosensory (areas 1 and 3b), visual (areas 17 and 18), motor (area 4), associative frontal (dorsolateral [areas 9, 10, 45, 46] and orbitary [areas 11, 12, 13, 14, 47], associative temporal (areas 20, 21, 22, and 38), and limbic cingulate (areas 24, 32) neocortical areas. Blocks from the different Brodmann’s areas of the cortex were selected from each brain according to their surface anatomy, using the patterns of the gyr and sulci. The identification of each cortical area was later confirmed by analyzing the distinctive cytoarchitectonic features of Nissl-stained sections.

After fixation, all the specimens were immersed in graded sucrose solutions and they were stored in a cryoprotectant solution at -20 °C. Serial sections (100 µm) of the cortical tissue were obtained using a vibratome, and the sections from each region and case were batch processed for immunocytochemical staining. The sections immediately adjacent to those stained immunocytochemically were Nissl stained in order to identify the cortical areas and the laminar boundaries.

**Immunostaining**

Sections were first treated for 30 min with a solution of 0.5% hydrogen peroxide and 50% ethanol in PB to inactivate the endogenous peroxidase activity. Subsequently, the sections were rinsed in PB and preincubated for 1 h at room temperature in a stock solution containing 3% normal goat or horse serum (Vector Laboratories, Burlingame, CA) in PB with Triton X-100 0.25%. Thereafter, the sections were incubated for 48 h at 4 °C in the same stock solution containing rabbit-anti-GAT-1 antiserum (1:500; Chemicon, Temecula, CA) or mouse-anti-neuron-specific nuclear protein (Neu-N) antibodies (1:4000; Chemicon). The sections were washed in PB, incubated in horse-anti-mouse or goat-anti-rabbit biotinylated secondary antibodies (1:200; Vector), and processed using the Vectorstain ABC immunoperoxidase kit (Vector). Antibody labeling was visualized with 0.05% 3,3′-diaminobenzidine tetrahydrochloride (Sigma, St Louis, MO) and 0.01% hydrogen peroxide. The sections were rinsed in PB, mounted on glass slides, dehydrated, cleared with xylene, and coverslipped. Controls were included in all the immunocytochemical procedures, either by replacing the primary antibody with preimmune goat or horse serum in some sections, omitting the secondary antibody, or replacing the secondary antibody with an inappropriate secondary antibody (i.e., an antibody directed against another species). No significant immunolabeling was detected under these control conditions.

**Quantification and Statistical Analysis**

A BX51 Olympus microscope equipped with a motorized stage and a DP70 digital camera, and the NeuroLucida package (MicroBrightField, Williston, VT) were used to plot all GAT-1-ir Ch-terminals visualized at a DP70 digital camera, and the Neurolucida package (MicroBrightField, MicroBrightField, Cary, NC) was used in this analysis. One-way analysis of variance with T3 Dunnet post hoc comparison was then performed with the SPSS statistical package software (SPSS Inc., Chicago, IL) in order to study the differences between the layers and areas. Spearman’s tests were used to study the possible correlations.

To generate the figures, light microscopic images were captured using a digital camera (Olympus DP50) attached to an Olympus light microscope, and Adobe Photoshop 7.0 software was used to generate the figure plates (Adobe Systems Inc., San Jose, CA).

**Results**

In the human cerebral cortex, GAT-1 immunocytochemistry labels numerous terminal-like puncta in the neuropil and around unstained cell bodies throughout cortical layers I–VI (Figs 1 and 2). However, as described previously the elements that are most intensely labeled are the Ch-terminals (DeFelipe and González-Albo 1998). GAT-1-ir Ch-terminals were found in

![Figure 1. Photomicrograph showing GAT-1-ir Ch-terminals (arrows) innervating the AIS of pyramidal cells in layer III of area 10. The asterisk indicates the position of the pyramidal cell soma. A small GAT-1-ir Ch-terminal indicated with 2 arrows also can be distinguished, despite the fact that the unlabeled cell of origin of the AIS is not visible in this section. Scale bar: 10, 5 µm.](image-url)
all cortical areas but by plotting their distribution it became apparent that there were dramatic differences between each cortical area and layer (Figs 3 and 4).

**Density of GAT-1-ir Ch-Terminals**

The global density of GAT-1-ir Ch-terminals was compared between each individual and it was seen to be highest in the tissue from M1 followed by that from M7. The lowest density of GAT-1-ir Ch-terminals was observed in the cortical tissue from the individual M8 (Fig. 5). However, the differences in the density of GAT-1-ir Ch-terminals were not statistically significant either between subjects or between replicates (the different measurements made in each layer, cortical area, and case). Nevertheless, there were clear differences in the mean density of GAT-1-ir Ch-terminals between different cortical areas and layers ($P < 0.0001$, see below). For this reason, we will present the data from both each individual case and the averages of the values obtained in the 3 cases.

When the densities observed in the 3 cases were averaged, there were clear differences in the mean density of GAT-1-ir Ch-terminals between different cortical areas ($P < 0.0001$, Fig. 6A). In general, the different cortical areas analyzed could be divided into 3 main groups according to the density of GAT-1-ir Ch-terminals. Group I contained the lowest density of GAT-1-ir Ch-terminals (mean ± standard error [SE]: 39.23 ± 2.84), and included the primary and secondary sensory areas, both visual areas 17 and 18 and somatosensory areas 3b and 1. In group II, the motor area 4 and associative frontolateral areas 45 and 46 displayed intermediate densities (80.15 ± 5.80). In contrast, group III displayed the highest mean density (124.66 ± 3.43) and it comprised the associative frontolateral areas 9 and 10, the frontal orbitary areas 11, 12, 13, 14, and 47, the associative temporal areas 20, 21, 22, and 38, and cingulate areas 24 and 32. No significant differences were found in the density of the GAT-1-ir Ch-terminals between individual layers or in the mean values of cortical areas within each group (Table 1). However, all the cortical areas of group I showed significant differences in...
the density of these terminals when compared with cortical areas in group III (Table 1). Only certain areas of group II showed significant differences in the density of GAT-1-ir Ch-terminals with the areas included in group I or III (Table 1).

Laminar Distribution of GAT-1-ir Ch-Terminals

When the data from all the cortical areas were averaged, each of the 3 brains showed a similar laminar distribution of GAT-1-ir Ch-terminals (Fig. 6B). The highest density of GAT-1-ir Ch-terminals corresponded to layer II (mean ± SE; 188.08 ± 7.34), which was significantly greater than that in the other layers ($P < 0.0001$). Layer III displayed an intermediate density of Ch-terminals (119.28 ± 5.28), significantly different to all layers except layer VI ($P < 0.01$). Finally, the lowest density of Ch-terminals was found in layers IV and V (80.43 ± 4.86 and 94.80 ± 4.66, respectively). Significant differences were found between the mean density of GAT-1-ir Ch-terminals in layers IV ($P < 0.001$) and V ($P < 0.05$) with that in other layers except layers V and IV, respectively. Finally, in layer VI the density of Ch-terminals (117.89 ± 5.03) was significantly different from that in all the other layers except that in layer III ($P < 0.05$).

The laminar distribution of GAT-1-ir Ch-terminals in sensory, motor, frontolateral associative, temporal associative, and cingulate areas is shown in Figures 3, 4, 7, and 8. Note that the
The distribution of these terminals is fairly similar in the 3 brains analyzed (Figs 7 and 8). The significance of the comparisons between the different layers across the different areas analyzed is illustrated in Table 1. In general, when significant differences were observed in the density of GAT-ir Ch-terminals between areas, they were mostly due to significant differences in layers III and VI. Layer II presented a homogeneously high density of GAT-1-ir Ch-terminals with no significant differences between most cortical areas. In contrast, the density of terminals in layer II of areas 1 and 18 was significantly lower when compared with most cortical areas of group III. In most areas other than the temporal lobe, a tendency toward a lower density of GAT-1-ir Ch-terminals was observed in layers IV and V, although the differences between areas did not generally reach statistical significance.

**Correlation between the Density of GAT-1-ir Ch-Terminals and that of Neu-N-ir Neurons**

In an attempt to detect possible correlations between the density of Neu-N-ir neurons and the number of GAT-ir Ch-terminals, we compared these parameters in 6 representative cortical areas: the sensory areas 17 and 18, motor area 4, associative areas 9 and 21, and cingulate area 24 (Figs 7-9). When these variables were analyzed in individual cortical layers from distinct cytoarchitectonic areas, an inverse correlation was found in layer III (Spearman’s rho -0.664, \( P = 0.03 \)). Thus, in

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**Figure 4.** Schematic drawings based on Neurolucida plots made with a ×40 objective showing the laminar patterns of GAT-1-ir Ch-terminals in associative frontal orbitary, associative temporal, and cingulate areas of the M1 brain. Note the similar distribution of GAT-1-ir Ch-terminals in the different cortical areas.
areas with a higher neuronal density in layer III (i.e., areas 17 and 18) there was a lower density of GAT-1-ir Ch-terminals (Figs 7–9). Likewise, a similar trend was found in layers II and IV but this did not reach statistical significance (Spearman's rho −0.457 \( P = 0.56 \) and Spearman's rho −0.493 \( P = 0.62 \), respectively). In contrast, the number of GAT-1-ir Ch-terminals was not correlated with neuronal density in layers V and VI.

When neuronal density and the density of GAT-1-ir Ch-terminals were analyzed in the cortical layers of each individual cytoarchitectonic area, a direct correlation was found in areas 4, 9, 17, and 24. As such, the higher density of GAT-1-ir Ch-terminals was associated with a higher density of neurons in the layers of these areas (Spearman's rho for areas 4, 9, 17, 24 = 0.83**, 0.65**, 0.68**, 0.53*, \( *P < 0.05, **P < 0.01 \)).

**Discussion**

Through studying GAT-1 immunohistochemistry, we have been able to quantify the density and distribution of Ch-terminals in different areas and layers of the human neocortex. This analysis has revealed both similarities and differences between distinct cytoarchitectonic areas and cortical layers. Thus, we found that the distribution of Ch-terminals is not homogeneous in the cortex and we consider that these differences are probably related to the different functional attributes of the cortical region or layer examined.

**Variation in the Density of GAT-1-ir Ch-Terminals between Individuals**

In this study, we found that the global density of GAT-1-ir Ch-terminals decreased with age. Indeed, there was a 15% decrease in the 69-year-old individual when compared with the tissue obtained from the 23 year old. However, this difference was not statistically significant and because we only analyzed one individual of each age, the differences could merely be due to interindividual variability. Thus, it is clear that further studies on tissue from more subjects will be necessary to verify the age-related decline in the density of GAT-1-ir Ch-terminals in the human neocortex. Nevertheless, these results are consistent with the age-related decline in GAT-1-ir Ch-terminals reported in layer III of the monkey cortex (Cruz et al. 2003). Such a decline does not seem to represent an age-dependent decrease in the number of neurons. Neither neuronal density (Pakkenberg et al. 2003) nor the density of PV-ir cell somata (including chandelier cells; Bu et al. 2003) have been seen to change as a function of age in the human neocortex. Thus, age-related axonal retraction by chandelier cells and/or a decrease of GAT-1 expression or antigenicity at Ch-terminals with age may well account for the current observations. However, because there are relatively few chandelier cells a loss of some these may pass unnoticed when the whole population of neurons is considered in stereological studies. It will be necessary to examine the pyramidal cell AISs by electron microscopy to better define the processes involved in this loss of GAT-1-labeled terminals.

**Variation in the Density of GAT-1-ir Ch-Terminals between Areas**

There were significant differences in the density of GAT-1-ir Ch-terminals between the distinct areas of the human neocortex analyzed, suggesting a regional specialization of the inhibitory circuits in which they are involved. In the 3 brains analyzed, the primary and secondary sensory areas (areas 17, 18, 3b, and 1) displayed the lowest density of GAT-1-ir Ch-terminals, the motor (area 4) and associative frontolateral areas 45 and 46 displayed intermediate values, whereas the frontolateral areas 9 and 10, the frontal orbital areas 11, 12, 13, 14, and 47, the temporal areas 20, 21, 22, and 38, and the cingulate areas 24 and 32 contained the highest mean density of GAT-1-ir Ch-terminals. Although detailed studies of the density and distribution of Ch-terminals have not been performed previously in the human neocortex, these results are consistent with observations that there is generally a higher density of Ch-terminals in high-order association areas than in primary sensory areas in the monkey (Lewis et al. 1989; Akil and Lewis 1992; Conde et al. 1996; Elston and Gonzalez-Albo 2003). Furthermore, the results are consistent with those showing that double bouquet cells, another important component of cortical GABAergic circuits, are not homogeneously distributed throughout the neocortex but that they also display rather dramatic differences in their density between areas (Yañez et al. 2005). Previous electron microscopy and tract tracing studies (Farinãas and DeFelipe 1991), as well as the analysis of Golgi-stained material (Lewis and Lund 1990) have shown that Ch-terminals are present in the cat and monkey visual cortex. However, it is difficult to obtain an idea about the distribution of Ch-terminals in electron microscope studies or in Golgi studies due to the inconsistency of the Golgi method and the relatively few AIS examined by electron microscopy. Therefore, the scarcity of GAT-1-ir Ch-terminals in the primary visual cortex observed here, as in other sensory areas, is best compared with other cortical areas examined using the same methodology. There are several possible explanations for the differences in the density of GAT-1-ir Ch-terminals between areas. Because not all pyramidal cells are necessarily innervated by Ch-terminals (e.g., see Farinãas and DeFelipe 1991), a smaller proportion of the pyramidal cells in sensory areas could be innervated by Ch-terminals than in associative areas. Alternatively, there may be less GAT-1 protein...
Figure 6. Charts indicating the average density ± SE of Ch-terminals immunostained for GAT-1 in the different cortical areas (A) and layers (B) of the human brains M1, M7, and M8. Note that similar values were obtained for each area in the 3 cases. When the average values from the 3 cases are considered (A), cortical areas can be grouped according to the density of GAT-1-ir Ch-terminals. Note also that similar laminar patterns of GAT-1-ir Ch-terminals were found in the 3 brains (B).
Table 1
Comparison of the laminar density of GAT-1-ir Ch-terminals between cortical areas

| Area | 1 | 3b | 17 | 18 | 4 | 45 | 46 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 |
| II   | 1  | 3b | 17 | 18 | 9 | 10 | 11 | 12 | 13 | 14 | 47 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | V |
| III  |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| IV   |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| II   | 3b |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| III  |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| IV   |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| II   | 17 |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| III  |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| IV   |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| II   | 18 |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| III  |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| IV   |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| II   | 4  |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| III  |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| IV   |    |    |    |    |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |

Note: Statistical comparisons and degree of significance (* 0.05; ** 0.01; *** 0.001) in the density of GAT-1-ir Ch-terminals between layers II, III, and IV (left) and V and VI (right). NA, not applicable.
in Ch-terminals in sensory areas implying that many terminals in these regions contain quantities of protein that are below the levels of detection for the immunocytochemical methods used. Furthermore, it is possible that at least some Ch-terminals in sensory cortical areas could use other types of GABA transporters.

**Laminar Distribution of GAT-1-ir Ch-Terminals in the Cerebral Cortex**

The present results also indicate that there are differences in the density of GAT-1-ir Ch-terminals between the distinct cortical layers. The highest density of GAT-1-ir Ch-terminals was observed in layer II followed by layers III, V, VI, and IV. Previous studies have shown that there are differences in the density of synaptic terminals that contact the AIS of pyramidal neurons in layers II–III are more densely innervated by chandelier cell synapses than those in layers V and VI (Sloper and Powell 1979; DeFelipe et al. 1985; Farinas and DeFelipe 1991; DeFelipe 1999). Because the pyramidal cells located in different layers project to different sites (Jones 1984; Inda et al.)

**Figure 7.** Graphs indicating the density of GAT-1-ir Ch-terminals in the different layers of sensory, motor, and associative frontal dorsolateral areas of the M1, M7, and M8 brains. Note that despite the differences in density, the same laminar patterns were generally found in each cortical area in the 3 individuals.
White 1989), the changes in the density of GAT-1-ir Ch-terminals observed between layers might be related to the laminar distribution of pyramidal cell populations projecting to particular sites.

In addition, it has been shown in the rat neocortex that postsynaptic GABA_A receptors at the AIS of supragranular pyramidal cells are enriched with the α2 subunit, whereas in infragranular layers the α3 subunit predominates (Fritschy et al., 2007).
Thus, it is possible that chandelier cells exert their activity through different types of postsynaptic GABA<sub>A</sub> receptors depending on the cortical layer in which they are found. Finally, a direct correlation was observed between the density of GAT-1-ir Ch-terminals and neuronal density in areas 4, 9, 17, and 24. This was not the case in areas 18 and 21 where there was no correlation between GAT-1-ir Ch-terminals and neuronal density. Hence, there is a remarkable heterogeneity in the density and distribution of GAT-1-ir Ch-terminals, suggesting that chandelier cells contribute differentially to cortical circuits (anatomically and physiologically) according to the cortical area or layer in which they are situated.

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References


Lewis DA, Hashimoto T, Volk DW. 2005. Cortical inhibitory neurons and schizophrenia. Nat Rev Neurosci. 6:312--324.


