Cell Tissue Res (1982) 227:319–342

Cell and Tissue Research

Neuronal types in the striatum of man

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Summary. Nerve cells of the human striatum were investigated with the use of a newly developed technique that reveals the pattern of pigmentation of individual nerve cells by means of transparent Golgi impregnations of their cell bodies and processes. Five types of neurons are distinguished:

Type I is a medium-sized spine-laden neuron with an axon giving off a great number of collateral branches. The vast majority of the cells in the striatum belong to this type. Numerous intensely stained lipofuscin granules are contained in one pole of the cell body and may also extend into adjacent portions of a dendrite.

Type II is a medium-sized to large neuron with long intertwining dendrites decorated with spines of uncommon shape. A distinguishing feature of this cell type is the presence of somal spines. This cell type is devoid of pigment or contains only a few tiny lipofuscin granules.

Type III is a large multipolar neuron. The cell body generates a few rather extended dendrites that are very sparsely spined. The finely granulated pigment is evenly dispersed within a large portion of the cytoplasm.

Type IV is a large aspiny neuron with rounded cell body and richly branching tortuous dendrites. The axon branches frequently in the vicinity of the parent soma. Large pigment granules are concentrated within a circumscribed part of the cell body close to the cell membrane.

Type V is a small to medium-sized aspiny neuron. The dendrites break up into a swirling mass of thin branches. More than one axon may be given off from the soma. The axons branch close to the soma into terminal twigs. Cells of this type contain numerous large and well-stained lipofuscin granules.

Each of the cell types has a characteristic pattern of pigmentation. The different varieties of nerve cells in the striatum can therefore be distinguished not only in Golgi impregnations but also in pigment-Nissl preparations.

Key words: Striatum – Golgi technique – Lipofuscin – Projection neuron – Local circuit neuron

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0302-766X/82/0227/0319/$04.80

The striatum is frequently considered as being composed of only two types of neurons: large and small cells (Vogt and Vogt 1920; Brockhaus 1942; Namba 1957; Feremutsch 1961; Adinolfi and Pappas 1968; Schröder et al. 1975). This simplified view is largely the result of the examination of Nissl preparations that provide little information about the real number of neuronal types occurring within the limits of a cortical area or a subcortical nucleus. In contrast, Golgi impregnations provide a much better basis for analyzing the various constituents of a given center. Golgi studies have clearly shown the existence of more than two neuronal types in the striatum of many mammalian species (Kemp 1968 cat; Fox et al. 1971/72a, b monkey; Mensah and Deadwyler 1974 rat; Chronister et al. 1976 rat, mouse; DiFiglia et al. 1976 monkey; Norton and Culver 1977 rat; Pasik et al. 1979, monkey).

The objective of the present study was to reexamine the human striatum with the aid of a newly-developed Golgi technique that allows one to study not only the specific characteristics of the processes of various nerve cell types but also the features of their cytoplasmic components. This was made possible by restricting the impregnation to only a thin and transparent coating of the cellular membranes stable enough to withstand counterstaining procedures (Braak and Braak 1982; Braak, in press). Preparations processed in this way can be used to study the pigmentation of Golgi impregnated nerve cells. This study is therefore aimed not only at distinguishing the various neuronal types constituting the human striatum but also attempts to demonstrate their characteristic pattern of pigmentation.

Materials and methods

Six brains obtained at autopsy and free of significant pathological alterations were used for this study. The brains were fixed by immersion in an aqueous solution of formaldehyde (4%). Age ranged from 44 years to 52 years in order to achieve the typical pattern of pigmentation of nerve cells of the human adult and to avoid age-related changes in cell processes (♂ aged 44, cardiac infarction; ♂ aged 45, peritonitis; ♂ aged 46, tuberculosis; ♀ aged 47, cardiac infarction; ♂ aged 50, suicide; ♂ aged 52, cardiac infarction).

Blocks, 3–5 mm thick, including the striatum and portions of adjoining structures were cut out of the brains and processed according to the Golgi technique proposed by Braitenberg et al. (1967; see also Millhouse 1981). After impregnation, the blocks were cut at 100 µm with the aid of a freezing microtome. Sections were directly transferred to 70% ethanol, quickly dehydrated, and mounted in synthetic resin (Permount, Fisher). A total number of 164 suitably impregnated nerve cells was chosen for documentation (23 type-I, 15 type-II, 19 type-III, 23 type-IV, and 84 type-V neurons). There is no correlation between these numbers and the frequency in which the cell types occur in the striatum, nor the frequency of successfully impregnated cellular images of a certain type. The vast majority of impregnated neurons belong to the type-I cells. About 10,000–20,000 neurons had to be checked to obtain a suitable number of cells of types II to V. Four to 12 photographs were taken from each of the documented nerve cells at different magnifications and various depths of focus. In addition, camera lucida drawings of several nerve cells were made with the aid of a drawing tube. Thereafter, sections containing the documented neurons were floated free of the slide and cover-slip by soaking in xylene. The sections were rehydrated and subjected to lixiviation of most of the silver chromate deposits that normally fill impregnated nerve cells. Lixiviation occurred in a diluted aqueous solution of ammonia leaving behind an only thin coating of the impregnated cells. This coating was made transparent by oxidation with an aqueous solution of potassium ferricyanide. For further details of the "de-impregnation" method the reader is referred to Braak (in press). Sections were then oxidized with performic acid and stained for pigment granules with aldehydefuchsin (Braak 1980). Preparations treated in this way revealed both the typical features of the cell processes and the pattern of pigmentation. Unfortunately, due to the thickness of the sections, the brilliancy of the photographs is considerably reduced.

Some additional blocks of the same material were embedded in paraffin and cut at 12 μm and 35 μm. Sections were stained either with cresyl violet or with a combination of aldehydefuchsin and gallocyanine chrome alum (Braak 1980).

Results

Medium-sized spiny nerve cell (Type I)

In Golgi preparations the most frequently impregnated neuronal type of the human striatum is a medium-sized cell with spiny dendrites (Koelliker 1896; Ramón y Cajal 1909). A comparable cell type has also been described in the striatum of monkeys (Fox et al. 1971/72a; DiFiglia et al. 1976, 1980; Rafols and Fox 1979), cats (Kemp 1968; Kemp and Powell 1971a), and rats (Mensah and Deadwyler 1974; Somogyi and Smith 1979; Preston et al. 1980; Wilson and Groves 1980). It is the commonest cell and comprises about 95% of the total cell population (Kemp 1968, cat).

Four to 10 dendrites are given off from a spindle-shaped or polygonal cell body. The dendrites radiate in all directions, but in places, especially close to thicker bundles of myelinated fibres, they are more or less strictly oriented in parallel to the fascicles. The dendrites do not differ appreciably in length. By no means can a main cell process be distinguished from a set of smaller dendrites as is typically found in the spiny nerve cells of the human claustrum (Braak and Braak 1982). The dendrites emerge from the cell body by way of a cone-shaped and spine-free stem. Close to the soma, they give rise to numerous secondary branches that follow a relatively straight course. Additional side branches are occasionally given off. The dendrites become progressively more slender as they extend distally (Figs. 1, 2, 12).

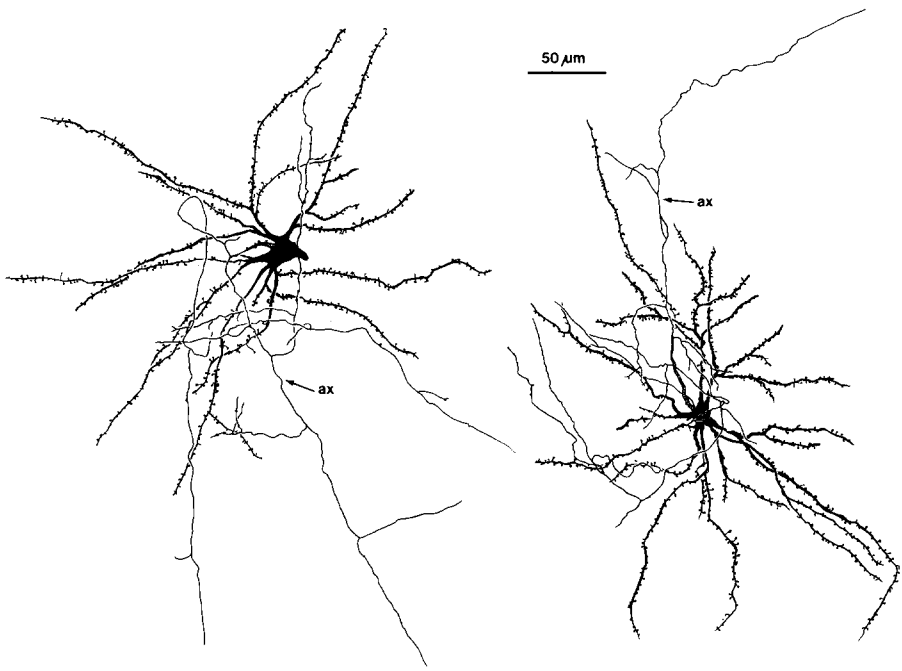

Fig. 1. Medium-sized spiny nerve cells of the striatum (type I). Note the rich axonal collateralization. The axon (*arrow*: *ax*) can be followed beyond the dendritic domain of the parent cell. Camera lucida drawing

Except at their proximal portions, the dendrites are densely covered with robust spines, most of which have bulbous knobs and thread-like stems tilted at various angles to the parent process. The types of spines that have been described to cover dendritic processes of cortical pyramidal cells (Jacobson 1967; Jones and Powell 1969; Peters and Kaiserman-Abramof 1970) can also be encountered along dendrites of the medium-sized spiny neurons in the striatum.

The axon originates at a thick conical elongation of either the cell body or one of the dendritic trunks. Frequently, the proximal axon shows a few stubby appendages (Fig. 1). Beyond its proximal portion, the axon assumes a relatively uniform caliber. At a certain distance from the cell body, the axon bends back abruptly giving off numerous collateral branches at short intervals. This occurs often within the dendritic domain of the parent cell. Most of the collaterals branch profusely to form an extensive plexus within the reaches of the spiny neuron (Fig. 1). The terminal twigs are very thin with irregularly spaced bead-like enlargements. A few of the collaterals leave the dendritic domain of the parent cell and take a straight course. As far as we could follow these processes, they give off no further side branches. Terminal arborizations of the axon or of the longer collaterals could not be found in the vicinity of the cell body.

Transparent Golgi impregnations combined with pigment staining show that the medium-sized spiny neurons contain considerable amounts of pigment (Figs. 2, 12). Most often, dense agglomerations of lipofuscin granules are located at one pole of the cell body whence they may even extend into adjacent portions of a dendritic trunk (Fig. 13, first row). A loose distribution of lipofuscin is contained in the remaining portions of the cell body. The granules are all approximately the same size and shape and are well stained by aldehydefuchsin.

A very sparse amount of basophilic material is more or less evenly distributed throughout the cell body and extends into the dendrites (Fig. 13, first row). The cell type belongs to the class of achromatic neurons. Its large and pallid nucleus is globular or only slightly ovoid in shape. It is centrally located and contains a distinct nucleolus. Extensive infoldings of the nuclear membrane do not occur.

Medium-sized to large nerve cells with somatic spines (Type II)

This cell type is sparsely distributed throughout all parts of the striatum. The cell body is triangular, spindle- or horn-shaped due to the emergence of only a few very thick dendrites that quickly reduce in diameter. The dendrites bifurcate repeatedly becoming thinner at each branch point. The thin terminal dendrites take a curved course intertwining with each other, thus forming only a small dendritic domain. The dendrites display a gnarled varicose outline. They are invested with a moderate number of spines which vary considerably in size and shape (Figs. 3–5). Besides stubby protuberances a fair number of spicular appendages with elongate pedicles are encountered.

The somal surface as well as the proximal portions of the dendrites are also lined with knobbed spines that in general have shorter stalks than those along the distal dendrites (Figs. 3–5). The presence of somatic spines appears to be a hallmark of the type-II neurons, since none of the other varieties of striatal nerve cells displays this feature in the adult.

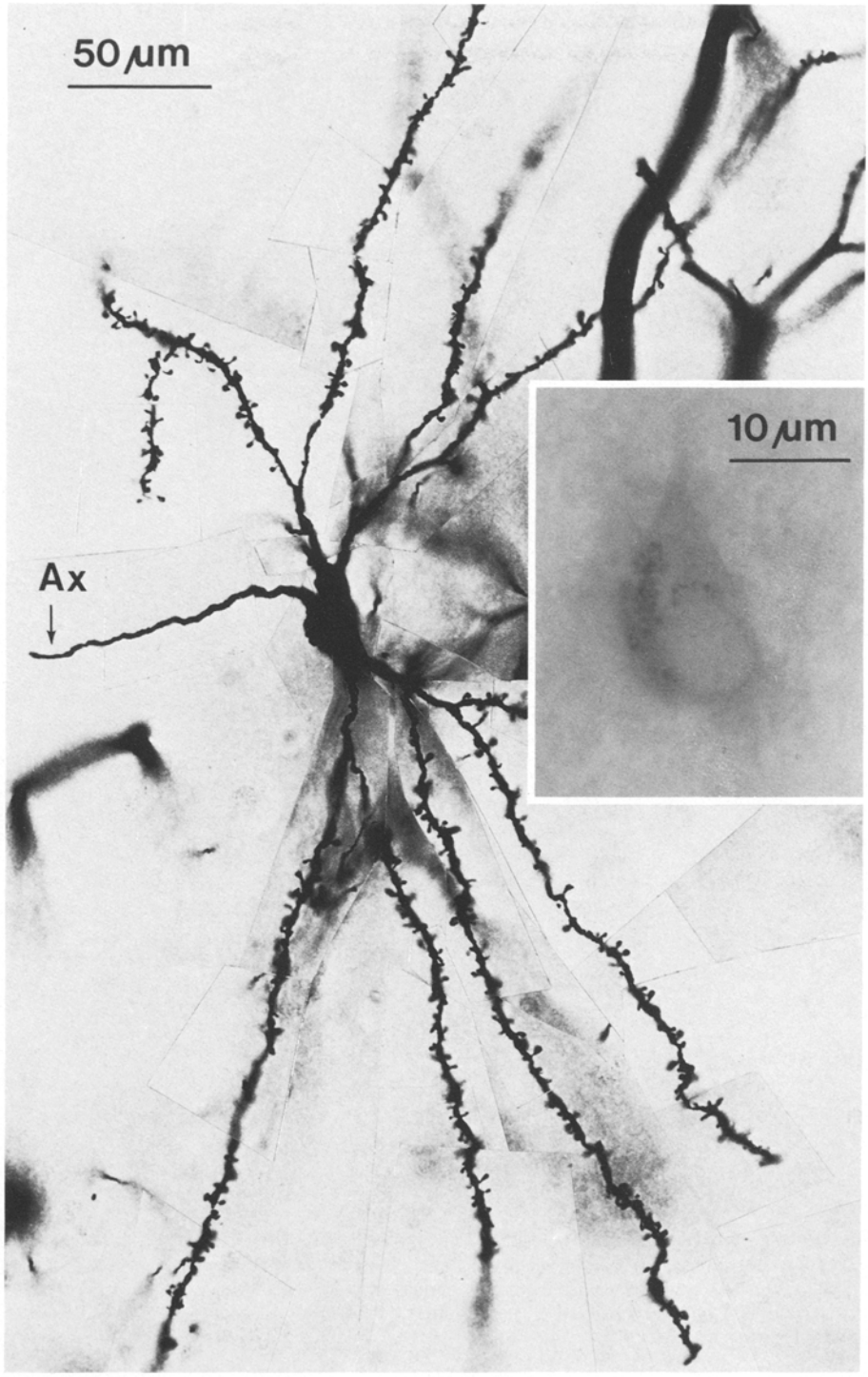

Fig. 2. Medium-sized spiny nerve cell (type I). *Arrow* indicates the axon (*ax*). Golgi impregnation, 100 µm. *Inset*: Same nerve cell as seen in transparent Golgi impregnation counterstained for pigment. The cell contains numerous lipofuscin granules located at one pole of the cell body

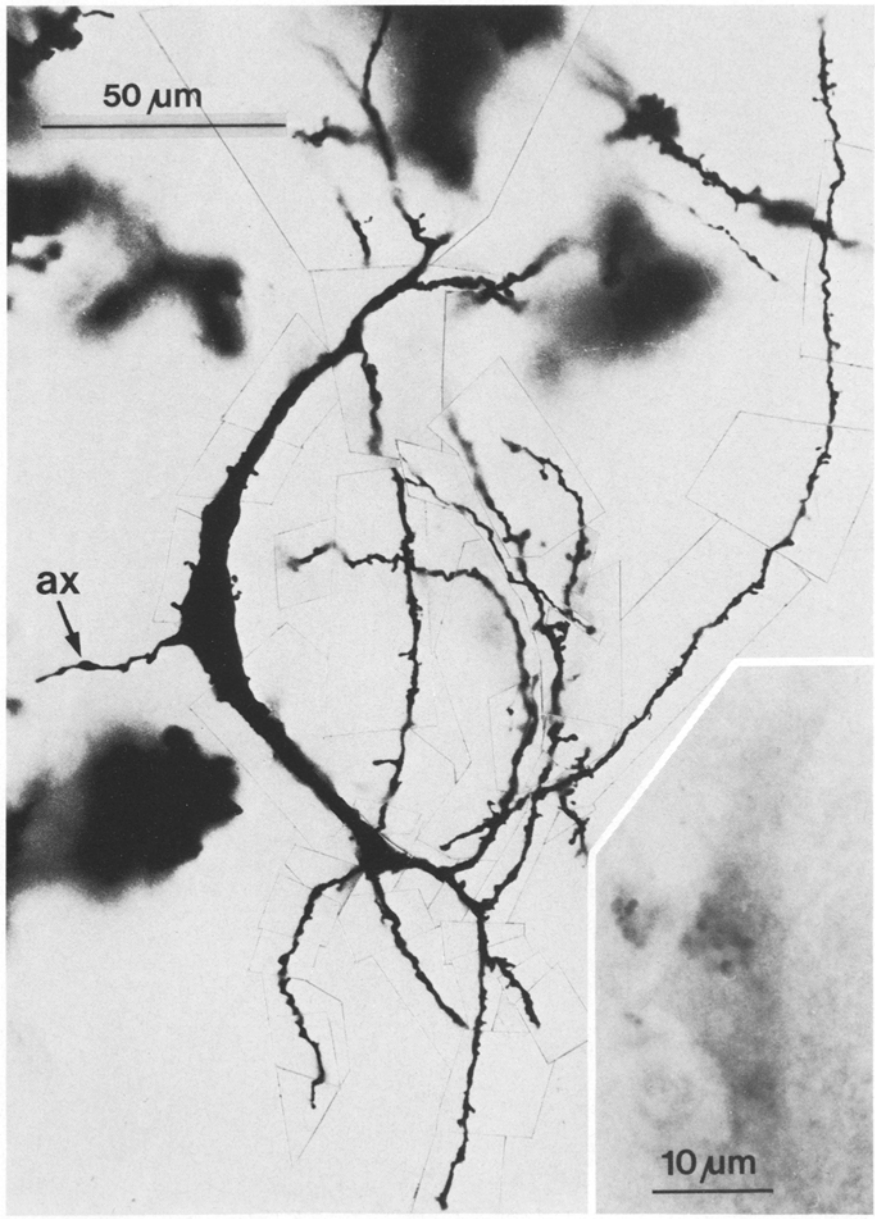

Fig. 3. Medium-sized to large nerve cell with somatic spines (type II). Only a few dendrites which take a curved course are given off from the cell body. Note the sparse distribution of spines along the dendrites and on the soma. An *arrow* points to the axon (*ax*). Golgi impregnation, 100 µm. *Inset*: Same nerve cell as seen in transparent Golgi impregnation counterstained for pigment granules. This cell type is almost devoid of pigment deposits

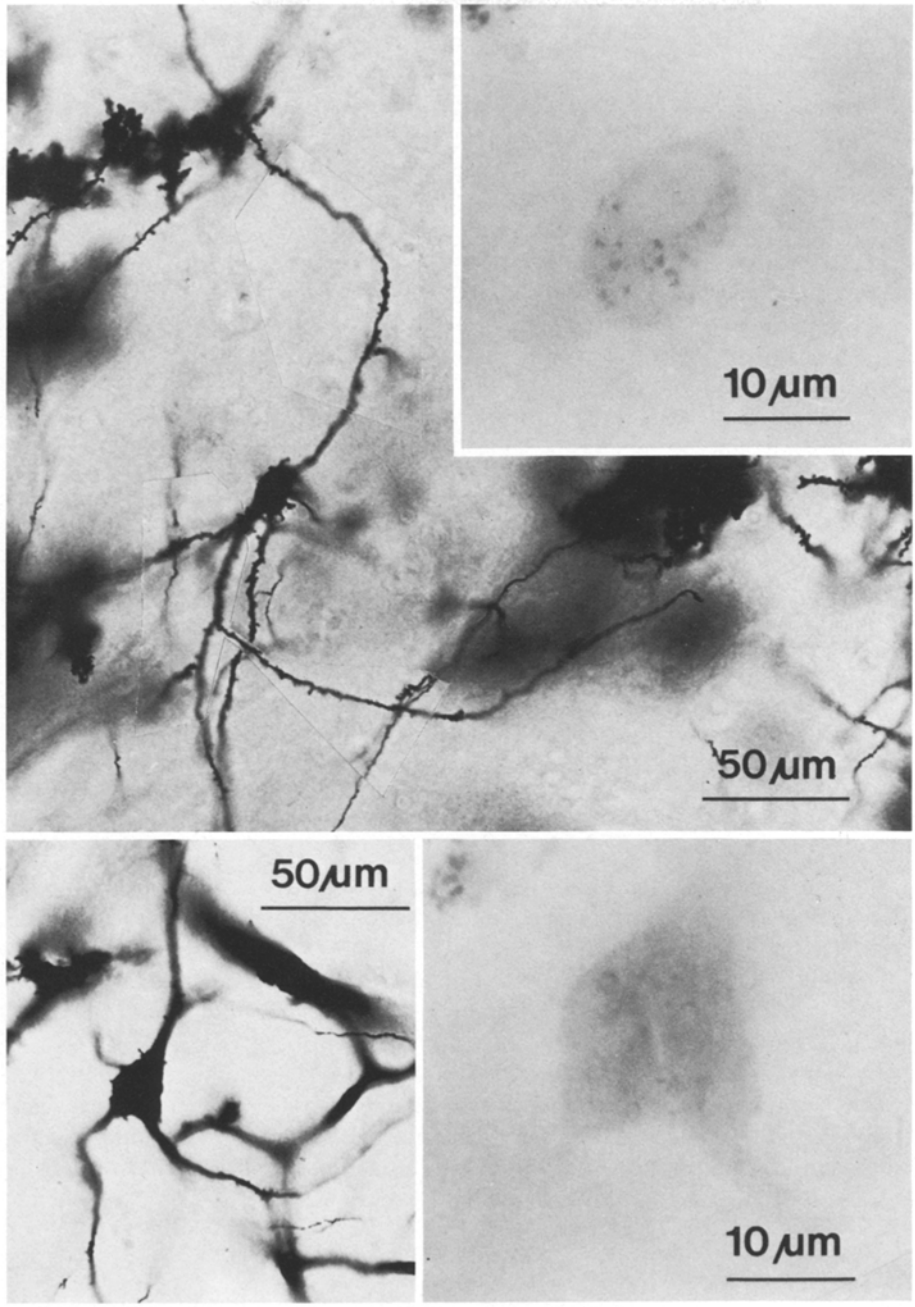

Fig. 4. Two nerve cells with somatic spines (type II). Golgi impregnation, 100 µm. *Insets:* Same nerve cells after de-impregnation and counterstaining. The cells contain only a few pigment granules that exhibit pallid vacuoles surrounded by a very thin rim of stainable material

The axon leaves the soma at a cone-shaped elongation. In the human adult, the impregnation of the axon ceases close to the soma, most probably due to the beginning of the myelin sheath.

In cell-stained material the type-II cells appear as only feebly tinged elements with foamy cytoplasm. Here and there, the sparse basophilic material may be concentrated to some extent. This occurs most often in peripheral portions of the soma. The basophilic substance extends into the thick dendrites and can sometimes even be followed into the secondary branches. Some of the somata of the type-II cells contain a few lipofuscin granules loosely distributed throughout the cell body and the proximal dendrites (Fig. 4). Often, the individual granule is formed of pallid vacuoles surrounded by a thin rim of dense material. Therefore, type-II cells appear very lightly pigmented or devoid of lipofuscin. In fact, some of these cells are completely devoid of pigment.

The ellipsoid nucleus is more or less centrally located and displays several deep infoldings of its nuclear membrane. One conspicuous nucleolus is contained in the clear nucleoplasm (Fig. 13, second row).

Large multipolar nerve cells with extended dendrites (Type III)

Cells of this type display a close resemblance to the neurons forming the globus pallidus. The spindle-shaped or multipolar nerve cells can be found in all portions of the caudate nucleus and the putamen, often close to large fascicles of myelinated fibres. Type-III cells are very obvious due to their large cell bodies from which a few coarse dendrites arise. The stout processes give off a very small number of side branches spreading for long distances in various directions. The dendrites maintain their thickness as they extend distally. Finally, most of them adopt a gently curved course without abrupt changes in direction. Thus a giant dendritic domain with a low density of branches is established.

The surface of the dendrites and the soma is smooth. Only occasionally are isolated spine-like appendages encountered along the distal portions of the dendrites (Figs. 5–7).

Initially, the axon shows the typical conical diminution of its diameter. It takes a straight course. Possibly due to myelination, the impregnation of the axon ceases close to the soma.

In pigment-Nissl preparations the type-III cells appear as large multipolar neurons with well-developed clumps of Nissl substance (Fig. 13, third row). The basophilic material extends far into the dendrites. Fine pigment granules are distributed throughout large portions of the soma. The large globular nucleus is centrally located and contains a conspicuous nucleolus.

Large aspiny nerve cells (Type IV)

Type-IV cells are the most frequently encountered of the large neurons. Dendrites emerge at any point from the more or less rounded soma either directly as thin processes or by way of short stout protrusions from which many fine branches are given off at short intervals (Figs. 8, 9). The dendrites lack a cone-shaped proximal portion but are already thin at their origin. They branch many times close to the

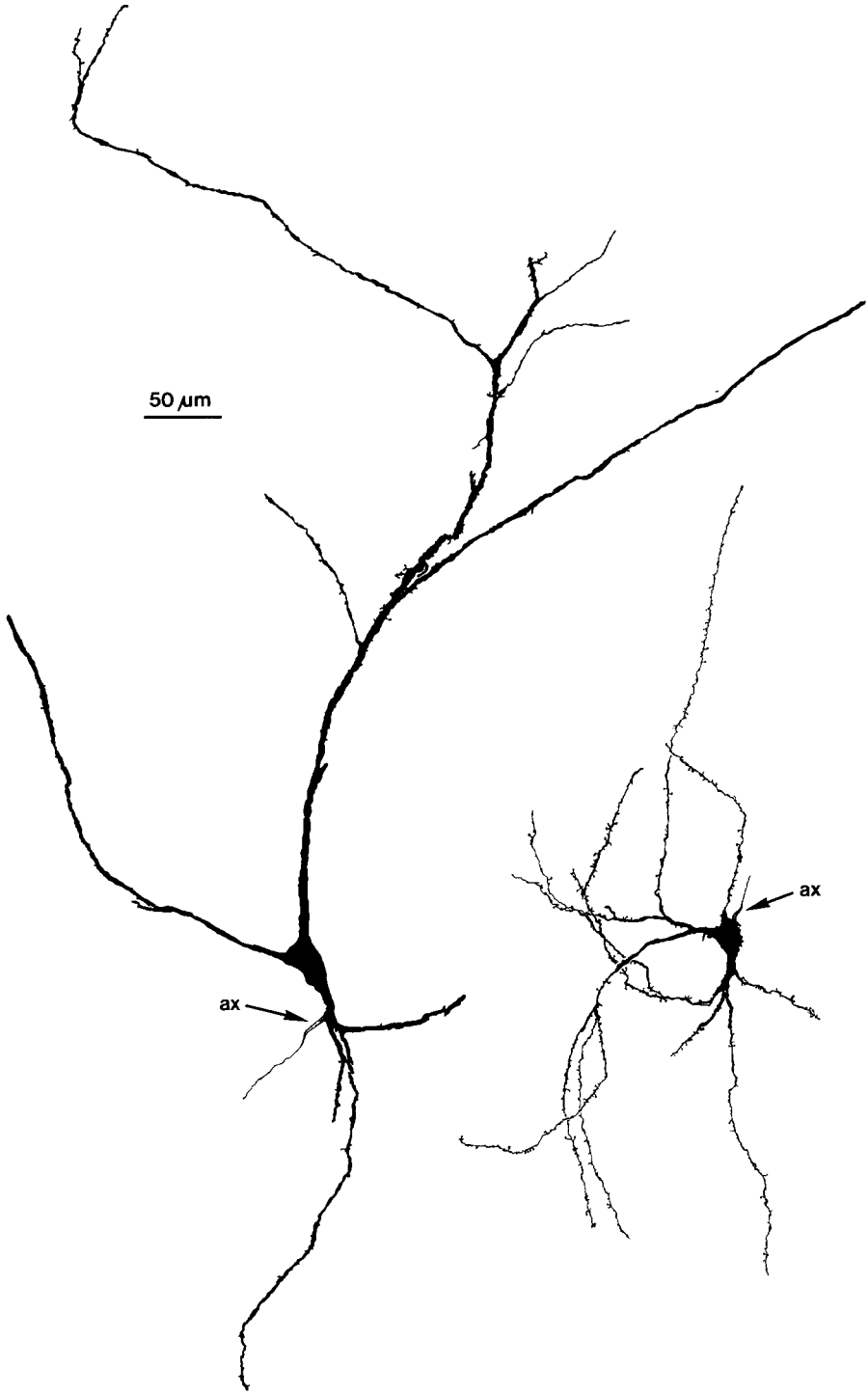

Fig. 5. Camera lucida drawing of a type-II neuron (*right*) and a type-III neuron (*left*). Note the sparsely spined wavy dendrites, the somatic spines of the type-II neuron, and the thick extended dendrites of the type-III neuron that are endowed with only a few spines. *Arrows* indicate the axons (*ax*)

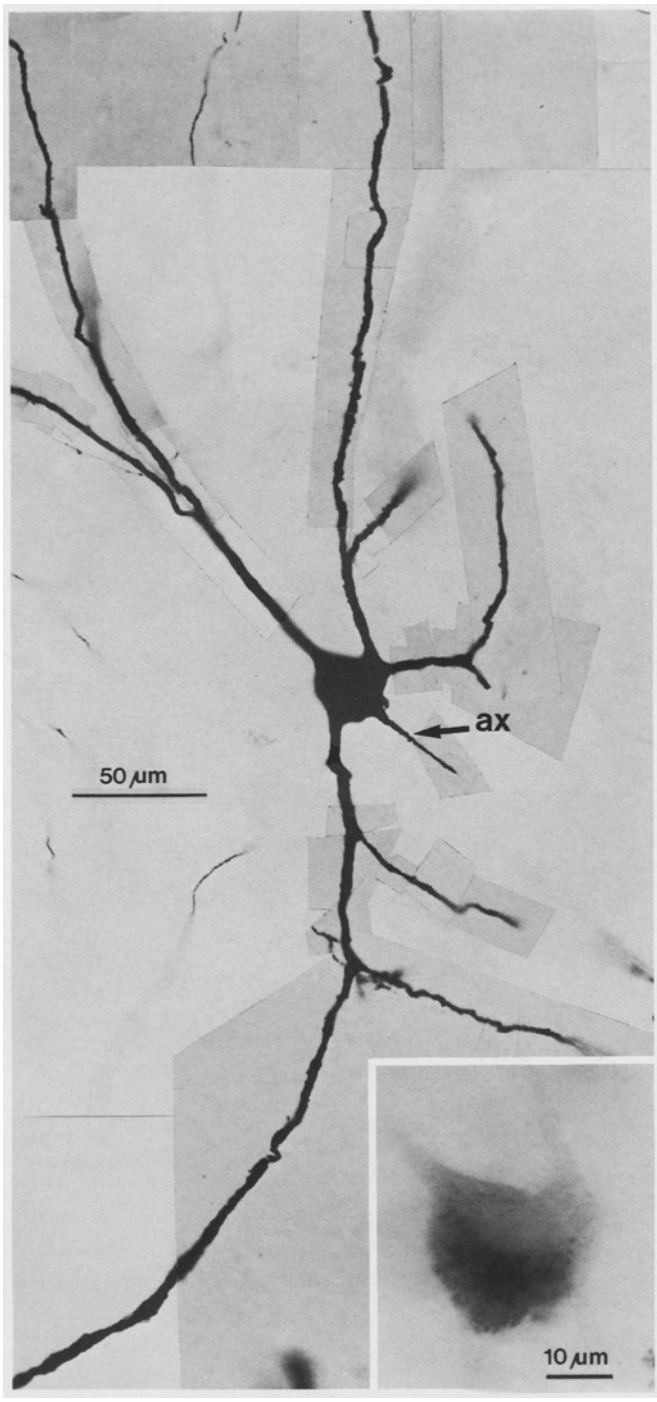

Fig. 6. Large nerve cell (type III). Only a few massive, sparsely spined dendrites arise from the soma, spreading out for very long distances. Golgi impregnation, 100 µm. *Inset*: Same nerve cell as seen in transparent Golgi impregnation counterstained for pigment granules. This cell type contains a finely granulated pigment that is evenly dispersed over a large portion of the cell body

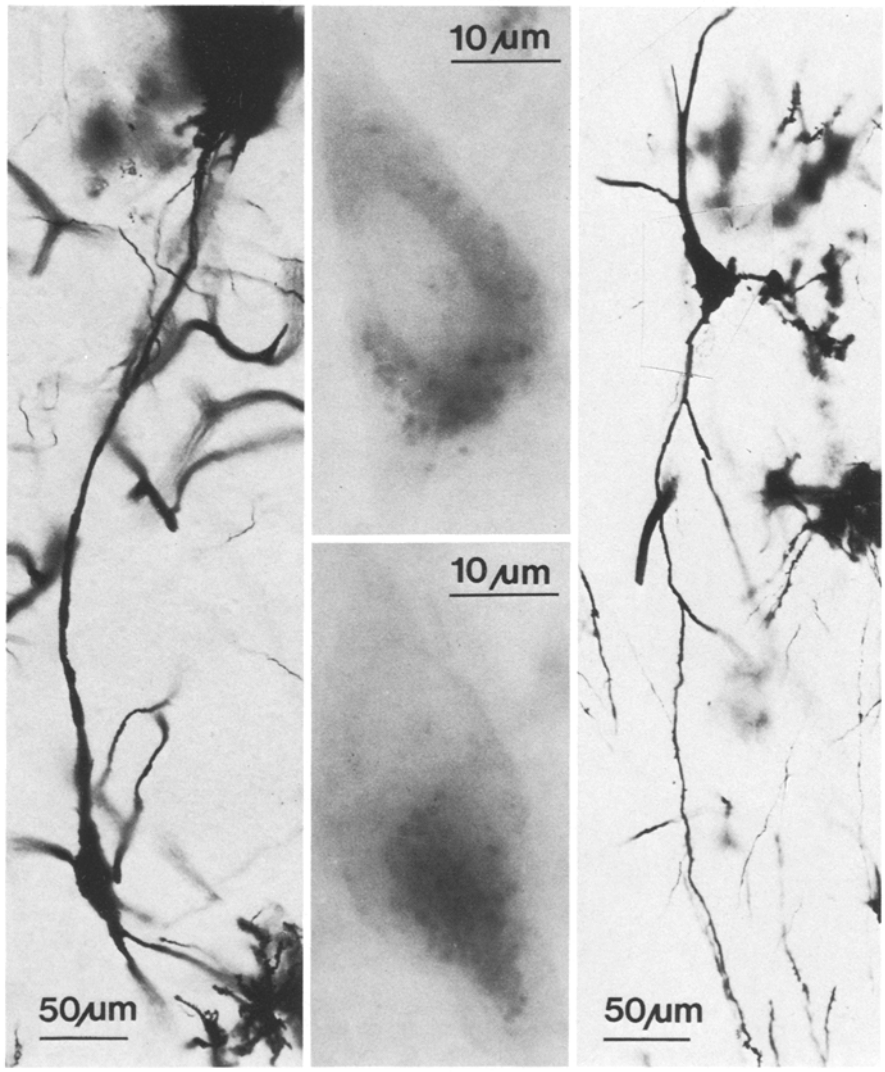

Fig. 7. Two large multipolar nerve cells with extended dendrites (type III). Golgi impregnation, 100 µm. Middle panel: Same nerve cells as seen in transparent Golgi impregnation counterstained for pigment. The pigment is finely granulated and widely dispersed throughout large portions of the cell body

parent soma. The terminal twigs are relatively long as compared to the primary or secondary dendrites. Most often, they bend around the soma interlacing and intertwining to form a dense, globular dendritic domain (Figs. 8, 9). In relation to the size of the cell body, the dendritic domain is surprisingly small. Most of the slender terminal branches have a rather gnarled appearance with many irregularly spaced varicosities and a few isolated peduncular spines.

The axon leaves the soma at a long cone-shaped trunk. The gradual diminution in size of the proximal axon as well as the absence of varicosities along the more distal portions facilitates differentiation of the axon from thinner dendrites.

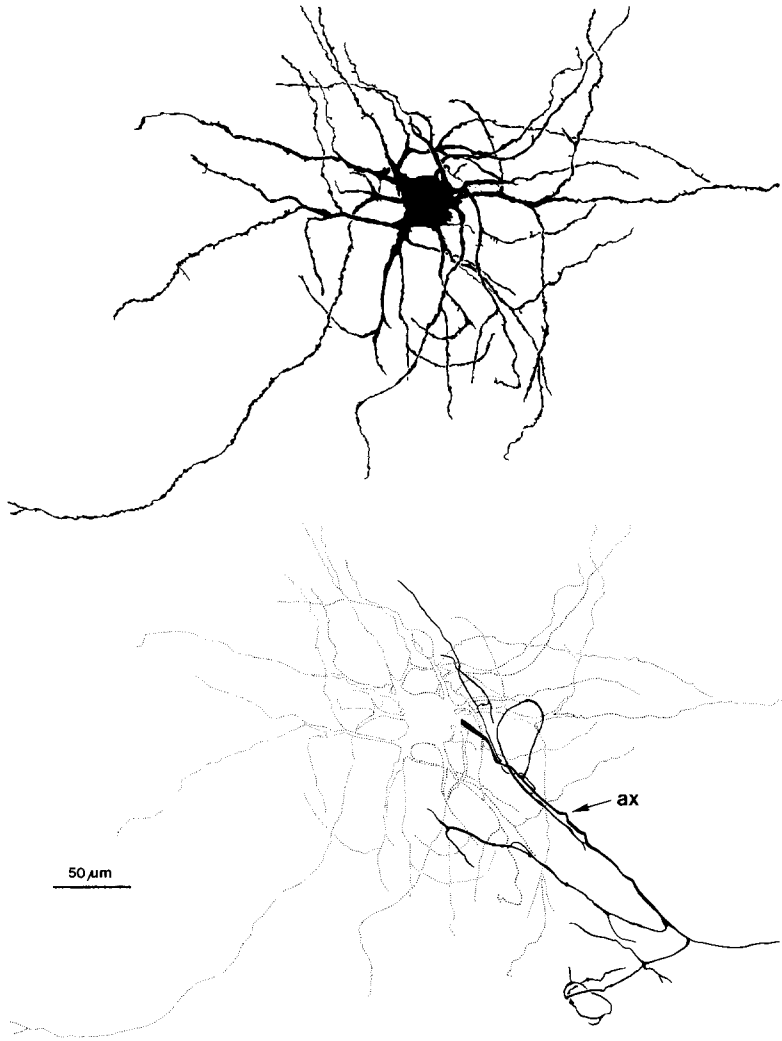

Fig. 8. Camera lucida drawing of a type-IV neuron. Note the dense dendritic domain established by the great number of relatively short dendrites. The axon of the cell is shown in the lower half of the Figure. Numerous collateral branches are given off close to the parent soma

Initially, the axon runs in a straight course giving off some collaterals. Before reaching the limits of the dendritic domain, the axon bifurcates into thin processes that loop around and break up into a large number of delicate branches. At each branch point the axon decreases in diameter. The proximal collaterals show similar characteristics and contribute to the rich axonal arborization, which seemingly does not extend far beyond the confines of the dendritic field (Fig. 8).

Pigment-Nissl preparations display large cells with rounded contours (Fig. 13, fourth row). Basophilic material in large quantities is found only in the peripheral portions of the soma, but does not penetrate into dendritic stems. The central portion of the perikarya is only slightly tinged.

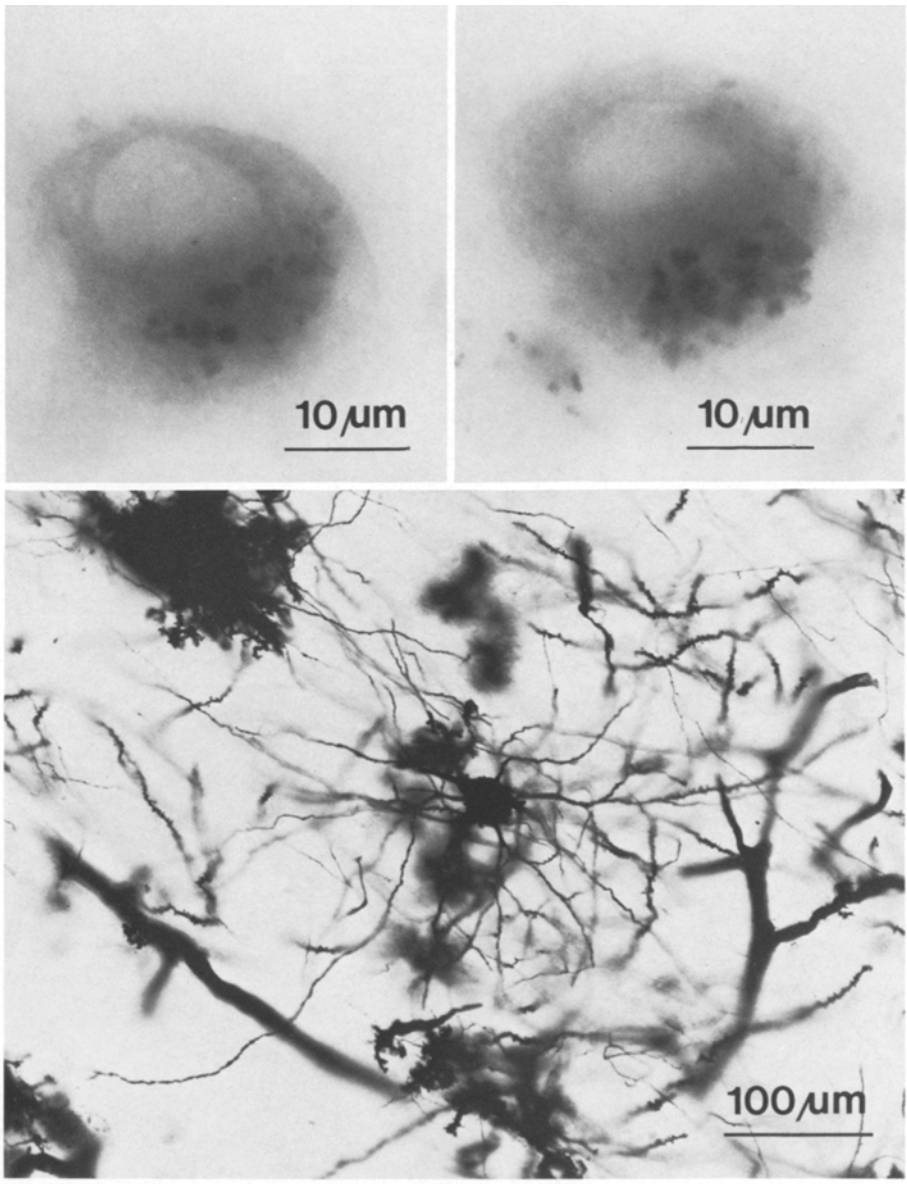

Fig. 9. Large aspiny nerve cell (type IV). Fig. 8 displays the camera lucida drawing of this cell. A great number of relatively thin and short, smoothly surfaced dendrites arise from the soma. Golgi impregnation, 100 µm. *Inset*: Same nerve cell after de-impregnation and counterstaining in two planes of focus. This cell contains a fair number of large pigment granules crowded together to one side of the cytoplasm opposite the eccentrically located nucleus

Pigment granules are likewise preferentially arranged in one segment of the cell body close to the periphery (Fig. 9). Typically, a small number of vacuolated granules coalesce to form larger units displaying bizarre outlines. These units are separated by relatively large distances; thus, type-IV neurons often appear as only modestly pigmented cells.

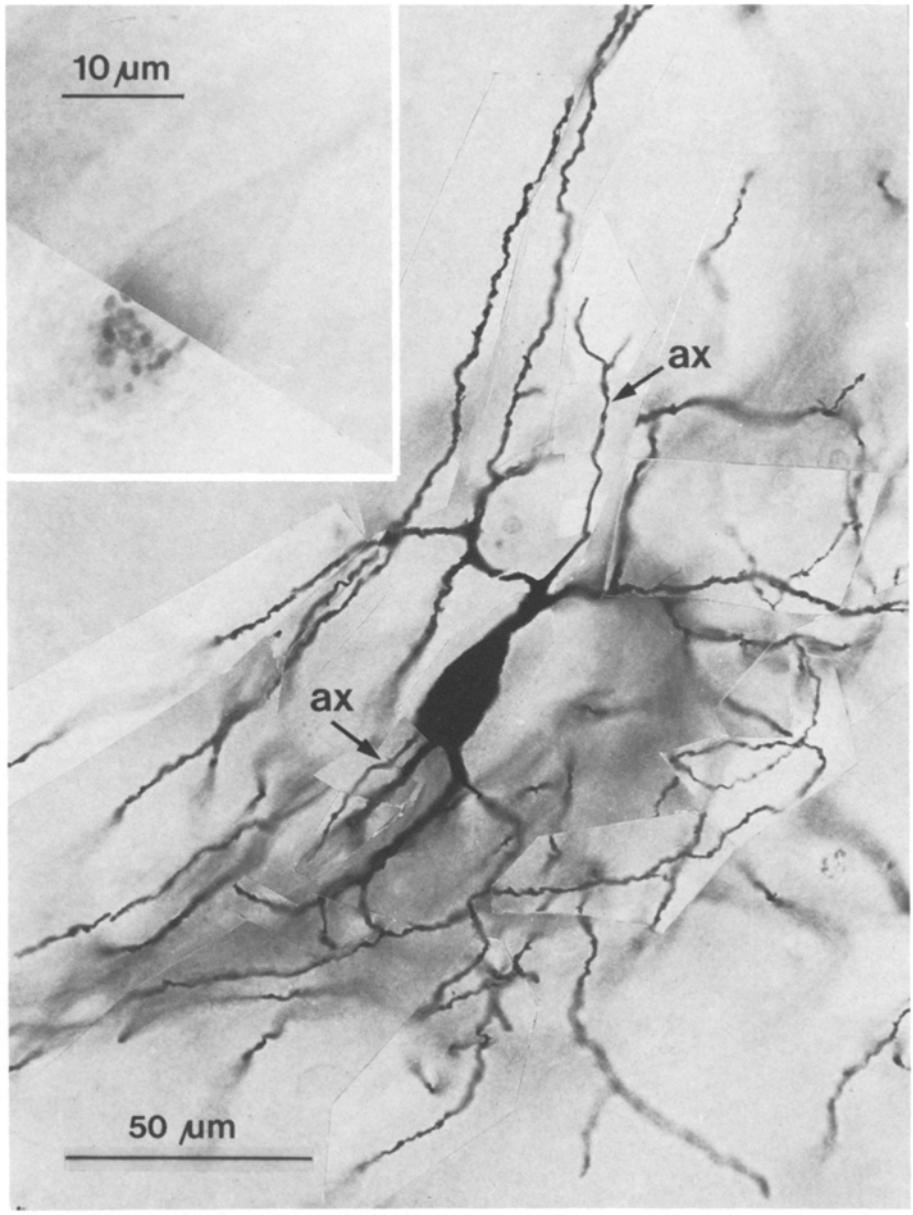

Fig. 10. Small to medium-sized aspiny nerve cell (type V). Numerous thin dendrites arise from the cell body and bifurcate repeatedly. Their distal portions take a tortuous course around the soma. Nerve cells of this type often generate two axons (*arrows: ax*) which mostly run in opposite directions. The axons break up into terminal ramifications close to the parent soma. Golgi impregnation, 100 µm. *Inset*: Same nerve cell as seen in transparent Golgi impregnation counterstained for pigment granules. The cell contains coarse, loosely arranged pigment granules

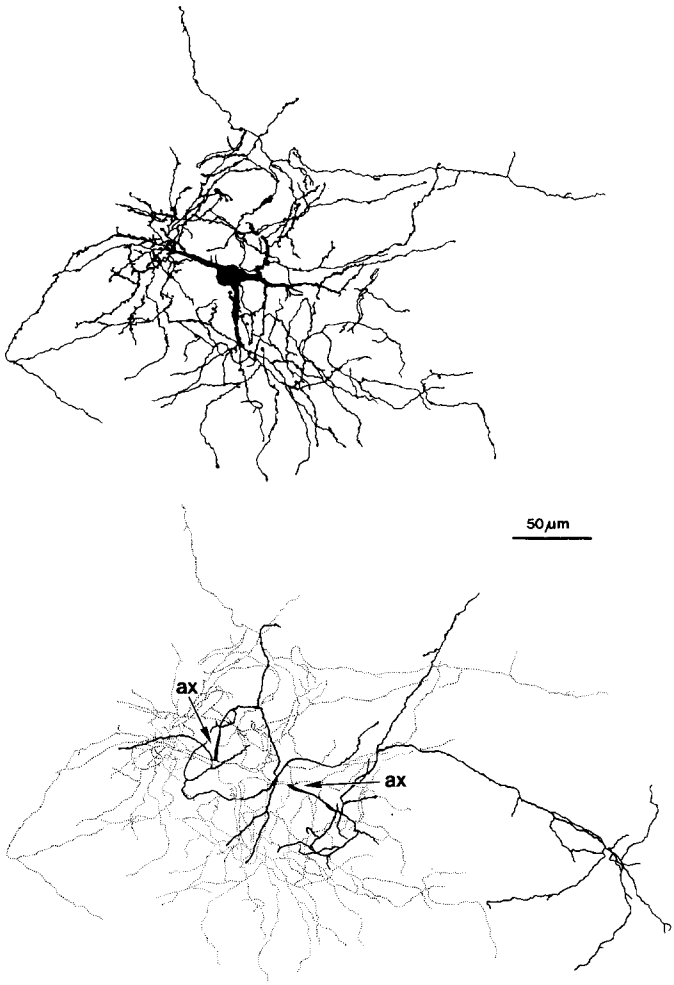

Fig. 11. Camera lucida drawing of a type-V neuron. Note the dense dendritic domain. The terminal dendrites are very delicate processes. This cell gives off two axons that are shown in the lower half of the figure. Both axons break up into terminal ramifications in the vicinity of the parent soma

The nucleus is strikingly small in relation to the large size of the soma. It is generally in an eccentric position opposite the pigment accumulation. Most often, it is ellipsoidal and slightly bent with a smoothly contoured convexity directed towards the soma membrane. The inner portion facing the pallid center of the cell is heavily crenated exhibiting numerous deep infoldings. A very large nucleolus is contained in the clear nucleoplasm (Fig. 13, fourth row).

Small to medium-sized aspiny nerve cells (Type V)

The soma of type-V cells is not generally as large as that of the medium-sized spiny neurons. It shows a rounded contour and gives off only a few relatively thick

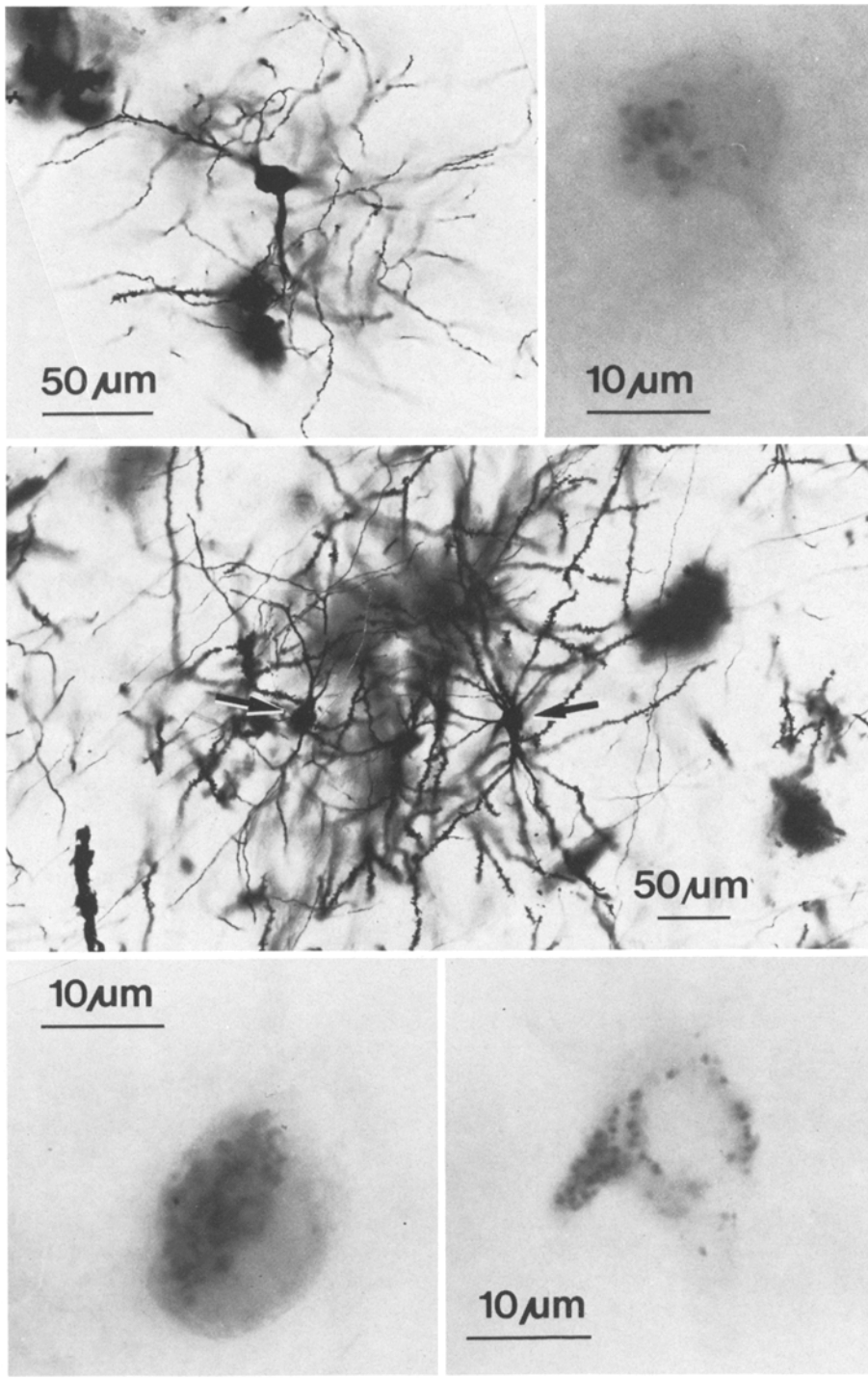

Fig. 12. Two medium-sized aspiny nerve cells (type V). Fig. 11 shows a camera lucida drawing of the cell depicted in the upper row. For direct comparison, the lower half of the Figure displays not only a type-V neuron on the left but also a characteristic type-I nerve cell on the right. Golgi impregnation, 100 µm. *Insets* display both nerve cells after de-impregnation and counterstaining. Type-V cells contain coarse pigment granules, the type-I cell shows finely granulated pigment concentrated at one pole of the cell body

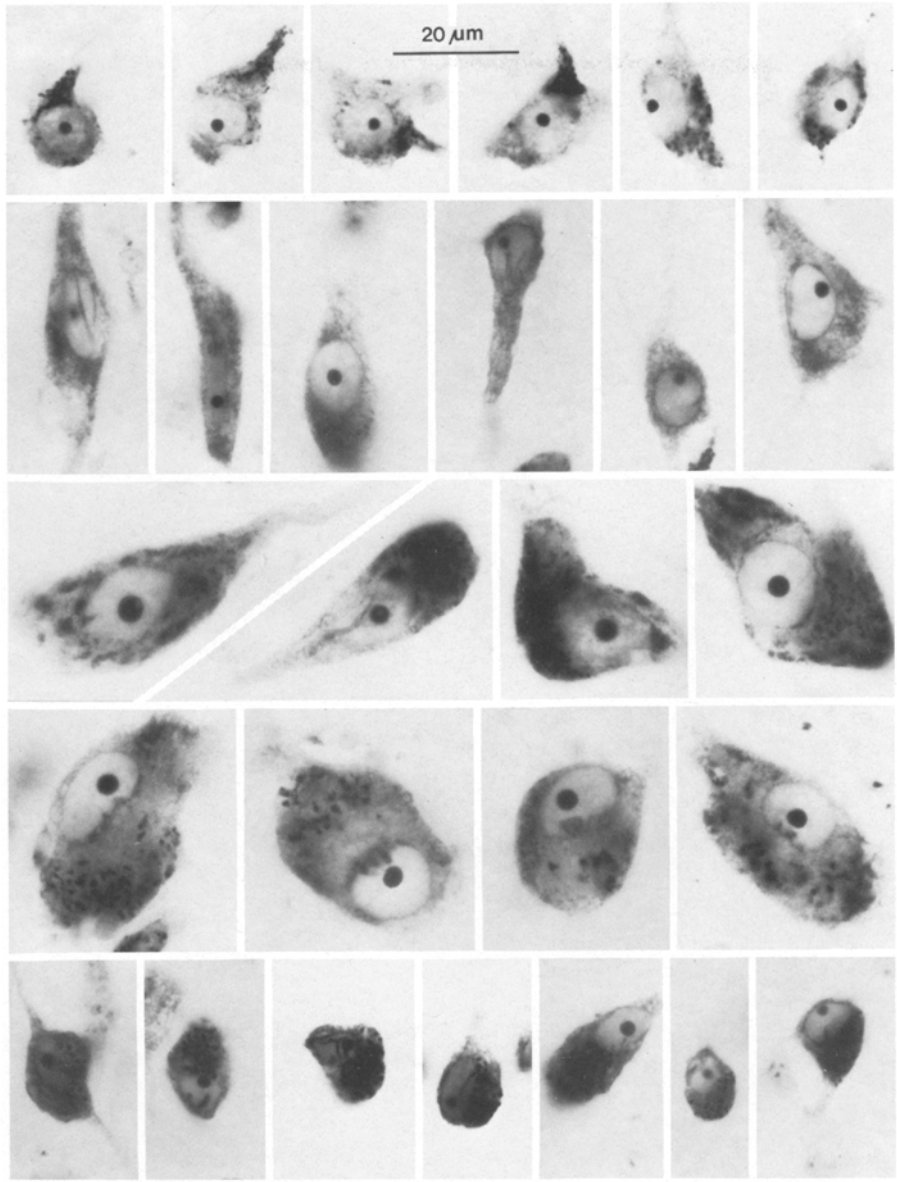

Fig. 13. Nerve cells of the striatum as seen in the combined Nissl-pigment preparation. *First row*: Medium-sized spiny nerve cells (type I) with globular, centrally located nucleus and a dense cluster of fine pigment granules that often extends into the proximal portion of one of the dendrites. *Second row*: Medium-sized to large nerve cells with somatic spines (type II). The cells are devoid of pigment or contain only a few very fine lipofuscin granules. *Third row:* Large, sparsely-spined nerve cells (type III) with centrally located nucleus, well developed clumps of basophilic material within the cytoplasm and finely granulated pigment. *Fourth row*: Large aspiny nerve cells (type IV) with eccentrically located nucleus, deep infoldings of the nuclear membrane directed towards the centre of the cell and large pigment granules. *Fifth row*: Small to medium-sized aspiny nerve cells (type V) with rounded cell body and eccentrically located nucleus. The cell body is rich in basophilic material and contains large intensely stained pigment granules. It should be stressed that cells depicted in Fig. 13 do not represent de-impregnated nerve cells. The classification shown here depends on the size and shape of the soma and characteristic features of the pigmentation

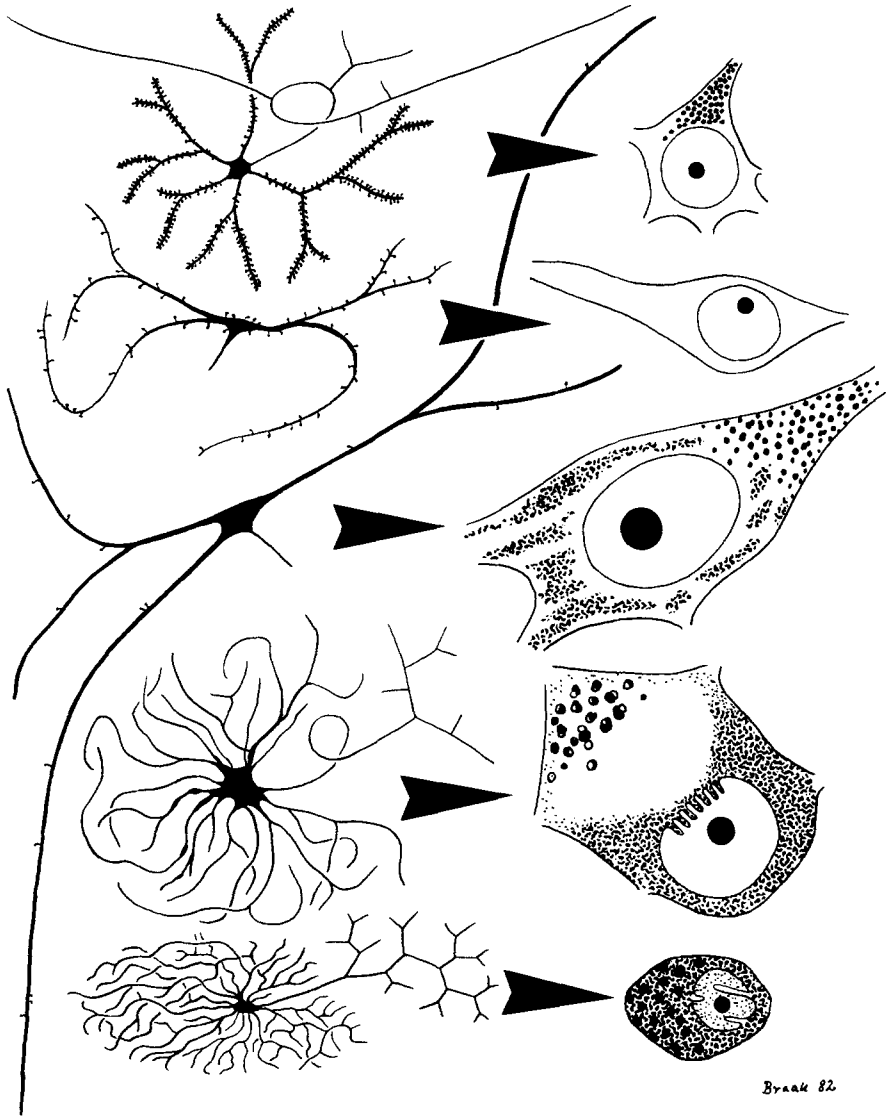

Fig. 14. Summary diagram of the neuronal types in the striatum of man. The cells are easily distinguished in Golgi impregnations by characteristic features of their processes. By means of the transparent Golgi technique it can be shown that each of these cell types can also be recognized in combined pigment-Nissl preparations because of characteristic features of their pigment deposits and other cellular details

dendrites. These bifurcate repeatedly and at short intervals close to the soma (Figs. 10–12). The diameter of the dendrites is considerably reduced at each branching point. The delicate terminal twigs bend back and follow a tortuous course around the nerve cell body. The ellipsoidal dendritic domain is small and mainly formed by the fine terminal branches that intertwine in a bewildering fashion (Figs. 10–12). These branches have a beaded appearance. They do not taper significantly as they extend distally. A few isolated and minute thorns can occasionally be encountered along the dendrites.

The axon takes origin either directly from the soma or from a primary dendrite. Now and then, sharp kinks can be observed along the conical proximal portion. The axon, while still close to its origin, emits a great number of collaterals. All these processes loop around within the confines of the dendritic tree. Only a few terminal branches can be seen to extend outside the dendritic field. Fine axonal twigs often show a varicose outline, a feature they share with the terminal dendrites. Nevertheless, the initial conical segment as well as the more distal thread-like portions with their characteristic loops allow one to delineate the axon from the dendrites (Fig. 11).

Type-V neurons often issue a second axon that generally arises from a conical elevation of the cell body opposite to the origin of the first axon (Fig. 11). The second axon is of similar thickness and shows the same branching pattern as the first one.

In cell-stained preparations, this type of local circuit neuron is obvious by its large content of basophilic material (Fig. 13, fifth row). The soma is ovoid or pear-shaped with rounded contours. The basophilic material does not extend into the proximal dendrites. It is concentrated to some extent in the vicinity of the nuclear membrane. Typically, lipofuscin granules are located in one pole of the cell body. The granules are slightly larger than those found in type-I cells. In places, rod-shaped particles are encountered, which may represent an amalgamation of smaller subunits. The granules are spaced apart from one another. Large clumps of pigment do not occur. The proximal portions of the dendrites are devoid of pigment (Figs. 10, 12).

The nucleus is often in an eccentric position and shows numerous deep infoldings of the nuclear membrane. Intensely stained clumps of basophilic material fill up the indentations. Infoldings are most common on the part of the nucleus which faces the pigment-free portion of the cytoplasm (Fig. 13, fifth row).

Discussion

Type-I neurons in the human striatum correspond most probably to the spiny neuron type I (S–I cells) of DiFiglia et al. (1976, monkey) and type-I neurons of Dimova et al. (1980, rat).

Anatomical and physiological investigations in experimental animals indicate that type-I neurons receive a massive input from the substantia nigra, the raphe nuclei, the locus coeruleus, the intralaminar nuclei of the thalamus, and the telencephalic cortex (Kemp and Powell 1971 b, c; Hattori et al. 1973; Hassler et al. 1975, 1978a, b; Chung et al. 1976, 1977; Usunoff et al. 1976; Kocsis et al. 1977; Pasquier et al. 1977; Grofova 1975; Frotscher et al. 1981; Somogyi et al. 1981). The axon of type-I cells gives rise to a very extensive collateral arborization. This has also been found in many subhuman mammalian brains (Kemp and Powell 1971 a, cat; Fox et al. 1971/1972a, monkey; Mensah and Deadwyler 1974, rat; DiFiglia et al. 1976, monkey; Preston et al. 1980, rat; Wilson and Groves 1980, rat; Somogyi et al. 1981, rat). Apparently the axon finally leaves the striatum and terminates in the globus pallidus and the substantia nigra, and in this way completes the circuit between the striatum and the substantia nigra (Grofova 1975; Bunney and Aghajanian 1976; Bak et al. 1978; Rafols and Fox 1979; Ribak et al. 1979; Somogyi and Smith 1979; Preston et al. 1980; Bolam et al. 1981).

Transparent Golgi impregnations counterstained with aldehydefuchsin permit a direct evaluation of the pigmentation of given nerve cells. The spine-laden type-I cells have a common pattern of pigmentation in all parts of the striatum, a fact that restrains us from proposing a further subdivision of this cell-type as was done by Danner and Pfister (1981a, rat).

Type-I cells have many features in common with cortical pyramidal cells. Both types of telencephalic projection cell are predominantly impregnated by the Golgi technique, show dendrites that are more or less heavily invested with spines, a pallid and centrally located nucleus, and basophilic material that extends from the soma into the proximal dendrites. The rare occurrence of axosomatic contacts (Hassler 1978; Frotscher et al. 1981) is a further feature common to both types.

Type-II neurons with somatic spines correspond most probably to the spiny neuron type II (S-II cells) of DiFiglia et al. (1976, monkey) and type-II-neurons of Dimova et al. (1980, rat). DiFiglia and coauthors could follow the axon of cells with somal spines far beyond the reach of the dendritic domain.

The occurrence of spines along the surface of the soma and the proximal dendrites is an enigmatic feature that is rarely encountered in telencephalic nerve cells of the human adult. Betz cells in the primitively organized cingulate gigantoganglionic field, for instance, show a fair number of such projections (Braak and Braak 1976). In the rat, spines are only occasionally encountered along the soma surface of isocortical pyramidal cells (Peters and Kaiserman-Abramof 1970). More regularly, somatic spines occur on the dwarf cells and pyramidal cells of the allocortical olfactory tubercle (Anderson and Westrum 1972, rat). Somatic appendages can frequently be seen during early ontogenesis but normally disappear as the maturing process advances (Meller et al. 1969). Outside the telencephalon, somatic spines have been noted in mature nerve cells of several nuclei as, for instance, the subthalamic nucleus (Rafols and Fox 1976, monkey), the lateral nucleus of the periaqueductal gray (Laemle 1979, man), the magnocellular portion of the red nucleus (Nakamura 1975, cat; King et al. 1971, monkey; Reid et al. 1975a, b, rat; Sadun and Pappas 1978, cat), and the raphe nuclei (Pfister and Danner 1980, rat; Diaz-Cintra et al. 1981, rat).

Type-III cells maintain a close relationship with the large nerve cells of the globus pallidus. One might even be inclined to consider them displaced constituents of the pallidum – a view that certainly has to await further confirmation.

Cells resembling type-III neurons of the human striatum were not mentioned by DiFiglia et al. (1976). Bolam et al. (1981) have found large multipolar nerve cells in the caudato-putamen of the rat that could correspond to type-III cells. The axons of these cells leave the striatum.

Type-IV and type-V cells can probably be considered local circuit neurons. Both types have several traits in common with cortical stellate cells. In Golgi preparations they display smoothly contoured dendrites and a profuse arborization of their axons close to the parent soma. The dendrites emerge abruptly and do not taper as they extend distally. In Nissl preparations, the nucleus is generally found in an eccentric position, and it shows numerous deep infoldings. A considerable

amount of basophilic material is contained in the cytoplasm but does not extend into the dendrites. The morphological resemblance to cortical stellate cells is concordant with the tentative classification of type-IV and type-V cells as local circuit neurons.

Of the neuronal types of the striatum, type-IV cells are the most difficult to visualize with the aid of the Golgi technique. Very often only the cell body and some coarser dendrites are impregnated whereas the finer arborization of the cell processes remains incomplete. Fox et al. (1971/72b) as well as DiFiglia et al. (1976) emphasize that they never could trace an axon of this cell type, despite the fact that they had well-fixed material of experimental animals. Our material displays a very rich local collateralization of the axon (Fig. 8); but the possible existence of longer branches cannot be excluded.

Type-V cells are the most common local circuit neurons in the human striatum. Fox et al. (1971/72b) did not mention these cells. DiFiglia et al. (1976) describe two varieties of small aspiny neurons: one endowed with varicose dendrites (type AS I), the other showing processes with an irregular surface but without significant varicosities (type AS III). In the human striatum we have not found an aspiny cell type with pronounced varicosities on the dendrites. The small aspiny neuron of our classification probably correponds, therefore, to type AS III.

Some of the type-V cells generate more than one axon (Fig. 11). Multiple-axoned cells occur only rarely in the mammalian central nervous system. Golgi cells of the cerebellar cortex commonly generate many axons (Palay and Chan-Palay 1974, rat). In the telencephalon, it is mainly the transitory Cajal-Retzius neuron of the molecular layer that occasionally has more than one axon (Ramón y Cajal 1891; Retzius 1893; Bradford et al. 1977), and recently Meyer (1982) described local circuit neurons in the visual cortex of the cat provided with two axon-like processes. Preston et al. (1980, rat) noted a second axon to originate from a spine-laden type-I cell in the striatum. In the light of this report we carefully re-examined our material but found no indication for the emergence of more than one axon from type-I cells.

The majority of type-V cells have a smaller cell body than the predominant type-I neurons. A few, however, are larger. A reliable basis for a further subdivision of type-V cells is not given by these size differences since all intermediate forms can also be encountered. All cells of this type are particularly richly endowed with basophilic material and also contain numerous intensely stained lipofuscin granules, which are characteristic features allowing one unequivocally to distinguish type-V local circuit neurons from type-I-projection cells in pigment-Nissl preparations.

Dwarf cells with a somal size of 6–10 μm have often been noted to occur in the striatum (Ramón y Cajal 1909, neuroglioform cells, man; Fox et al. 1974, neuroglioform cells, monkey; DiFiglia et al. 1976, aspiny type-III cells, monkey; Danner and Pfister 1981b, spiny dwarf cells and neuroglioform neurons, rat). Indications for the existence of minute nerve cells could be found neither in our Golgi material, nor in the pigment-Nissl preparations.

We cannot explain why striatal cell types are so differently pigmented. It is possible that transmitter substances influence the formation of intraneuronal

pigment deposits. More knowledge about the transmitters utilized by the various cell types would be helpful to interpret the characteristic differences in pigmentation. Whatever the basis for these differences in pigmentation, each of the types which can be distinguished with the aid of the Golgi technique can also be recognized in pigment-Nissl preparations (Fig. 14) thereby enabling one to evaluate their relative numbers. The Golgi technique stains only a small and not necessarily representative percentage of the neurons present. Conclusions concerning the arrangement and packing density of neuronal populations can therefore not be drawn from Golgi studies. Such quantitative investigations are nevertheless of particular significance if one attempts to explain the normal functions of the striatum on the basis of its anatomy and disturbances of these functions on the basis of pathologically altered centers of the extrapyramidal system.

Acknowledgement. This study was sponsored by grants from the Deutsche Forschungsgemeinschaft.

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Accepted June 28, 1982