Neurogliaform or Spiderweb Cells

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1. Background

Ramón y Cajal (1909–1911) described small neurons resembling neuroglial cells in both the striatum and the cerebral cortex (Fig. 1) (see also Fig. 1 of Chapter 8). Usually Ramón y Cajal termed these *cellules neurogliiformes.* He notes that in the cerebral cortex, he had first observed them in the human visual area in 1899. His most extensive description of the cells comes in his general account of layer II of the cortex, though he notes that they are found in all layers and are especially common in the deeper layers. In layer II he refers to them as "cellules name ou neurogliiforme" and he illustrates them by reference to preparations of the human motor cortex (his Fig. 345) and of the cat visual cortex (his Fig. 547). Elsewhere he describes them in human visual and auditory cortex and in cat auditory cortex as well.

According to Ramón y Cajal the neurogliaform cell is very small, even "minuscula" (1922) with a "feeble" cell body and a large number of fine, radiating dendrites that are short, varicose, and rarely branched. The short length and lack of lateral branches on the dendrites, coupled with the difficulty of identifying an axon, was what in Ramón y Cajal's eyes caused these neurons to resemble neuroglial cells. The axon, when seen, is extremely thin, and never deeply im-
pregnated. Shortly after its origin, it breaks up into a very dense, highly ramified arborization composed of delicate beaded intertwined branches. Later, in his description of the visual cortex, he emphasizes the fact that the axonal arborization tends to remain within the territory of the dendrites. The cells, he says, are less common in the dog and cat than in man but in those species are remarkable for their larger size and extreme richness of their axonal arborizations.

As Ramón y Cajal’s account of the cerebral cortex proceeds, he commences using the term cellule aracnoïdiforme or spiderweb cell as a synonym for neurogliaform, sometimes referring to a drawing of a cell by one name in the text and by the other in the figure legend (e.g., Fig. 387). By the time he wrote his account of the cat visual cortex (1922), he had generally come to refer to the cells as aracnoïdiforme, aracnoïforme, or ipfrastructure, all terms with the connotation of a spiderweb and emphasizing the axonal arborization as the distinguishing feature of the cell.

It seems doubtful that spiderweb or neurogliaform cells were clearly identified for more than half a century following Ramón y Cajal’s last account. Neither term is mentioned by Lorente de Nó (1922), in his description of what he took to be the mouse auditory cortex but which we now know to be somatosensory cortex. Certain small cells shown in his drawings of layer IV have the dendritic patterns of spiderweb cells, and axonal ramifications that intertwine in what he called a “glomerular” or “basket” manner among the terminal ramifications of thalamic afferents. In both this and his later work (1949), he emphasized the extremely local nature of the effect that such cells should exert. The axonal ramifications drawn on some cells by O’Leary (1941) and O’Leary and Bishop (1988) in the visual cortex of the cat and rabbit are too incomplete for a positive identification, and even in more recent times it is doubtful that many workers have been successful in fully impregnating the axon and, therefore, in recognizing spiderweb cells.

2. Recent Studies

2.1. Distribution

Probably the first author to draw attention to spiderweb cells in recent times was Valverde (1971, 1978) who refers to them as cleaved cells, that is, the name, again, emphasizing the distinctive axonal plexus. Valverde’s first description of such cells was from the visual cortex of the monkey. He found the cells to be especially characteristic of layer IV and, from the extent of their axonal plexus, considered that each should embrace some 500–500 somata of the small spiny cells that also dominate layer IV. Both cleaved and spiny cells were described as major recipients of the terminations of thalamic afferents. The composite arrangement of thalamic afferent terminations, cleaved cell axons, and contained layer IV somata, he termed a glomerulus.

Spiderweb cells were also identified in the somatosensory and motor cortex of monkeys by Jones (1975) who referred to them as type 3 cells. They were especially concentrated in layer IV of the sensory area but could be observed in layer III of the motor area and in layer II of both areas. Jones confirmed Valverde’s account of the extent of the axonal plexus showing an almost invariable diameter in all dimensions of 90–400 μm. Peters and Regidor (1981) later reported the presence of neurogliaform or spiderweb cells in all layers of area 17 of the cat visual cortex, noting that they are the smallest nonpyramidal cells in the cortex. Fairen and Valverde (1980) and Feldman and Peters (1978) have remarked on the apparent absence of these cells from the visual cortex of rodents. Tombol (1978) has observed them in all layers of monkey visual cortex but has found them especially concentrated in layers I, II, and IV and V. See Chapter 6 for other accounts.

2.2. Description

The identification of a cell as a spiderweb cell depends always on the ability to stain the distinctive axonal plexus (Figs. 2, 3). When only the dendrites are stained, the cell, though obviously small, could easily be mistaken for any one of a number of other nonpyramidal cell types.

* Clew, a very old English word, means a ball of thread or yarn.
The soma is spherical and rarely more than 10–12 μm in diameter. Seven to ten thin dendrites radiate out symmetrically from the soma; some branch once or twice, many do not. Single and branched dendrites are of approximately equal length and extend for 50–72 μm, rarely more. Together, they form a very symmetrical, spherical dendritic field. Within this, it is common for some of the dendrites to curve back toward the soma. The dendrites are thin (1–2 μm), occasionally beaded, though not overtly so, and virtually never bear dendritic spines. Even those occasional spines seen intermittently on somatopyramidal neurons appear to be lacking.

The axon is extremely thin (0.5–1 μm) and can arise from any part of the soma or from the base of the dendrite. Almost immediately it branches and rebranches so frequently and the branches become so entangled that it is difficult to follow all the branches in continuity. Though there is a tendency for the

**Figures 2 and 5.** Photomicrographs of spiderweb or type 5 cells, from material illustrated in Jones (1972). Golgi–Kopsch preparations, from layer IV of the somatosensory cortex of squirrel monkeys. Parts of the complicated axonal plexus are out of the plane of focus or in the two adjacent sections. Bars represent 100 μm.

**Figure 4.** Camera lucida drawings of spiderweb cells from layer IV of the squirrel monkey somatosensory cortex. From material illustrated in Jones (1972). Only the parts of the axon found in one section are drawn; the axonal plexus formed by each cell usually extends through three or four 100-μm-thick sections. Lower cell in (B) has axon omitted to show dendritic field. Bars represent 100 μm and 1 mm (inset).
branches of the axon to be beaded, the diameter of each bead is not much greater than that of the axon, so the appearance is one of sinuosity rather than of a heavy bouton investment. Such an axon is presumably unmyelinated. The axon branches suffer very little reduction in diameter so that the plexus has a homogeneous appearance. Characteristically, small "holes" appear in the plexus, representing the positions occupied by the unstained somata of other cells (Fig. 4).

![Image](image-url)

**Figure 5.** Camera lucida drawing (A) and computer reconstruction (B) of a spiderweb cell to show small extent and symmetry of dendritic field. In (A), dendrites and axon are drawn separately. In (B), lines represent surfaces of section. Bars represent 100 µm (A) and 50 µm (B). From Jones (1975).

Though the greater part of the axonal plexus is confined to the general vicinity of the dendritic field, in the monkey at least, it can extend for considerable distances beyond that. Figure 2 shows a spiderweb cell from the monkey somatosensory cortex with a dendritic field approximately 175 µm in diameter and an axonal field approximately 350 µm in diameter. Figures 4 and 5 show cells with even smaller dendritic fields.

To date there has been no direct identification of the spiderweb cell at the electron microscopic level. A cell from layer I of the visual cortex of an immature cat shown by LeVay (1973) to have an axon that gives rise to symmetrical synapses is the only possible example. The smallest nonpyramidal cells of layer IV, from the accounts of Powell and his colleagues (Sloper et al., 1979; Wüthrich et al., 1980), have a rather low density of cytoplasmic organelles and receive relatively few axosomatic synapses, by contrast with larger nonpyramidal cells. At the electron microscopic level, layer IV contains a relatively dense plexus of fine, unmyelinated axons that are mildly beaded, contain flattened synaptic vesicles, and give off repeated en passant, symmetrical synapses (Jones and Powell, 1970).

Axons of this type would be expected for the spiderweb cell, from its light microscopic appearances, but this also remains to be verified.

### 2.5. Are They GABAergic?

A substantial proportion (approximately 40%; Fig. 6) of the small cell somata in layer IV of the monkey and rat cerebral cortex concentrate [3H]GABA and stain immunocytochemically for GAD (Ribak, 1979; Hendry and Jones, 1981; Hendry et al., 1985; Houser et al., 1985). It is rarely possible to stain the dendrites of such cells much beyond their proximal parts, though it can be confirmed that they are nonspiny. Sometimes dendrites that recur toward the soma, like those of spiderweb cells, can be discerned but it would be premature to state that the spiderweb cells are proven GABAergic interneurons. Similarly, at the fine structural level, long segments of thin, beaded, unmyelinated GAD-positive axons can be seen making multiple en passant synapses on GAD-positive and GAD-negative neurons in layer IV (Hendry et al., 1985), but as pointed out above, these axons have not been established as belonging to spiderweb cells.

### 3. Functions

No cells resembling spiderweb cells have been labeled by intracellular dye injections to date and it seems doubtful that many such small cells have been encountered electrophysiologically. Certainly none have been positively identified. In the absence of any physiological information and with no positively confirmed data regarding the synaptic relationships of the spiderweb cells, it is not possible to make more than extremely tentative suggestions as to their functions.

The highly branched and tightly intertwined axon of the spiderweb cell gives the cell some resemblance to the Golgi neuron of the cerebellum and to other known inhibitory interneurons elsewhere. If it can be tentatively thought
of an inhibitory interneuron, and if all of the slight dilations on its highly branched axon are synaptic terminals, then the spiderweb cell would be in a position to exert a powerful inhibitory effect on a large number of neurons in a local area. Concentrated as it is in layer IV, where it probably receives thalamic axon terminations (Valverde, 1971), and possibly making synapses mainly on the small spiny neurons of that layer, the spiderweb cell, as an inhibitory interneuron, could play an important role in setting up surround inhibition. Suppose its action were similar to that of a Golgi cell in the cerebellum, the spiderweb cell could serve to inhibit the spiny and other layer IV cells less powerfully excited at the periphery of a zone of focal thalamic input. In this way it could serve to maintain the focal nature of the input, much as a Golgi cell is thought to focus mossy fiber inputs to granule cells in the cerebellum. Such focusing would seem to be an essential prerequisite for setting up the columnar nature of information flow through other cortical layers (Fig. 7). Such a theory (Jones, 1981) is entirely speculative and requires much additional work before it can be said to be confirmed or disapproved.

4. References


Figure 7. Schematic figure from Jones (1981) illustrating hypothetical mode of action of spiderweb cells, assuming they are inhibitory. Focal bundle of thalamocortical axons (A) terminates on a small group of spiny cells of layer IV whose vertical axons synapse on pyramidal cells of all layers (arrows, B) converging focus into a column. Focus and cells are maintained (C, D) by putatively inhibitory spiderweb cells which inhibit spiny cells less strongly excited at perimeter of thalamic input zone. Synaptic relationships shown do not exclude thalamocortical synapses on other cell types in cortex.
Smooth and Sparsely Spinous Nonpyramidal Cells Forming Local Axonal Plexuses

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1. Introduction

In the cerebral cortex there exists a population of nonpyramidal cells with locally ramifying axonal plexuses which partially or completely overlap their dendritic trees. These neurons have smooth or sparsely spinous dendrites and, in addition to the local plexus, the axons of many of these neurons have branches which extend into cortical layers either above or below the one containing the cell body. In some cases, it has been shown that these branches give rise to a second plexus. So far as is known, the axons of these neurons do not leave the cerebral cortex and so these cells are variously referred to as short-axon, local-circuit, or Golgi type II neurons. Further, their axons do not form easily characterized terminal arborizations, as do the axons of chandelier cells (Chapter 10) and basket cells (Chapter 8).

The group of neurons with smooth or sparsely spinous dendrites and locally distributed axonal collaterals lacking distinctive terminal arborizations have not yet been systematically classified, although Valverde (1976) and Fairén and Val-