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# MORPHOLOGICAL TRANSFORMATION OF SENSORY GANGLION NEURONS AND SATELLITE CELLS

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*The development of sensory ganglion neurons and satellite cells examined by scanning electron microscopy after removal of the connective tissue is reviewed. Sensory neurons are bipolar at early stages of development and later became pseudounipolar. This maturation event starts earlier but proceeds more slowly in chick than in rat embryos. These may due to the difference in the extent and intimacy of satellite cell investments between these two animal species. The neuronal perikaryal projections are observed by scanning electron microscopy after removal of the connective tissue and satellite cells. The morphometric analysis reveals that perikaryal projections are more numerous on the surface of mature pseudounipolar neurons than on that of premature bipolar neurons; they increase in number as the neuronal cell bodies grow larger. This may support the hypothesis that perikaryal projections are structural devices for increasing the neuron-satellite interface and for improving the efficiency of metabolic exchange between these two cell types.The important role of satellite cells in neuronal maturation is discussed.*
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## INTRODUCTION

Sensory ganglion neurons undergo a unique transformation from spindle-shaped bipolar to pseudounipolar cells during development (1-5). Satellite cells are present from the beginning of this pseudounipolarization, but intricate networks of branching satellite cell processes only develop after about day 17 in rat embryos (4). The important role of satellite cells in the pseudounipolarization was reported *in vitro* (2) and *in vivo* (4). Perikaryal projections on the surface of sensory ganglion neurons, which were first thought to be a technical artifact or an instrument for the attachment between neurons and satellite cells, considerably enlarge the perikaryal surface (6). By expanding the area available for exchange of metabolites they may be important in neuronal metabolism in adult animals (6-8). We also supported the above hypothesis by showing the neuronal shape- and size-dependent increase in perikaryal projections during development (5).

In this review we show the morphological change of sensory ganglion neurons, perikaryal projections and satellite cells

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to evaluate the functional significance of neuron-satellite cell interactions.

## PSEUDOUNIPOLARIZATION OF SENSORY NEURONS

Pseudounipolarization has been examined in histological sections using classical silver impregnation methods (1,9-11), by transmission electron microscopy (12,13), and more recently using immunohistochemistry for cytoskeletal markers (14,15). However, the precise time course of pseudounipolarization cannot be accurately determined, because the neurons are visualized in only two dimensions and only a few can be seen in their entirety with the above methods. Furthermore, there is little detailed information about the development of dorsal root ganglion (DRG) neurons in birds, although these have been widely used as the source material for tissue culture studies (14).

Scanning electron microscopy (SEM) has overcome some of these limitations of observing neurons. Using this technique, the three-dimensional appearance of the neuronal cell bodies and processes in embryonic rat and chick DRG was described (3-5,16,17).

In the early stages, most DRG neurons are spindle-shaped bipolar; a few have an eccentrically bulging cytoplasm. The angle formed by the extensions of the central and peripheral processes of these neurons is greater than 90 degrees and the central process is thinner than the peripheral one (Fig. 1a,b). The two processes approach each other as the cell body bulge more in a direction opposite to the initial segments of the processes. The extensions of these processes form an angle less than 90 degrees, and thus the processes and cell body exhibit a bell-shaped conformation (Fig. 1c-f). At the same developmental stages, there are some more advanced ganglion neurons whose cell bodies elongate between the initial segments of two processes to form a primitive stem process (Fig. 1f-h). Initially, the stem process is larger in diameter than the sum of the central and peripheral processes, shorter in length than the diameter of the cell body (Fig.1g) and gradually becomes thinner as it elongates (Fig. 1h). On the postnatal days, the stem process is so long that the bifurcation of the central and peripheral processes is hardly visible in SEM.

No sign of close apposition of the central process to the peripheral one is noted in any of the neurons examined and the primitive stem processes are always thicker than the sum of the diameters of the two individual processes. From these findings, one may exclude the possibility that both processes contact and fuse with each other to yield a common stem process. A further elongation of the primitive stem process without fusion of the central and peripheral processes appears to result in the formation of a long-stem pseudounipolar neuron (3,18-21).

## COMPARISON OF PSEUDOUNIPOLARIZATION IN RAT AND CHICK

The development of each DRG is much different at early stages. Especially, as shown in Figure 2, the appearance differs considerably between the cervical and the thoracic ganglia. For this reason, we always used DRG of Th.2-7.

The examination of dissociated ganglion neurons gathered on the Millipore filter facilitates the observation of the morphological characteristics of neurons with SEM. The proportions of different types of chick and rat neurons observed at different developmental stages are presented in Table 1, 2. Percentages of unipolar neurons at successive stage of development in chick and rat DRG are shown in Figure 3. From this figure, the formula to compare the early development of chick and that of rat is estimated as follows: (chick embryonal days)/2 + 10 days = rat embryonal days. Although it is not sure that this formula is applied widely, it is useful to at least compare the development of the spinal cord or the DRG in these two animal species.

Several marked differences are noted between the dissociated chick and rat ganglion neurons during development. First, pseudounipolarization begins to take place during E8 to E10 in the chick and around E14 in the rat (Fig. 3). Second, the percentage of pseudounipolar neurons increase abruptly in the prenatal rat after day E16, whereas in the chick, it increases relatively gradually after day E10 (Fig. 3). Third, the percentage of bell-shaped bipolar neurons is higher in the rat during E14 to E17 than that in the chick throughout the embryonic periods (Tables 1, 2). Last, very few immature neurons (3%) are found in the rat ganglia, one day after birth, whereas in 2-day-old chicks many immature neurons (13% not unipolar) are still present (Fig.4). It is likely that in the chick, the estimated 13% immature neurons at post hatching day 2 continue developing into mature forms, because such bipolar neurons comprise only about 2% of the total in adult chick sensory ganglia (22,23).

## ROLE OF SATELLITE CELLS IN PSEUDOUNIPOLARIZATION

The findings described above suggest that DRG neurons remain in a more immature condition for longer during prenatal development in chicks than in rats. A possible explanation for this difference may be that the extent and intimacy of satellite cell investment is more developed in the rat than in the chick (24,25). In line with this speculation, cultured chick spinal ganglion neurons maintain bipolar form for periods of up to 1 month if grow in the absence of satellite cells or Schwann cells (Fig. 5). However, when purified Schwann cells were added, the morphology of the neurons changed from the bipolar to the pseudounipolar form (2). Moreover, the time required for this change to occur is related to the number of Schwann cells added; the more Schwann cells are added, the

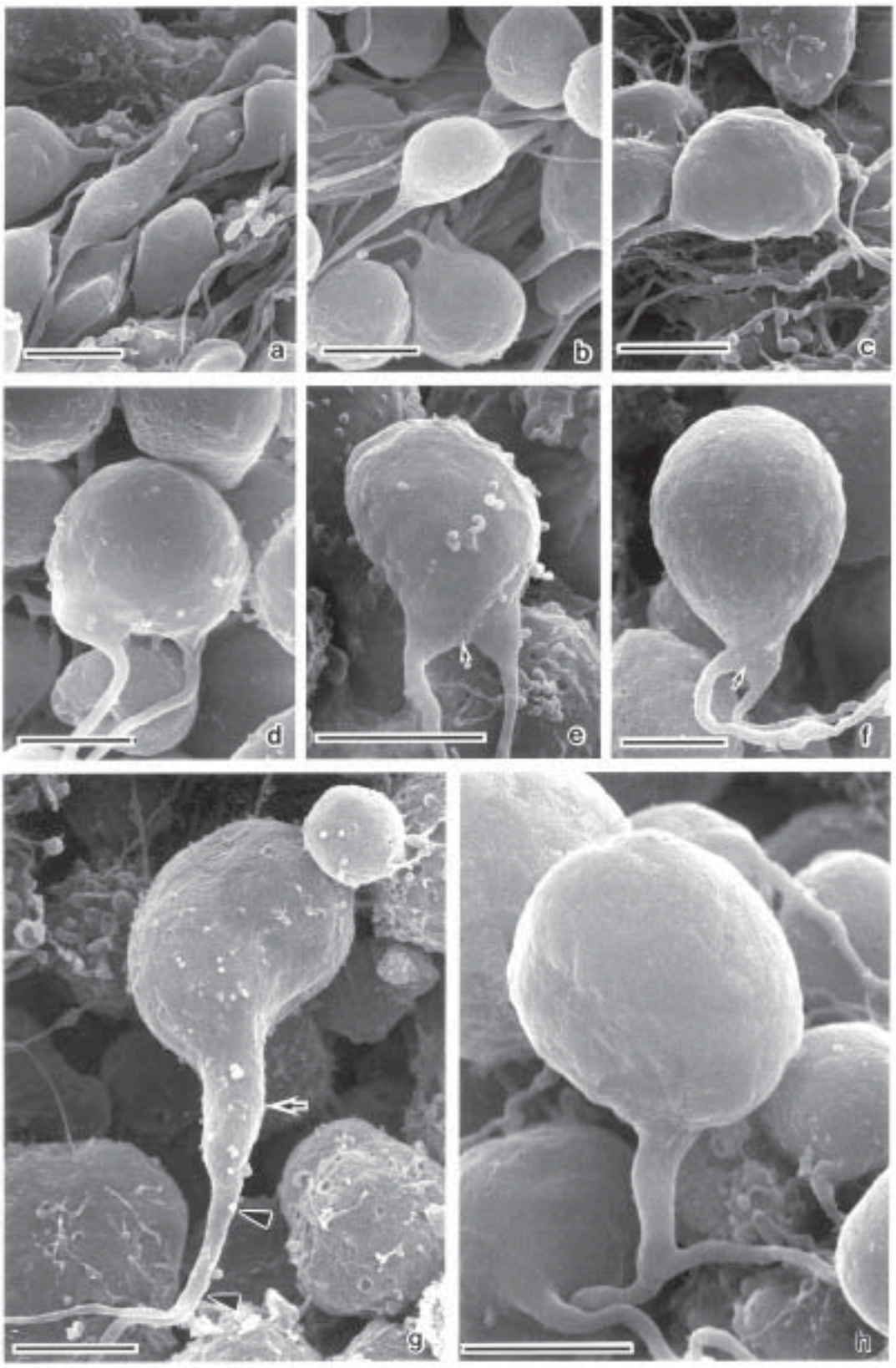


***Figure. 1****. Scanning electron micrographs of sensory neuron types at successive stages of development in the rat dorsal root ganglion. Spindle-shaped bipolar neuron on embryonic day 14 (**a**), on day 16 (**b**). Bell-shaped intermediate neuroblasts on day 14 (**c**), on day 16 (**d,f**), on day 17 (**e**). Short-stem unipolar neuron on embryonic day 18 (**g**), on day 16 (**h**). Note that the connecting piece (arrow) elongates and a primitive stem process is formed (arrowhead). Bars, 5 μm. From Ref 3, with permission of Springer Verlag.*

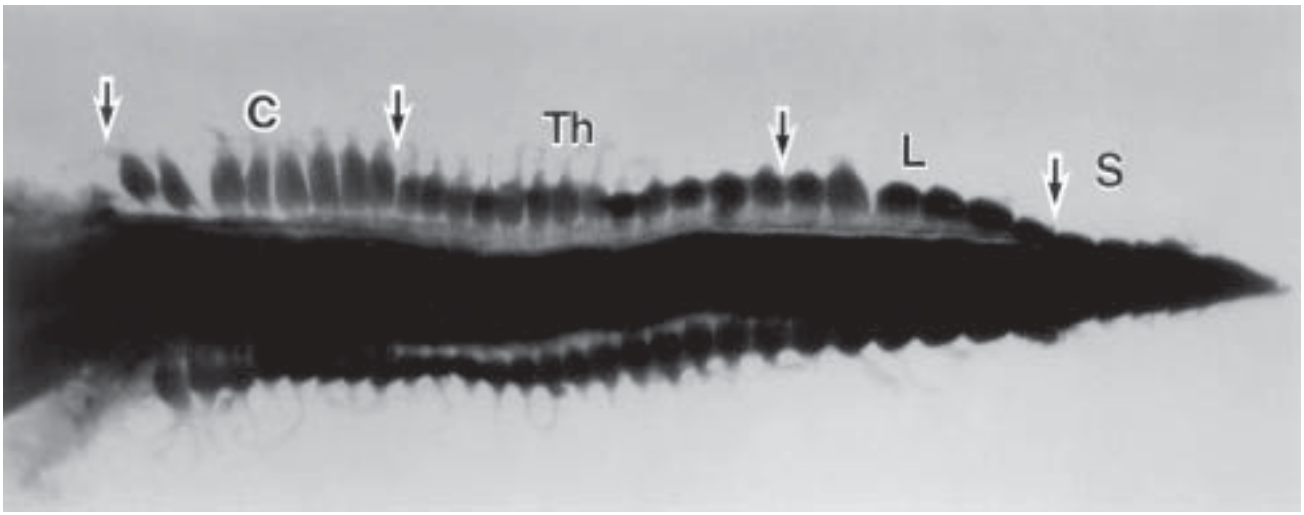


***Figure 2***. *An embryonic rat spinal cord and dorsal root ganglia (DRG) stained with methylene blue. Note that the cervical DRG are much bigger than the thoracic DRG .*

***Table 1.*** *Percentage of different neuron types at successive stages in chick dorsal root ganglion.*

| | 6 | 8 | 10 | 14 | 18 | P2 |
|---|---|---|---|---|---|---|
| **Multipolar** | 3 | 5 | | 1 | | |
| **Spindle shaped bipolar** | 31 | 12 | 5 | 2 | 1 | 1 |
| **Eccentric bipolar** | 66 | 69 | 73 | 27 | 10 | 6 |
| **Bell-shaped bipolar** | | 14 | 12 | 13 | 11 | 6 |
| **Short stem unipolar** | | | 5 | 4 | 6 | 5 |
| **Long stem unipolar** | | | 5 | 53 | 72 | 82 |
| **Unipolar** | 0 | 0 | 10 | 57 | 78 | 87 |

***Table 2.*** *Percentage of different neuron types at succesive stages in rat dorsal root ganglion.*

| | 14 | 15 | 16 | 17 | 18 | 19 | P1 |
|---|---|---|---|---|---|---|---|
| **Multipolar** | 2 | | 1 | | | | |
| **Spindle shaped bipolar** | 4 | 3 | 4 | | 1 | | |
| **Eccentric bipolar** | 56 | 30 | 18 | 13 | 2 | 1 | 1 |
| **Bell-shaped bipolar** | 31 | 46 | 47 | 24 | 8 | 5 | 2 |
| **Short stem unipolar** | 4 | 6 | 9 | 8 | 7 | 12 | 5 |
| **Long stem unipolar** | 3 | 15 | 21 | 55 | 82 | 82 | 92 |
| **Unipolar** | 7 | 21 | 30 | 63 | 89 | 94 | 97 |

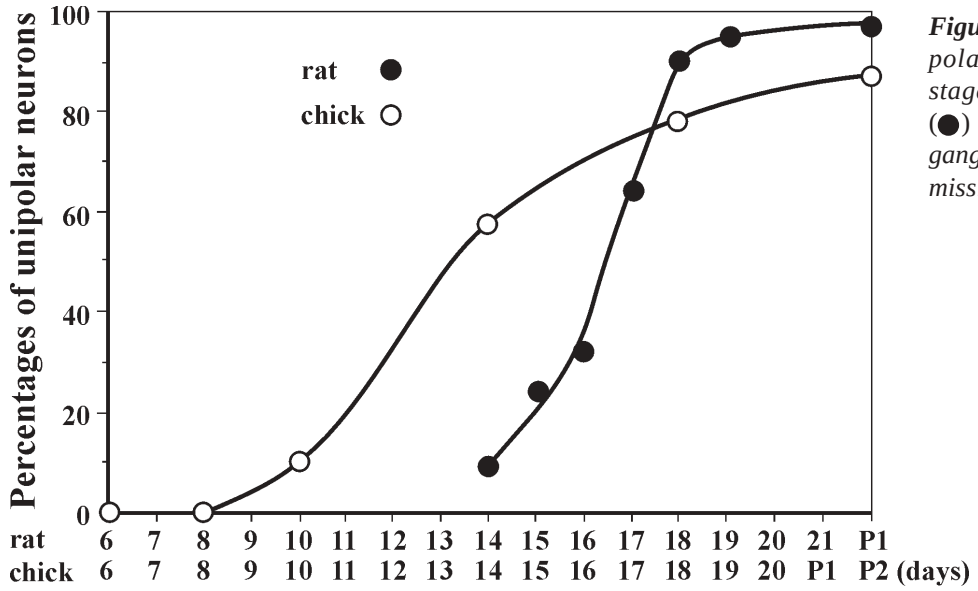


***Figure 3***. *Percentages of unipolar neurons at successive stages of development in rat (●) and chick (○) dorsal root ganglion. From Ref 4, with permission of Springer Verlag.*

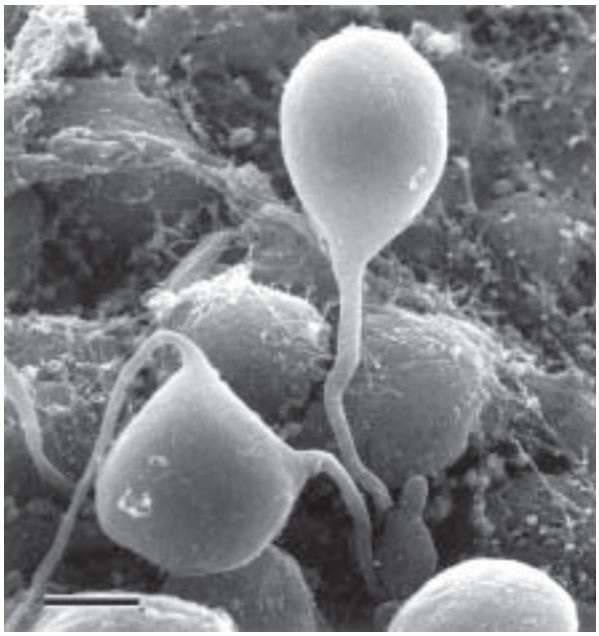

***Figure 4***. *Long-stem unipolar neuron and bell-shaped bipolar neuron in chick dorsal root ganglion on postnatal day 1. Bar, 5 μm.*

sooner pseudounipolarization occurs (2). The addition of supernatant from Schwann cell or satellite cell culture could not induce this transformation. This suggests that neuron-satellite cell contact is important for pseudounipolarization (2).

Figure 6 shows a possible sequence in the maturation of satellite cells of the rat DRG. On day 14, a few stellate-shaped cells can be found among neurons (Fig.6a,d). Later, cells with a few thin processes embrace the neuronal cell body (Fig. 6b,e). At a more advanced stage, they have a number of ramifying and interconnected processes which form a delicate network surrounding the nerve cell body (Fig. 6c,f). Although the reasons why the satellite cells invest the ganglion neurons are not fully understood, some growth factors like basic fibroblast growth factor produced in the neurons (Fig. 7) (26) may stimulate the proliferation and investment of the satellite cells.

## FUNCTIONAL SIGNIFICANCE OF PSEUDOUNIPOLARIZATION

Not all sensory neurons are pseudounipolar. The vestibular and spiral ganglion neurons with pericellular myelin sheaths remain bipolar even in the adult life (Fig.8) . The reason why these sensory ganglia of the eight cranial nerve keep the bipolar form is not understood. Do the pericellular myelin sheaths or surrounding bone prevent the pseudounipolarization? Or is it inhibited genetically? Although the molecular basis for the mechanism to switch on or off pseudounipolarization remains to be determined, Schwann (satellite) cells are likely to play a key role in the transforming event (2,4,15,24). What are the advantages of pseudounipolarization for the neuronal function? While bipolar neurons are slender, their cell bodies are not so big obstructions on the course of nerve fibers. However, as the nerve cell bodies become enlarged, neuronal processes become tortuous (Fig. 9a). In contrast, in the case with pseudounipolar neurons, central and proximal processes

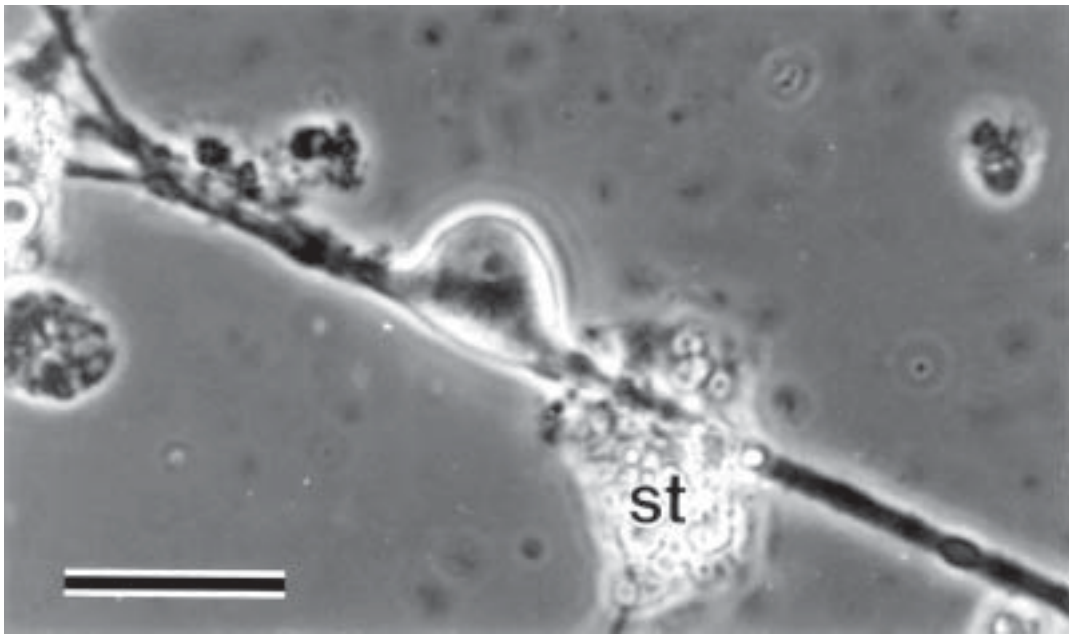


***Figure 5***. *A cultured bipolar neuron and a satellite cell (st) from dorsal root ganglion. Bar, 10 μm.*

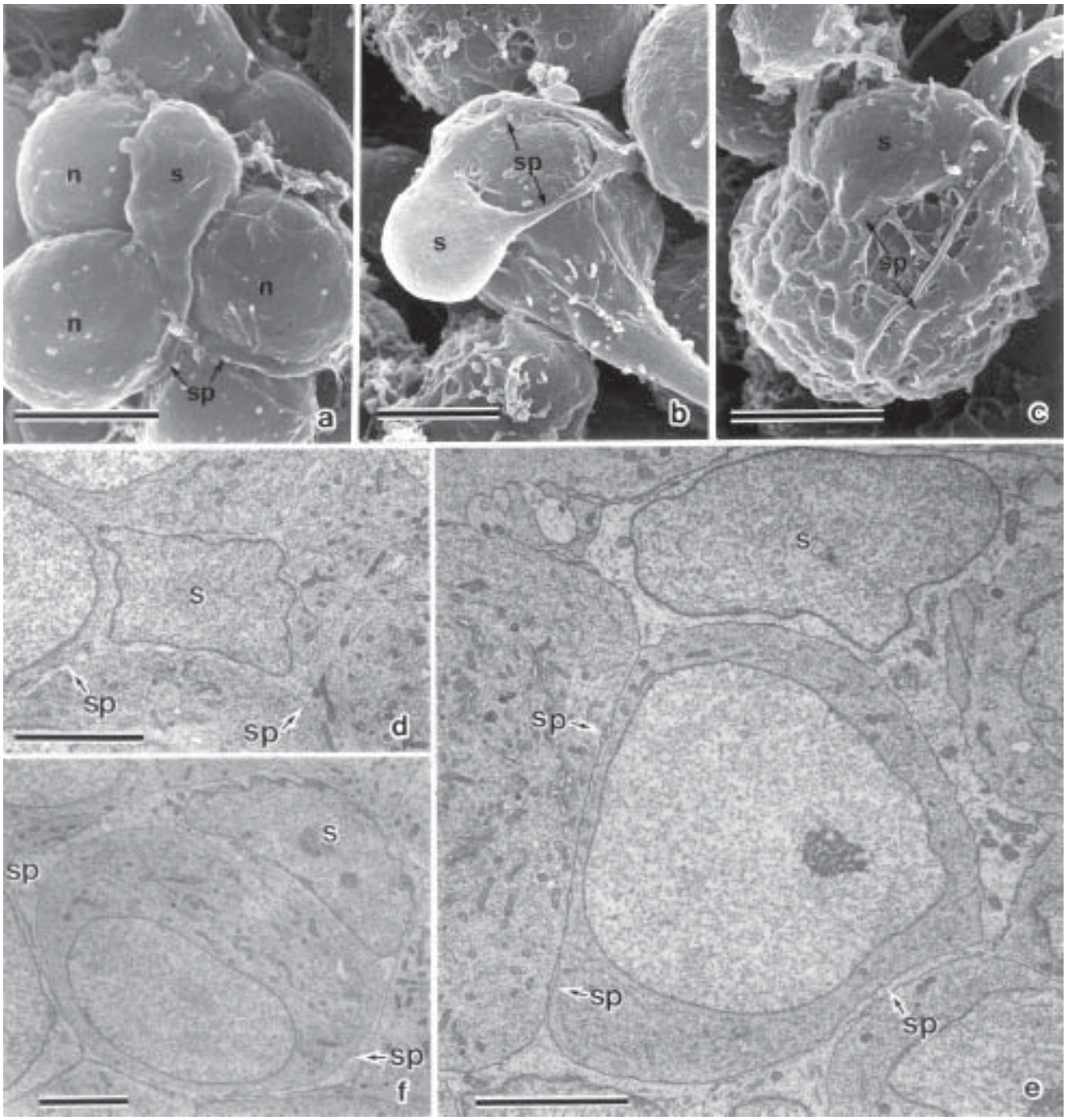


***Figure 6***. *The maturation process of the satellite cell in the rat dorsal root ganglion is illustrated. Processes (sp) of satellite cells (s) are seen between some neurons (n)* ***(a,d)****. Satellite cell (s) with processes (sp) embraces a neuron (n)* ***(b,e)****. Satellite cells (s) display a number of ramifying and interconnected processes (sp)* ***(c,f)****. Bars, 5 μm. From Ref 3, with permission of Springer Verlag.*

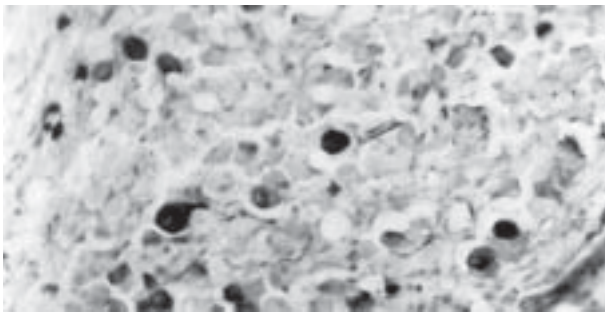

***Figure 7**. Light micrograph showing basic fibroblast growth factor-containing dorsal root ganglion neurons of an E13 chick embryo.*

run straightly in the center of the ganglia (Fig. 9b). Furthermore, to avoid the decline of the conduction velocity in the perikaryon, bipolar neurons should be surrounded by myelin sheaths. The perikaryal myelin sheath around the ganglion neurons of eighth cranial nerve, unlike the axonal myelin sheath, is loose. It would forgive the exchange of substances between the nerve cell body and connective tissue space, but it would act as an incomplete ionic insulator. In contrast, cell bodies of pseudounipolar neurons of DRG are surrounded by the satellite cell sheath and their processes for conduction have complete myelin sheath. In this manner, pseudounipolarization saves the space in the ganglia, the neuronal processes and the time for transduction.

## NERVE FIBER THICKNESS

One process of bipolar neuron of the adult spiral ganglia, which is directed toward the periphery (peripheral process), is thicker than the one directed towards the brain stem (central process) (Fig. 8). Bipolar neurons of the immature sensory ganglia also have a thicker peripheral process and a thinner central process (Fig. 10). But after pseudounipolarization, the size of both processes are almost the same (Fig. 1h). Also in the adult cat and rat, no consistent differences were reported in the diameter spectra of myelinated fibers proximal and distal to the ganglia after careful measurements of osmicated nerve roots and trunks (27,28) except for uncommon unequal branching processes (29,30).

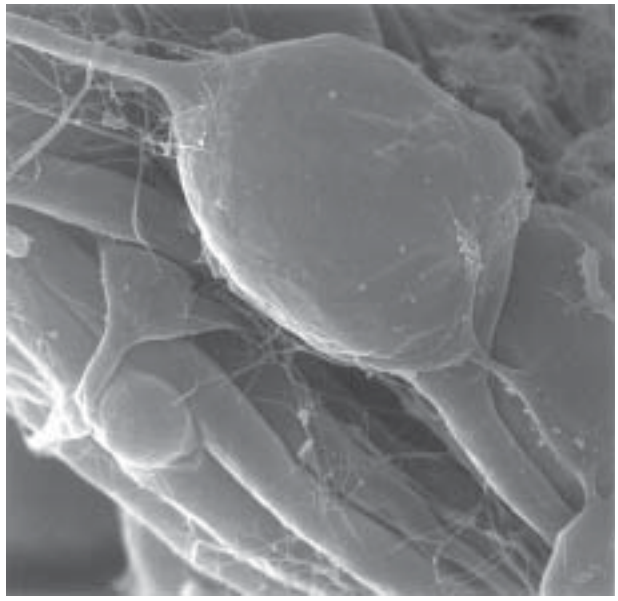

***Figure 8**. A bipolar myelinated neuron of the spiral ganglion of the adult guinea pig.*

## INITIAL GLOMERULUS OF CAJAL

Another interesting structure is the initial glomerulus of Cajal (31). The complexity of the initial glomeruli varies consider-

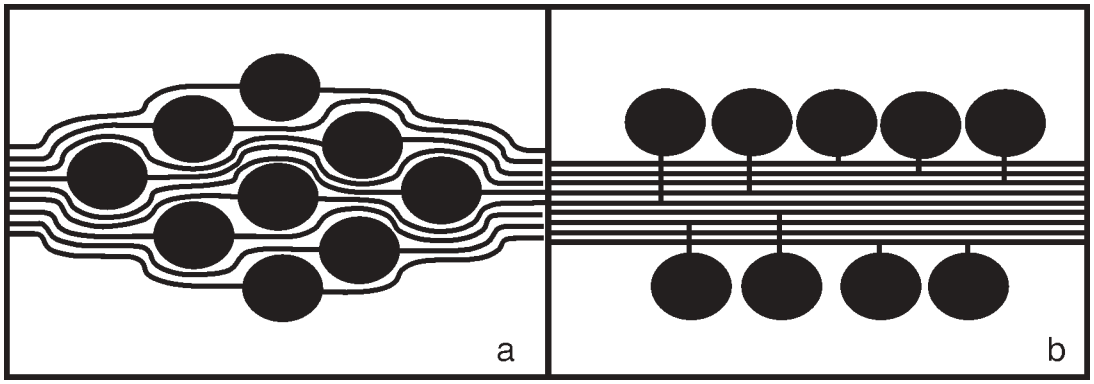


***Figure 9**. Schematic representation of ganglia with bipolar neurons (**a**) and pseudounipolar neurons (**b**).*

ably; large neurons tend to give rise to more prominent glomeruli than do smaller neurons (Fig. 11). Initial glomeruli are more prominent in the higher vertebrate than lower one. The advantage of the initial glomeruli for the conduction or cell metabolism is not clear.

## PERIKARYAL PROJECTIONS OF DEVELOPING SENSORY NEURONS

The neuron-satellite cell boundary is very complicated in sensory ganglia, mainly by the presence of many perikaryal projections from the neurons (Fig. 12). The neuronal perikaryal projections have long been believed to rise from shrinkage of the nerve cell body or other technical artifact (32). However, Levi (33) suggested that the enlargement of neuronal surface area may facilitate the metabolic exchange between the neurons and its environment. Using quantitative transmission electron microscopic studies, Pannese *et al* (7, 8) supported Levi's hypothesis. We tried to observe the perikaryal projection using SEM in the adult animals (34, 35) and embryos (5). In DRG treated with collagenase and trypsin, a small population of nerve cell bodies was surrounded partly by satellite cells. These satellite cells were not seen in contact with the corresponding neuronal surface and were apparently separated from it (Fig. 13a,b). The other nerve cell bodies were completely devoid of any enveloping sheaths, and the profiles of perikaryal projections could be seen on or near the neuronal surface in single electron micrograph (Fig. 13c). These projections appeared to be similar to the perikaryal protrusions in ganglia not treated enzymatically (Fig.12,13), and the fine structure of nerve cell bodies subjected to

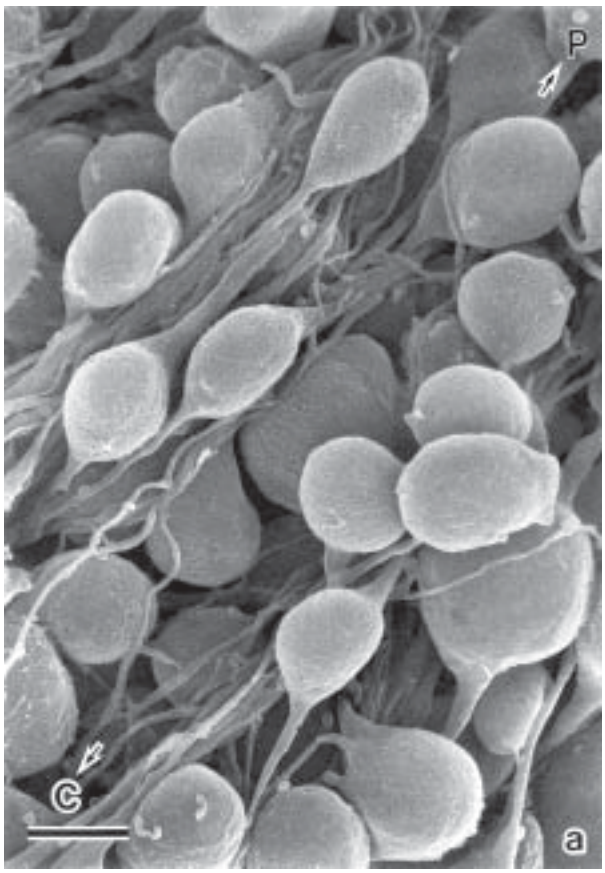


***Figure 10**. Bipolar neurons with thick peripheral and thin central processes on embryonic day 14. P, peripheral axis; C, central axis. Bar, 5 μm.*

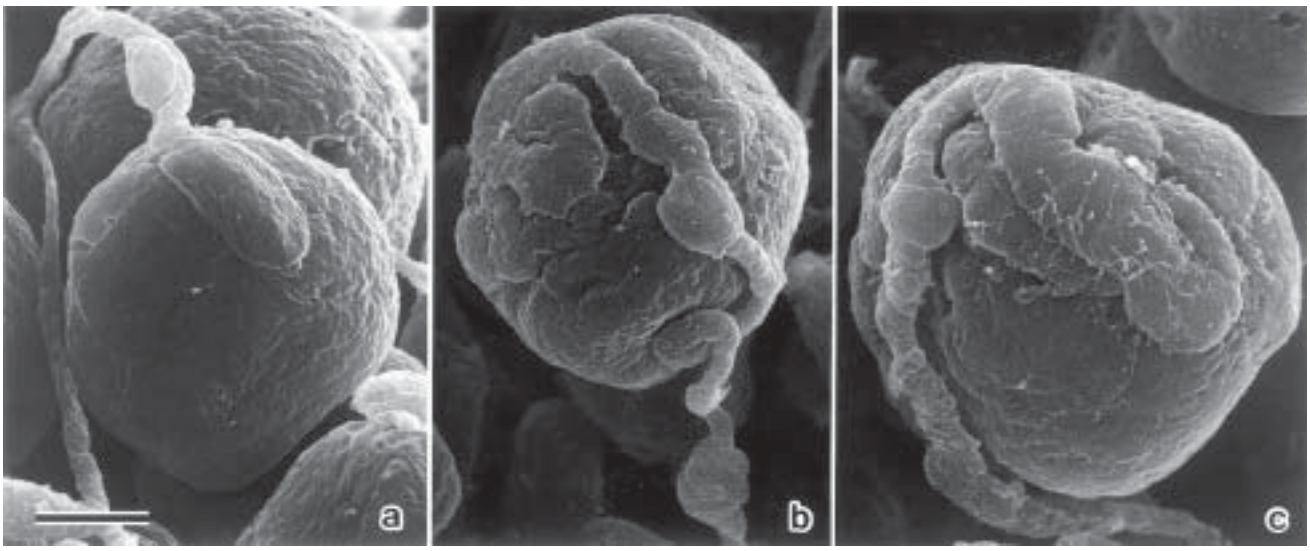


***Figure 11**. Pseudounipolar dorsal root ganglion neurons with a simple stem process (**a**) or a highly convoluted stem process (Cajal's initial glomerulus) (**b, c**). Bar, 5 μm.*

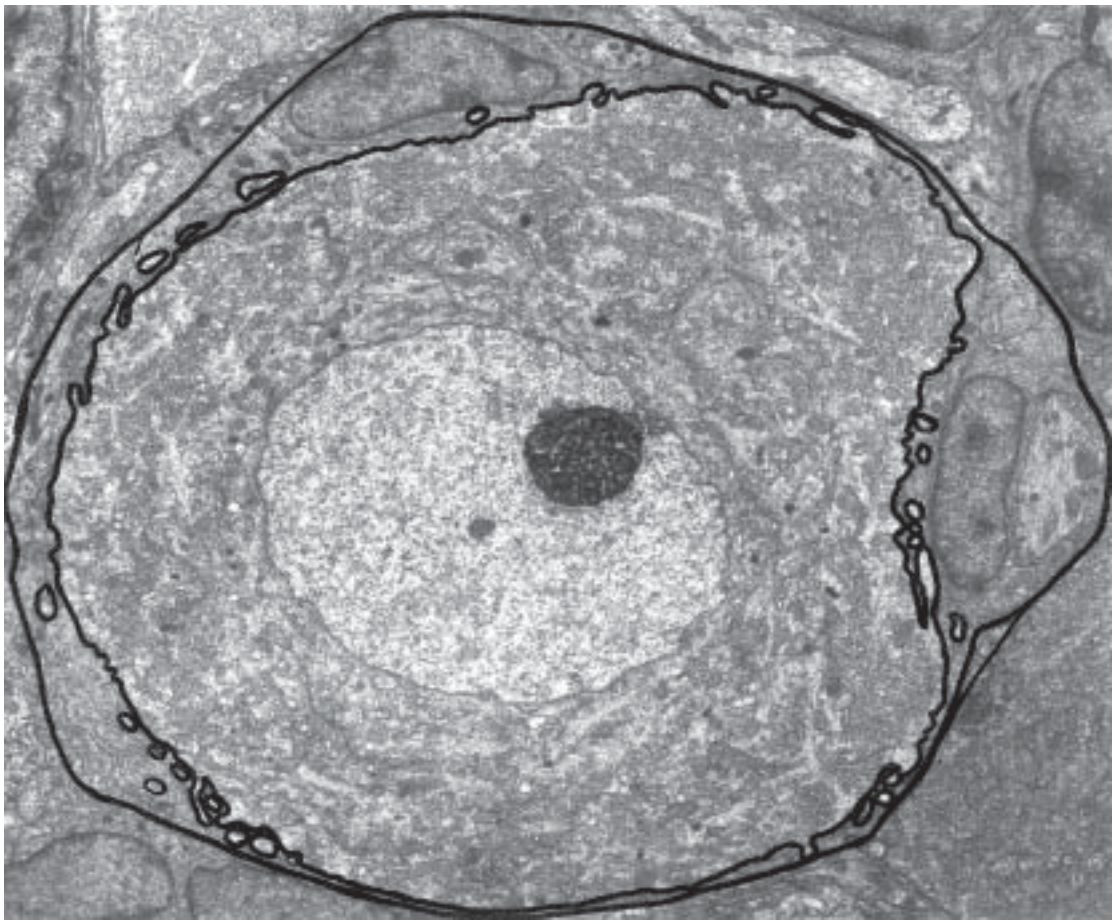

***Figure 12****. On postnatal day 2, sensory nerve cell body is completely enveloped by satellite cell sheath. The neuron-satellite cell boundary are outlined in ink to show its complicated course due to finger-like projections arising from the neuron surface.*

enzymatic digestion was well preserved (Fig.13c), suggesting these projections are not artifacts.

The mean transverse diameter and length of perikaryal projections were calculated. The surface area (s) and the volume (v) of individual neurons were estimated from micrographs at a magnification of 6 000 with the same system. Total surface area (S') of these projections on each neuron were calculated by the following formula: $S' = l\pi LS/50$, where l = mean transverse diameter (= 0.173 μm), L = total length of neuronal projections in 50 $\mu m^2$ of surface area, S = estimated surface area of the nerve cell body.

The perikaryal projections were observed more frequently on large nerve cell bodies than on small nerve cell bodies at all stages examined (Fig. 14a,b,15). The relationship between the surface area of projections and the volume of the corresponding nerve cell body is shown in Figure 16 with double-logarithmic plotting (5). In this graph, the volume of the nerve cell body (V) is plotted on the abscissa and the surface area of the projections (S') on the ordinate. The neuron size-dependent increase in the surface area of perikaryal projections was evident ($p<0.0001$) at later developmental stages when the majority of ganglion neurons differentiated into pseudo-unipolar cells (Fig. 16). The surface areas of the projections of immature bipolar neurons were smaller than those of mature ganglion neurons (Fig. 14).

The total surface area of perikaryal projections correlates positively with the volume of the corresponding soma of a pseudounipolar neuron, which is spherical in shape. In contrast, spindle-shaped bipolar neurons, even though they lack perikaryal projections, are endowed with a surface area per unit volume about two times that of spherical pseudo-unipolar neurons (Fig. 16). This may account for the finding that bipolar neurons do not have perikaryal projections which increase the cell surface area.

The functional significance of the perikaryal projections has been a subject of discussion for years. The hypothesis that the perikaryal projections of sensory ganglion neurons are vestiges of retracted neuronal processes during embryonic life is difficult to be supported, because the perikaryal projections increase continuously even after the disappearance of the thick projections that are seen transiently on E6 and E8 (5). A satisfactory interpretation of this structure is that the

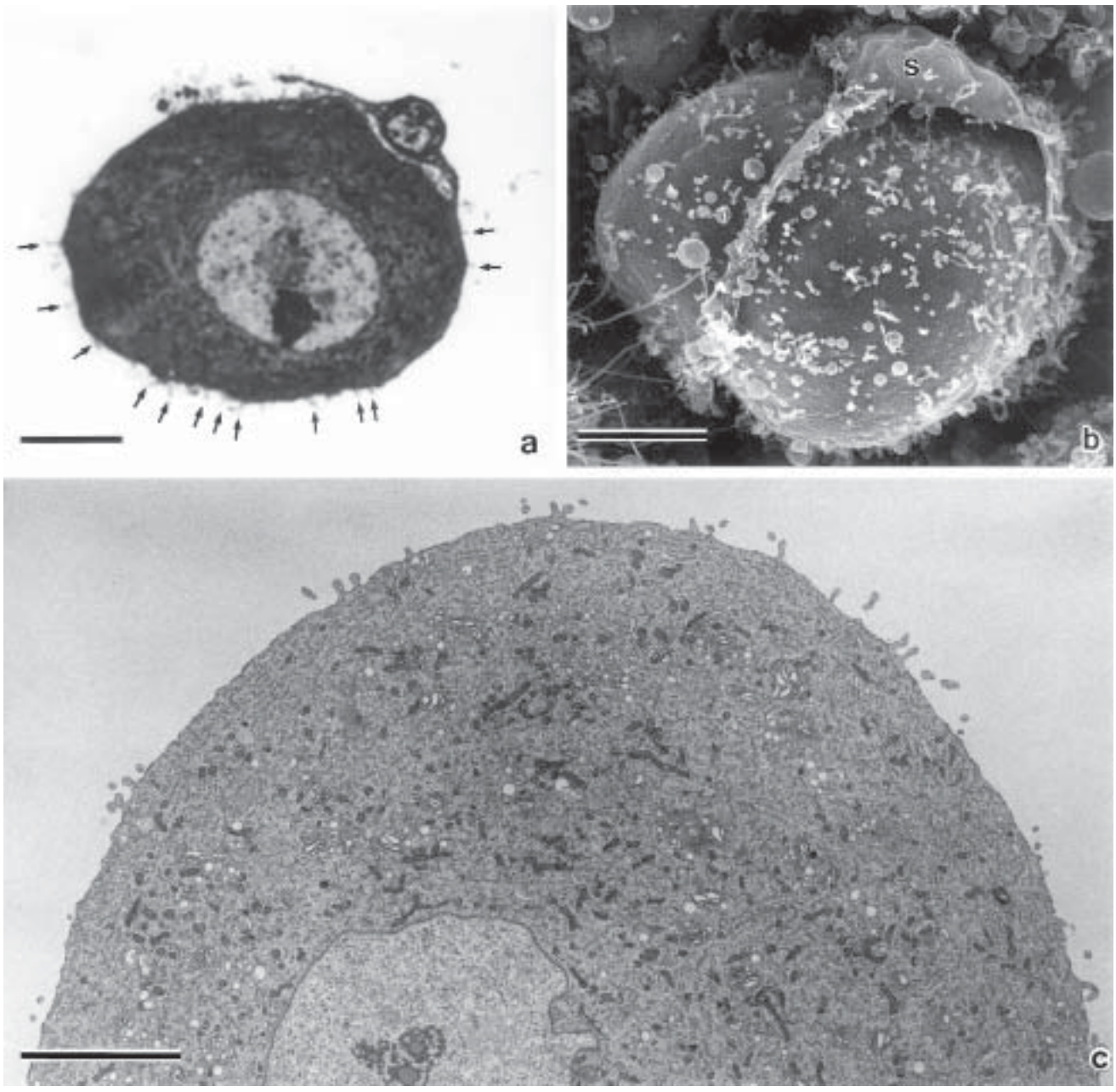


***Figure 13***. *Light micrograph (**a**), scanning electron micrograph (**b**) and transmission electron micrograph (**c**) of nerve cells from dorsal root ganglion at postnatal day 2 (P2) after enzymatic digestion. A nerve cell body surrounded partly by satellite cell sheath (**a, b**). Note perikaryal projections (arrows) protruding from the nerve cell body (**a**). Another nerve cell body completely devoid of satellite cell sheath (**c**). Note that the fine structure of the neuron is well preserved. Bars, 5 μm. From Ref 3, with permission of Springer Verlag.*

cell body is the metabolic hub of the neuron, and therefore its surface, including that of its perikaryal projections, must be large enough to meet the metabolic exigency of microenvironmental changes (7,8,30) (Fig.17). Since DRG neurons have no ramified dendritic trees to make their neuronal surfaces larger, they may need perikaryal projections. As described by Fawcett (36), in living organisms most physiologically important events take place at cell surfaces or at interfaces between intracellular compartments. The rate of activity per unit area of surface probably cannot be increased above a

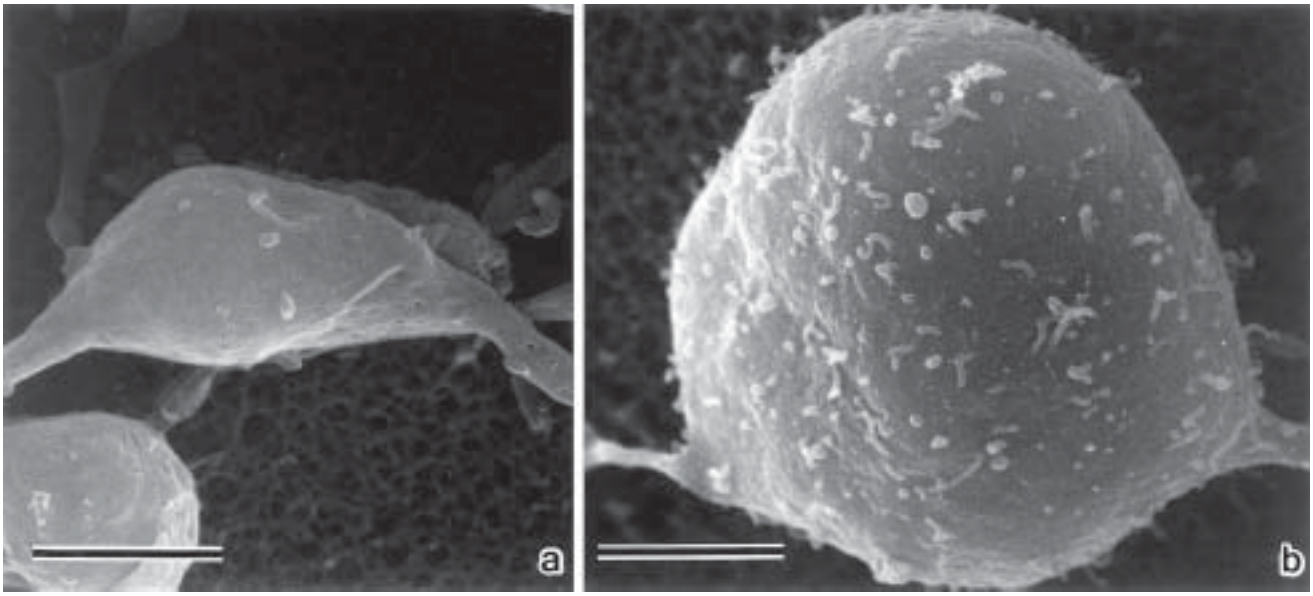


***Figure 14***. *Scanning electron micrographs showing spindle-shaped bipolar neuron on day E8 (**a**), and eccentrically bulging bipolar neuron at postnatal day 2 (P2) (**b**). Note that the latter has more perikaryal projections than the former. Bars, 5 μm. From Ref 5, with permission of Springer Verlag.*

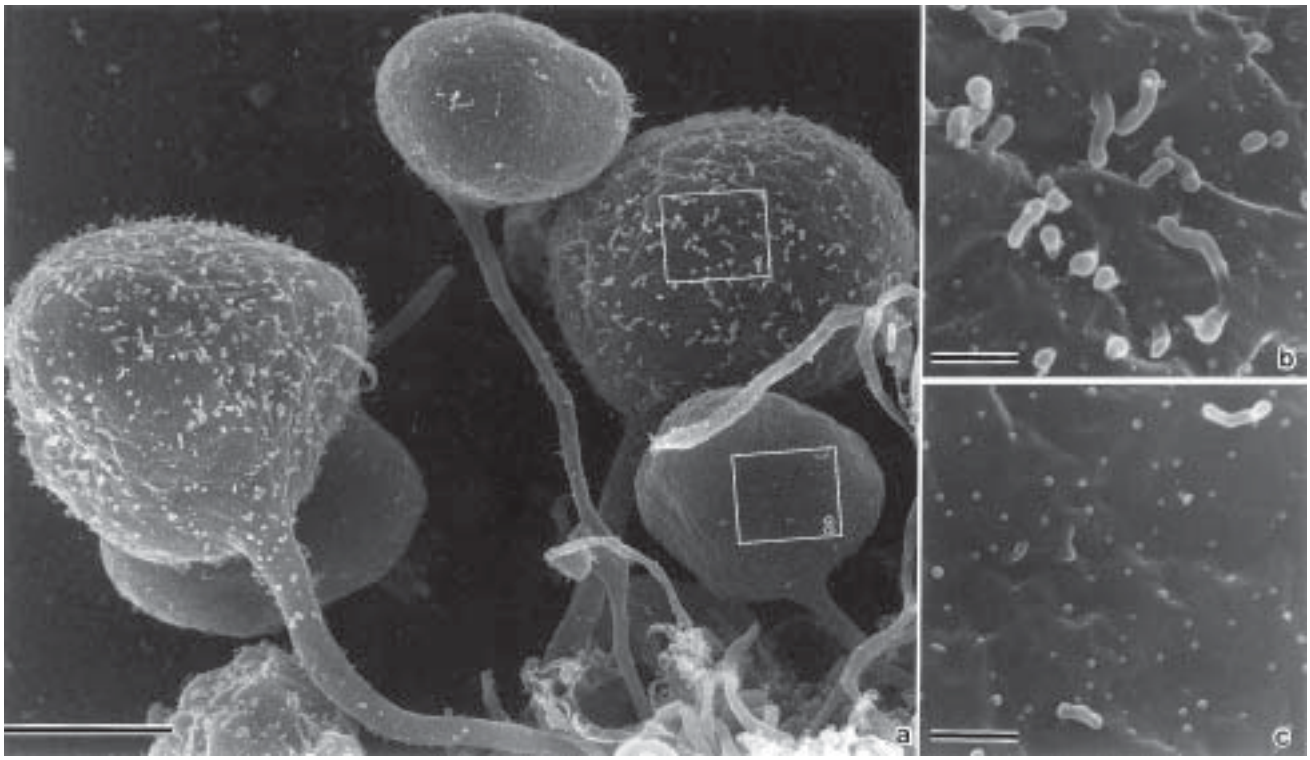


***Figure 15***. *Scanning electron micrograph showing, at low magnification, difference in number of perikaryal projections between large and small ganglion neurons at postnatal day 2 (P2) in the rat dorsal root ganglion (**a**). Bar, 10 μm. Scanning electron micrographs showing perikaryal projections in area indicated by rectangle 1 (**b**) and 2 (**c**) in (**a**). Bars, 1 μm. From Ref 5, with permission of Springer Verlag.*

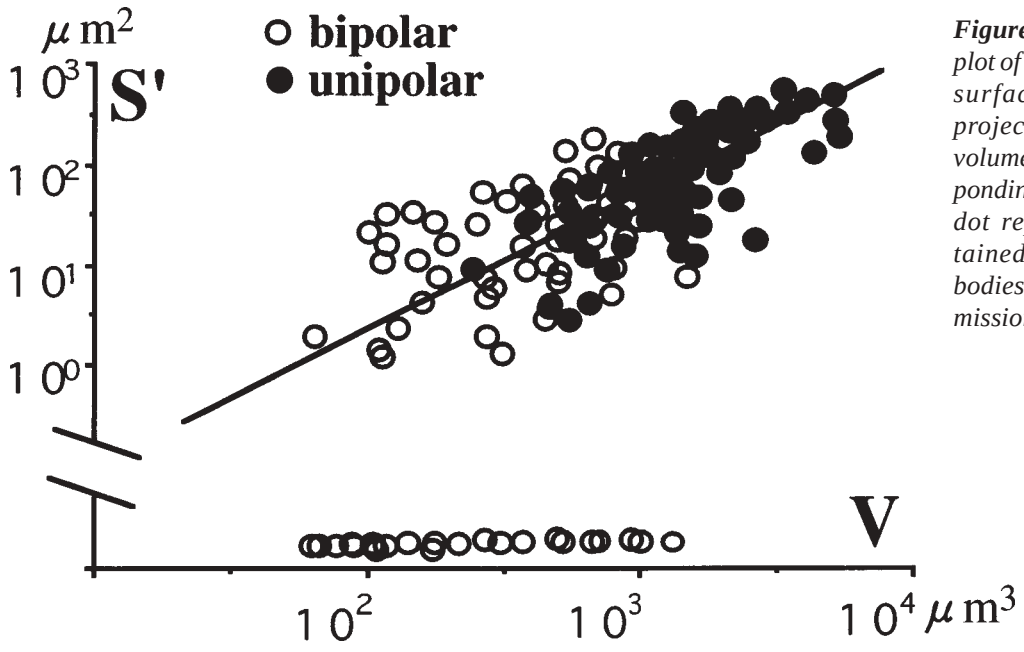


***Figure 16**. Double-logarithmic plot of relationship between total surface area of perikaryal projections (S', ordinate) and volume (V, abscissa) of corresponding nerve cell body. Each dot represents the values obtained from single nerve cell bodies. From Ref 5, with permission of Springer Verlag.*

certain limit, so structural devices for increasing the available surface area appear to be necessary.

## CONCLUSION

Pseudounipolarization is a striking model of neuronal transformation and neuron-satellite cell interface in sensory ganglia is also a useful model for the study of cell-cell interaction. The perikaryal projections which increase the area of neuron-satellite cell interface may play a crucial role in the development of DRG neurons. Pseudounipolarization, increase in the number of perikaryal projections and synaptogenesis in the gray matter of the spinal cord (37-39) proceed in the similar period of development. Further work is required to establish the precise relationships in these events related to the primary sensory tract.

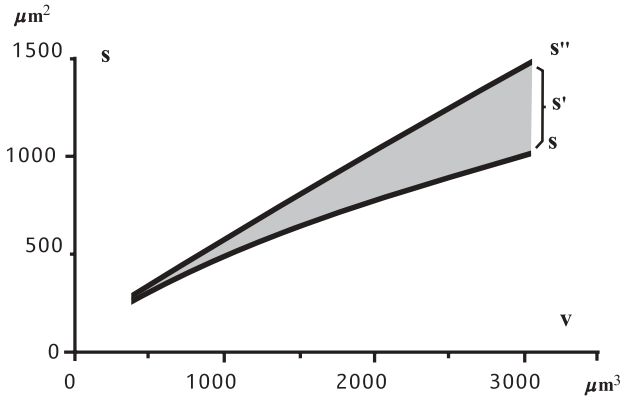


***Figure 17**. Relationships between both the total and smooth surface areas (S" and S, respectively) and the volume (V) of the nerve cell body. The dotted area (S') represents the total surface area of perikaryal projections.*

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## REFERENCES

1. Ramon y Cajal S. Sur l'origin et les ramification des fibres nerveuses de la molle embryonnaire. *Anat Anz* 1890; 5: 85-95.
2. Mudge AW. Schwann cells induce morphological transformation of sensory neurons in vitro. *Nature* 1984; 309: 367-369.

3. Matsuda S, Uehara Y. Prenatal development of the rat dorsal root ganglia. A scanning electron-microscopic study. *Cell Tissue Res* 1984; 235: 13-18.
4. Matsuda S, Baluk P, Shimizu D, Fujiwara T. Dorsal root ganglion neuron development in chick and rat. *Anat Embryol* 1996; 193: 475-480.
5. Matsuda S, Desaki J, Aburaya J, Sakanaka M. Perikaryal projections of developing spinal ganglion neurons in the chick demonstrated by scanning electron microscopy. *Anat Embryol* 1997; 195:137-146.
6. Pannese E, Ledda M, Conte V, Procacci P. The perikaryal projections of rabbit spinal ganglion neurons. A comparison of thin section reconstructions and scanning microscopy views. *Anat Embryol* 1990; 181: 427-432.
7. Pannese E, Gioia M, Carandente O, Ventura R. A quantitative electron microscope study of the perikaryal projections of sensory ganglion neurons. *J Comp Neurol* 1983; 214: 239-250.
8. Pannese E, Bianchi R, Gioia M, Ventura R. A quantitative electron microscope study of the perikaryal projections of sensory ganglion neurons. II. Gecko and lizard. *J Comp Neurol* 1985; 240: 212-218.
9. His W. Zur Geschichte des menschlichen Rukenmarks und der Nervenwurzeln. *Abh math-phys Kl d Kgl sachs Gas Wiss* 1886; 13: 479-513.
10. Rezius G. Zur Kenntnis des centralen Nervensystems; quoted by Scharf JH. In: *von Mollendorffs Handbuch der mikroskopischen Anatomie des Menschen*, vol 4, 1, Sensible Ganglien. Springer, Berlin, Gottingen, Heidelberg. 1891.
11. Lenhossek M. Beobachtungen an der Spinalganglien und dem Rukenmark von Pristiurusembryonen. *Anat Anz* 1892; 7: 519-539.
12. Tennyson V. Developing sensory neuroblasts *J Comp Neurol* 1965; 124: 267-318.
13. Pannese E. Developmental changes of endoplasmic reticulum and ribosomes in nerve cells of the spinal ganglia of the domestic fowl. *J Comp Neurol* 1968; 132: 331-364.
14. Riederer BM, Barakat-Walter I. Differential distribution of microtuble-associated proteins, MAP2 and MAP5, during chick dorsal root ganglion development in situ and in culture. *Dev Brain Res* 1992; 68:111-123
15. De Koninck P, Carbonetto S, Cooper E. NGF induces neonatal rat sensory neurons to extend dendrites in culture after removal of satellite cells. *J Neurosci* 1993; 13: 577-585.
16. Matsuda S, Uehara Y. Cytoarchitecture of the rat dorsal root ganglia as revealed by scanning electron microscopy. *J Electron Microsc* 1981; 30: 136-140.
17. Matsuda S, Uehara Y. Scanning electron microscopy of neuronal development in ganglia after removal of connective tissue components. In: Shahar A, editor. *A Dissection and Tissue Culture Manual of the Nervous System*. Alan R. Liss.1989; 272-273.
18. Ramon y Cajal S. Neue Darstellung vom histologischen Bau des Centralnervensystems. *Arch Anat Physiol Anat Abt* 1883; 319-428.
19. His W. Die Entwicklung der ersten Nervenbahnen beim menschlichen Embryo. *Arch Anat U Abt* 1887; 368-378.
20. Murnaghan DP. Studies on living spinal ganglion cells. *Anat Rec* 1941; 81: 183-203.
21. Ninomiya T. Morphological changes of rat dorsal root ganglion cells in the process forming period. *Sapporo Med J* 1985; 54: 1-10.
22. Smith EV. Histology of the sensory ganglia of birds. *Am J Anat* 1913; 14: 251-297.
23. Truex R. Observations on the chicken Gasserian ganglion with special reference to the bipolar neurons. *J Comp Neurol* 1939; 71: 473-486.
24. Pannese E. The histogenesis of the spinal ganglia *Adv Anat Embryol Cell Biol* 1974; 47: 1-97.
25. Pannese E. The satellite cells of the sensory ganglia *Adv Anat Embryol Cell Biol* 1981; 65: 1-111.
26. Funakoshi Y, Matsuda S, Uryu K, Fujita H, Okumura N, Sakanaka M. An immunohistochemical study of basic fibroblast growth factor in the developing chick. *Anat Embryol* 1993; 187: 415-423.
27. Dale HH. On some numerical comparisons of the centripetal and centrifugal medullated nerve fibers arising in the spinal ganglia of the mammal. *J Physiol* 1900; 25: 196-206
28. Rexed B, Sourander P. The caliber of central and peripheral neurites of spinal ganglion cells and variations in fiber size at different levels of dorsal spinal root. *J Comp Neurol* 1949; 91: 297-306.
29. Ha H. Axonal bifurcation in the dorsal root ganglion of the cat: a light and electron microscopic study. *J Comp Neurol* 1970; 140: 227-240.
30. Lieberman AR. Sensory Ganglia. In: Landon D, editor. *The Peripheral Nerve*. Chapman and Hall, London. 1976; 188-278.
31. Ramon y Cajal S. Die Struktur der sensiblen Ganglien des Menschen und der Tiere. *Ergeb Anat Entwickl Gesch* 1907; 16: 177-215.
32. Pannese E. *Neurocytology: Fine Structure of Neurons, Nerve Processes, and Neuroglial Cells*. Georg Thieme Verlag, Stuttgart, New York. 1994.
33. Levi G. I gangli cerebrospinali. *Arch Ital Anat Embriol* 1908; 7(Suppl): 1-39.
34. Pannese E, Ledda M, Conte V, Marini E, Matsuda S. A technique for studying the perikaryal projections of spinal ganglion neurons by scanning electron microscopy. In: Motta PM, editor. *Cells and Tissues: A Three-*

*Dimensional Approach by Modern Techniques in Microscopy.* Alan R. Liss. 1989; 371-376.
35. Pannese E, Ledda M, Conte V, Procacci P, Matsuda S. Scanning electron-microscope observations of the perikaryal projections of rabbit spinal ganglion neurons after enzymatic removal of connective tissue and satellite cells. *Cell Tissue Res* 1989; 260: 167-173.
36. Fawcett FA. *The Cell.* 2nd edition. W.B. Saunders, Philadelphia, London, Toronto. 1981.
37. Kanemitsu A, Matsuda S. Synaptogenesis in the chick cervical cord and possible initial central pathways from dorsal root fibers to motor neurons. Golgi and electron microscopic studies. *Neurosci Lett* 1984; 48: 1-6.
38. Kanemitsu A, Matsuda S. Growth of the initial dendrite of early differentiated inter neurons in the zonk inter media of the embryonic chick cervical cord: A morphometric study with the Golgi method. *Neurosci Lett* 1985; 53: 267-272.
39. Kanemitsu A, Matsuda S, Kobayashi Y. Morphological aspects of formation of neuronal pathways in the chick spinal cord - Golgi and electron microscopic studies. *Acta Neurochir* 1987; 41 (Suppl): 78-84.