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CORRELATION OF CELL BODY SIZE, AXON SIZE, AND SIGNAL CONDUCTION VELOCITY FOR INDIVIDUALLY LABELLED DORSAL ROOT GANGLION CELLS IN THE CAT

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= Abstract =

Measurements of cell body and peripheral and central axon sized were made for primary sensory neurons outlined by the intracellular injection of HRP. Conduction velocities were also measured on the outlined processes The sensory neurons were then subdivided into A and C cells on the basis of the conduction velocity of the impulses carried by the processes of these cells.

Central processes of both A and C cells are smaller than the peripheral processes, but the size differential is greater for the C cells. For A cells, there is a linear relation between the size of the peripheral axon and the conduction velocity of the impulses carried by these axons, but the confidence limits are wide. For C cells, there is a linear relation between the size of the central process and conduction velocity of the impulses carried by the processes, but for the peripheral processes, 2 aberrant processes resulted in no correlation between process size and conduction velocity For A cells, the size of the central and peripheral processes and the conduction velocity of the impulses carried by the peripheral processes are linearly correlated with cell body size. By contrast no such correlations can be demonstrated for C cells. This presumably implies an important difference in that the size of the cell body is correlated with axon size impulse conduction velocity for A cells but not for C cells.

A widely accepted generalization is that large sensory cells give rise to myelinated axons and small sensory cells to unmyelinated axons In this study, myelinated and unmyelinated are defined on the basis of impulse conduction velocity. For those cells that are clearly large (greater

than 50 μm in diameter), the conduction velocity of the impulses carried by their processes is always greater than 2.5 m/sec and for those cells that are clearly small (less than 35 μm in diameter) the conduction velocity is always less than 2.5 m/sec. Thus for these cells the above generalization holds. For the intermediate sized cells (35 ~ 50 μm), however, the size of the cell body bears no predictable relation to the conduction velocity of the impulses carried by those processes, and thus to whether the axons are myelinated or unmyelinated. Thus the above generalization does not hold for this intermediate group of cells, and since there are many cells in this size range, we feel that the generalization that large cells give rise to myelinated axons and small cells to unmyelinated axons is an oversiplification.

Ⅰ. INTRODUCTION

The sizes of neuronal cell bodies and their axons and the conduction velocities of the potentials carried by the axons are thought to be correlated and related to the function of the cell. With some exceptions, however, these relationships are derived from population data such as compound action potentials and histograms of cell and axon sizes. To provide further insight, it would be desirable to determine cell and axon sizes and conduction velocities in individual neurons and see if the same relationships can be derived from these data. With the development of markers that can be injected from microelectrodes into individual cells, this is now possible.

The present study is concerned with dorsal root ganglion cells in the cat. These neurons, which are primary sensory cells, are classically depicted as unipolar neurons with a stem process that bifurcates into a central process that travels in the dorsal root and a peripheral process that travels in a peripheral nerve. For individual dorsal root ganglion cells, we measured; 1) cell body size, 2) size of the central process, 3) size of the peripheral process, 4) conduction velocity of potentials carried by the central process and 5) conduction velocity of potentials carried by the peripheral process. We then attempt to answer four questions : 1) what is the relation of central axon size to peripheral axons size, 2) what is the relation of the size of the axon to the conduction velocity of the signals carried by the axon 3) what is the relation of cell body size to the size of the axons and the signal conduction velocities carried by the axon of that particular cell and 4) do large cells always give rise to myelinated axons and small cells to unmyelinated axons?

Some of this material has been presented in an abstract (Lee et al., 1983).[29]

Ⅱ. MATERIALS AND METHODS

Animal preparation

Cats of either sex weighting 1.5 ~ 3.5 kg were used. Anesthesia was with sodium pento-

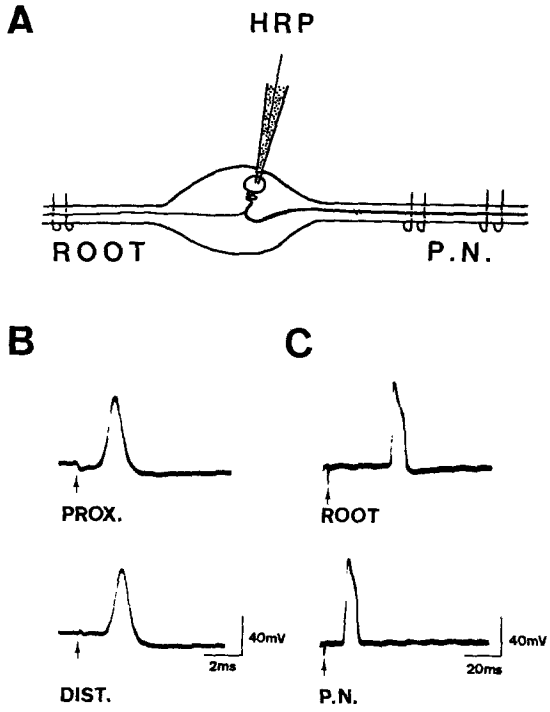

Fig. 1. A A diagram showing the experimental preparation which consists of a dorsal root ganglion with attached dorsal root (ROOT) and peripheral nerve (P.N). One pair of stimulating electrodes is placed on the root and 2 pairs on the nerve. Then a microelectrode containing 5% horseradish peroxidase (HRP) is placed in a dorsal root ganglion cell body. Action potentials are elicited by stimulation from any of the 3 pairs of electrodes. B. For conduction velocities in the nerve (P.N), the proximal electrode pair is stimulated (PROX. arrow, conduction distance 15 mm), and the potential is recorded in the cell body. The distal pair is then stimulated (DIST arrow, conduction distance 21 mm), and the resulting potential again recorded in the cell body Conduction velocity is calculated as the distance between the electrode pairs, divided by the time between the spike at PROX. and the spike at DIST. The illustrated action potential in this case is from an A cell (see text) C Two action potentials from a C cell are illustrated. The first is recorded in the cell body after stimulation of the pair of electrodes in the root (ROOT, arrow, conduction distance 26 mm), and the second from stimulation of the proximal electrode pair on the peripheral nerve (P.N, arrow, conduction distance 16 mm).

barbital (Nembutal) 40 mg/kg intraperitoneally. When anesthesia was deep, the chest was opened and heart exposed. Intracardiac infusion was done with 1500 cc of Kreb's solution (Higashi & Nishi, 1982)[21] which had been oxygenated by bubbling 95% O_2 and 5% CO_2 through it. Laminectomies were then done and the L5-S3 dorsal root ganglia with attached dorsal roots and peripheral nerves were removed and put in the oxygenated Kreb's solution. The lengths of the removed roots and nerves were approximately 2.5 and 5.0 cm, respectively. Ganglia, roots and nerves were then placed in a stimulating-recording chamber superfused with oxygenated Kreb's solution, and the temperature was maintained at 37℃ throughout the study. The roots were placed on a single pair of electrodes, and the peripheral nerve was placed on 2 pairs of electrodes (Fig. 1). The stimulating electrodes were at least 15 mm from the ganglion (range 16.0 ~ 29.5 mm) and the usual distance between the two pairs of electrodes on the peripheral nerve was 15 mm. To increase stimulus effectiveness, the junctions between the ganglion on the one hand and the root and peripheral nerve on the other were lined with stop-cock grease and the compartments containing the roots and nerves had the saline replaced with mineral oil warmed to 37℃. The capsule of each ganglion was then opened with jeweler's forceps and iris scissors along the long axis of the ganglion, and the edges were retracted and pinned to the floor of the chamber with small pins.

Recording and Stimulation

After opening the capsule, ganglion cells could be visualized in the dissecting microscope The exposed cells were impaled with glass micropipettes filled with 5% M/V horseradish peroxidase (HRP) in Tris buffer (0.05 M, pH 8.6) containing 0.2 M KCl. The impedances of the recording electrodes ranged from 40 ~ 80 MΩ. Intracellular recordings were made with a high voltage electrometer (Eutectic Electronics, Model 400A). The stimuli consisted of constant current square wave pulses whose intensity was adjusted to a level just above the threshold to activate the cell. The pulse duration was 50 ~ 100 μs for A cells and 500 ~ 1,000 μs for C cells. The threshold intensity varied widely with a range from less than 100 μA to several mA.

After the above measurements were made, depolarizing current pulses were applied to the cell body via the microelectrode (0.5 ~ 1.0 nA for 15 m/sec at 20 m/sec intervals for 5 ~ 10 min for A cells; and 0.3 ~ 0.5 nA for 10 m/sec at 20 m/sec intervals for 1 ~ 5 min for

Table 1.

ABBREVIATIONS:

DBC = Cell Body Diameter
DCP = Diameter of Central Process
DPP = Diameter of Peripheral Process
CVC = Conduction Velocity of Central Process
CVP = Conduction Velocity of Peripheral Process

Parameters Correlated	N	r	Regression Lines
		A CELLS	
1. DPP/DCB	76	0.470	DPP = 0.08 × DCB + 1.06
2. DCP/DCB	70	0.480	DCP = 0.07 × DCB + 0.01
3. DCP/DPP	78	0.914	DCP = 0.87 × DPP − 0.67
4. CVP/DPP	45	0.724	CVP = 6.10 × DPP − 7.91
5. CVP/DCB	38	0.474	CVP = 0.84 × DCB − 20.3
		C CELLS	
6. DPP/DCB	33	0.245	Not Significant
7. DCP/DCB	33	0.176	Not Significant
8. DCP/DPP	35	0.669	DCP = 0.44 × DPP + 0.02
9. CVC/CVP	16	0.772	CVC = 0.33 × CVP + 0.24
10. CVP/DPP	23	0.345	Not Significant
11. CVC/DCP	25	0.636	CVC = 0.40 × DCP + 0.29
12. CVP/DCB	29	− 0.219	Not Significant
13. CVC/DCB	30	− 0.075	Not Significat

C cells). One or 2 cells from each ganglion were injected After injection, the ganglia were incubated in the warm oxygenated Kreb's solution for 6 ~ 12 hours. The ganglia were then fixed in 0.75% paraformaldehyde and 1.25% glutaraldehyde in 0.1 M phosphate buffer overnight The next day, each ganglion was frozen and serially sectioned at 50 μm. All sections were collected in phosphate buffer and then reacted by a nickel-cobalt diaminobenzidine reaction (Adams, 1981).[2]

Following the above procedure, the sections were placed on slides, dried, and coverslipped in permount. Cell body diameters were determined by measuring the long axis of the cell body and the axis at right angles and dividing by 2 Because of the variability in diameter of the processes of the labelled cells, a single measurement did not give an accurate measure of diameter (Hursh, 1939; Sunderland & Roche, 1958).[24,11] Accordingly the bifurcation was located and the central and peripheral processes were measured at 25 μm or 50 μm intervals from the bifurcation by an ocular micrometer calibrated by a stage micrometer. Ten to 25 measurements were made on each axon and the mean values were taken as the size of the process

Shrinkage of the histological material was evaluated in the following way. Fine needles, separated by 500 μm, were placed in a rectangular pattern in a living ganglion The ganglion was then fixed and processed as above The distances between 2 holes were then measured in histological sections, and no demonstrable shrinkage was observed

Data Analysis

Linear regression analysis and calculation of correlation coefficients (r) were done with the aid of a PDP 11/45 computer. A P value of less than 0.01, as determined from r and the degrees of freedom, was chosen as the level of significance.

Ⅲ. RESULTS

Anatomical Data

Dorsal root ganglion cells outlined by the intracellular injection of HRP do not differ in any obvious way from cells similarly outlined

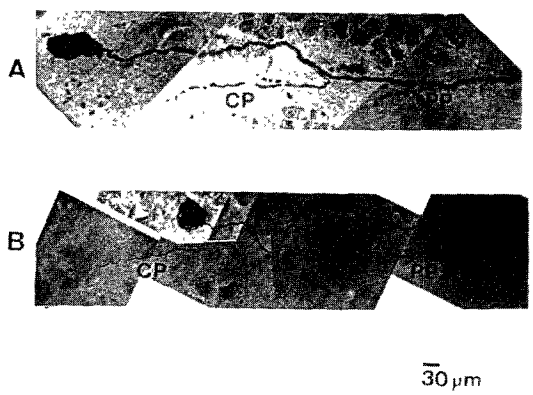

Fig. 2. A A montage of light micrographs showing an A cell outlined by the injection of peroxidase into the cell body. Note the stem process and its bifurcation into the peripheral process (PP) and the central process (CP) The impulse conduction velocity over the peripheral process of this cell is 30.0 m/sec B A montage of light micrographs showing a C cell outlined by the injection of peroxidase into the cell body Note the stem process and its bifurcation into a peripheral (PP) and a central process (CP). Note that the central process is much finer than the peripheral process Impulse conduction velocity over this peripheral process is 0.89 m/sec and over this central process 0.46 m/sec

in previous work (Yoshida & Matsuda, 1979),[18] or from cells as depicted in classic work (Dogiel, 1908).[13] A photograph of a dorsal root ganglion cell whose processes conduct more rapidly than 2.5 m/sec is shown in Fig. 2A and a photograph of a dorsal root ganglion cell whose processes conduct more slowly than 2.5 m/sec is shown in Fig. 2B. Note the relatively spherical cell body with its stem process, which then divides into a central process that travels in the dorsal root and a peripheral process that travels in the peripheral nerve. No unequivocal branching of either the central or peripheral process distal to the stem bifurcation was seen in our material in spite of previous reports indicating that such branching might be significant (Langford & Coggeshall, 1981).[27]

Two hundred and thirty dorsal root ganglia were taken from 30 cats and from these, 129 labelled cells were obtained. Eighty-four of these cells gave rise to axons that conducted impulses more rapidly than 2.5 m/sec. These cells will be referred to as A cells (see Discussion). Seventy of the A cells had cell body, peripheral process and central process labelled, 8 cells had the processes labelled but not the cell body and 6 cells had the cell body and peripheral axon labelled but not the central process. Forty-five of the labelled cells gave rise to axons that conducted impulses at less than 2.5 m/sec. These will be referred to as C cells (see Discussion). Thirth-three of these cells had all parts of the cell labelled, 10 had only the cell body labelled and 2 had only the peripheral and central processes labelled.

Diameters of A cell bodies ranged from 36.0 ~ 97.5 μm, and the mean diameter was 54.8 μm ± 12.2 S.D. (Fig. 3B). The C cell bodies were smaller, their range of diameters was 20.5 ~ 48.9 μm, and the mean diameter

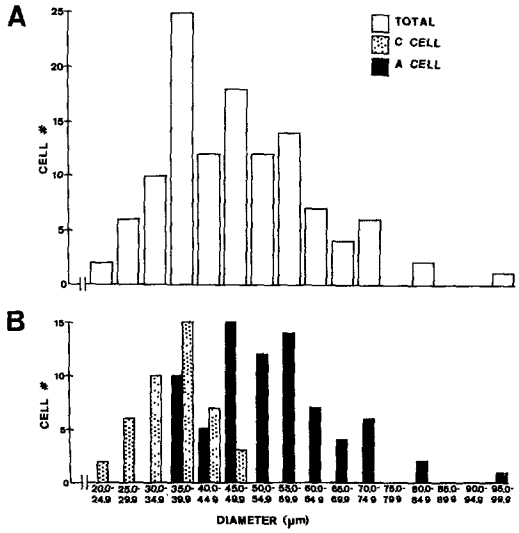

Fig. 3. A. Histogram of cell body sizes for all cells outlined by intracellular injection of HRP in this study. Note the histogram has a vaguely bimodal shape with 1 peak at 35.0 ~ 39.9 μm and the other at 45.0 ~ 49.9 μm. B. Histograms of 43 cell body sizes for C cells (stippled bars) and 76 A cells (black bars). Note that the 2 populations appear to be separate but that there is much overlapping in the diameter ranges from 35.0 ~ 49.9 μm

was 35.7 μm ± 6.3 S.D. (Fig. 3B). Note that there is a bimodal appearance to the histogram of Fig. 3A, but that the peaks are not distinct.

The mean diameter of the peripheral process of A cells was 5.36 μm ± 2.06 S.D. (Fig. 4A), and the mean diameter of the central processes of A cells was 3.98 μm ± 1.88 S.D. (Fig 4A). The mean diameter of the peripheral processes of the C cells was 1.27 μm ± 0.43 S.D. (Fig. 4B) and the mean diameter of the central processes 0.57 μm ± 0.28 S.D (Fig. 4B).

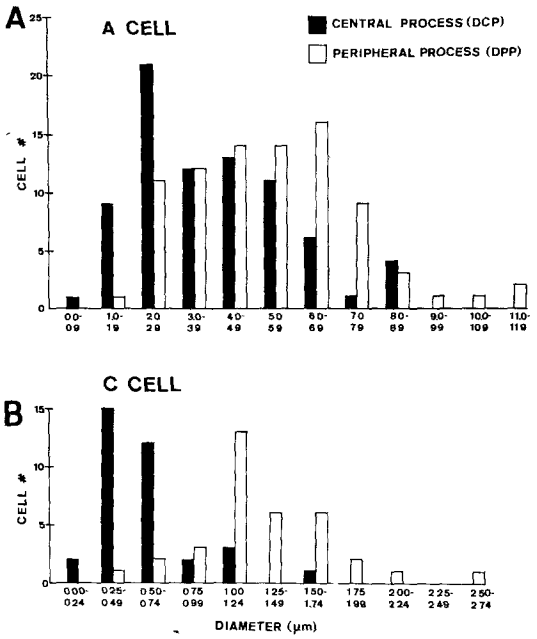

Fig. 4. A Histograms of the sizes of 78 central processes (black bars) and 84 peripheral processes (clear bars) of the A cells labelled in this study Note that although there is intermingling, the means of the 2 populations are clearly separate B Histograms of the sizes of 35 central processes (black bars) and 35 peripheral processes (clear bars) of the C cells labelled in this study. Although there is some intermingling, the 2 populations are more clearly separated than those in A.

Physiological Data

All recorded cells showed a stable resting membrane potential and no spontaneous action potentials were seen except from obviously injured cells during electrode penetration. Action potential peaks were $+20 \sim +30$ mV The duration of the action potential was much wider for the C cells than for A cells (Fig. 1). The resting membrane potential for the A cells was higher than for the C cells; the average resting potential for A cells was -51.1 mV $\pm$ 6.1 (n= 35, range $-43 \sim -63$ mV) and for C cells -42.9 mV $\pm$ 8.5 (n=28), range $-28 \sim -55$ mV. These values are similar to those seen in in vivo studies (Sato & Austin, 1960).[39]

The usual way to measure conduction velocity is to determine the distance between stimulating and recording sites and divide by the time it takes for an impulse to get between the 2 sites. There is, however, the delay between onset of stimulus and beginning of action potential (stimulusutilization time). In addition for dorsal root ganglion cells there are the particular problems of the unmeasured length of the stem process which tends to be thin and convoluted in large cells (the glomerulus) (Dogiel, 1908),[13] and the probable conduction delays at the bifurcation of the stem process (Dun, 1955)[17] and where the stem process joins the cell body (Tagini & Camino, 1973).[43] For peripheral processes of dorsal root ganglion cells we dealt with these problems by using 2 pairs of stimulating electrodes and calculating conduction velocity by determining the distance and conduction time from 2 different stimulus sites to the cell body and calculating conduction velocity by the difference between the two sets of measurements. Utilization times and conduction delays are thus cancelled out and the cell body and stem process are not involved in the distance measurements. We were not able to obtain as long a length of root as of nerve, however, and thus 2 pairs of stimulating electrodes could not be adequately separated on the root Accordingly we were 'forced to determine central conduction velocities the classic way (conduction distance divided by latency) which requires only a single pair of stimulating electrodes and a recording electrode in the cell body. To determine whether the 2 methods

gave comparable results, conduction velocities for 35 peripheral A cell axons and 28 peripheral C cell processes were measured by both methods. For the C cell processes the velocity calculated as distance divided by latency (the classic method) is 0.63 m/sec ± 0.19 S.D. and calculated as distance between 2 pairs of stimulation electrodes divided by latency, it is 0.65 m/sec ± 0.20 S.D. These values are not statistically different ($p < 0.1$, paired t-test). Thus conduction velocity for C cell processes can be measured either way and root conduction velocities can be determined. For A cell processes, however, conduction velocity measured as distance divided by latency was 19.02 m/sec ± 6.87 S.D., and when measured as distance between the pairs of stimulating electrodes divided by the latency difference, it is 40.09 m/sec ± 26.99 S.D. The first value is undoubtedly too low due to the problems mentioned above. Thus we cannot accurately measure the conduction velocity of the central processes of the A cells with only one pair of stimulating electrodes. In summary, we are able to measure conduction velocities for both central and peripheral processes of C cells but only for peripheral processes of A cells

The average conduction velocity of potentials carried by the peripheral processes of A cells was 26.6 m/sec ± 19.3 S.D. (Fig. 5A). The average conduction velocity of potentials carried by central processes of C cells was 0.55 m/sec ± 0.23 S.D. and the velocity of impulses carried by the peripheral processes was 0.76 m/sec ± 0.51 S.D. (Fig. 5B).

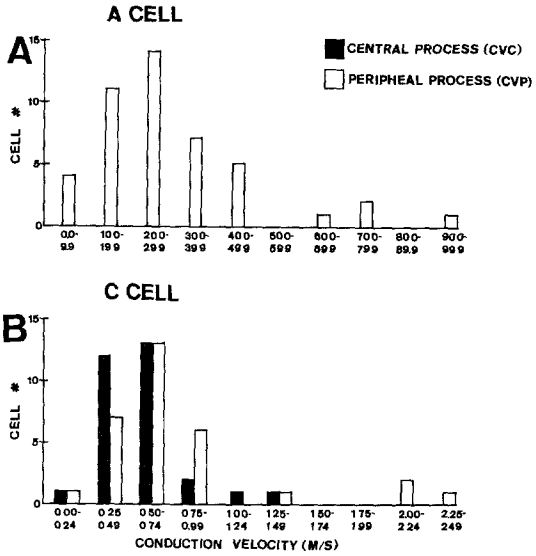

Fig. 5. A Histograms of the conduction velocities of impulses carried by 45 peripheral process of A cells. Note that the majority of recordings cluster in or around the 30.0 ~ 29.9 m/sec range with relatively few readings at higher conduction velocities B. Histograms of the conduction velocities of impulses carried by 30 central processes (black bars) and 31 peripheral processes (clear bars) of C cells. Although there is some overlap, note that the mean conduction velocities are different.

Correlations

We have done linear regression analysis and also determined correlation coefficients for our data (Figs. 6 ~ 9). Since we measured 5 parameters (cell body size, central and peripheral axon size, central and peripheral axon conduction velocity) and are separating A and C cells, there would theoretically be 20 such correlations; 10 for the A cells and 10 for the C cells. We were unable to measure the central conduction velocities for A cells, however, which removes 4 correlations. In addition, there is little sense in correlating the size of a central process with peripheral conduction velocity and vice-versa. Thus this leaves 13 correlations that would be useful, 5 for the A cells and 8 for the

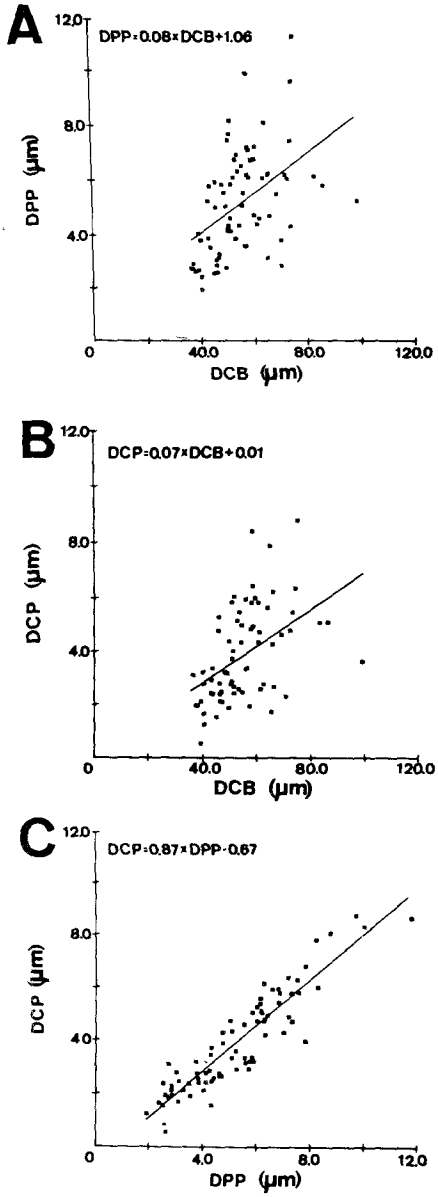

Fig. 6. A Plot of the relation between diameter of the peripheral process (DPP) and diameter of the cell body (DCB) for A cells B. Plot of the relation between the diameter of the central process (DCP) and the diameter of the cell body (DCB) for A cells. C. Plot of the relation between the diameter of the central process (DCP) and the diameter of the peripheral process (DPP) for A cells.

C cells. The pertinent conclusions from these correlations are presented in Table 1 and the plots of the 13 sets of data are presented in Figures 6 ~ 9. Note that significant regression lines can be found for all variables correlated for the A cells but for only 3 of the C cell comparisons.

Ⅳ. DISCUSSION

The Relative Sizes of Central and Peripheral Processes of Dorsal Root Ganglion Cells

In classic studies, the central processes of dorsal root ganglion cells are depicted as being finer than the peripheral processes (Dogiel, 1908; Ramon y Cajal, 1909; Lieberman, 1976)[13,33,30] This observation has been extensively confirmed for small dorsal root ganglion cells (Ranson, 1912; Ranson & Davenport, 1931; Gasser, 1955; Ha, 1970; Suh et al., 1984),[34,35,17,19,40] but it is denied for large cells with myelinated sensory processes (Lieberman, 1976).[30] In support of the denial are 1) reports of equal average diameters of myelinated axons central and peripheral to the dorsal root ganglion (Dale, 1900, Rexed & Sourander, 1949; Ochs et al., 1978),[11,36,32] 2) a Golgi impregnation study claiming that central and peripheral processes of large dorsal root cells are the same size (Ha, 1970),[19], 3) reports stating that fast conduction velocities carried by central and peripheral sensory processes of at least some dorsal root ganglion cells are equal (Gasser, 1955; Kirkwood & Sears, 1982; Rindos et al., 1984)[17,26,37] and 4) a report that the conduction velocities carried by central sensory processes are faster than those by peripheral sensory processes (Wiesenfeld & Tapper, 1976).[46] Thus it is now stated that the central process is finer

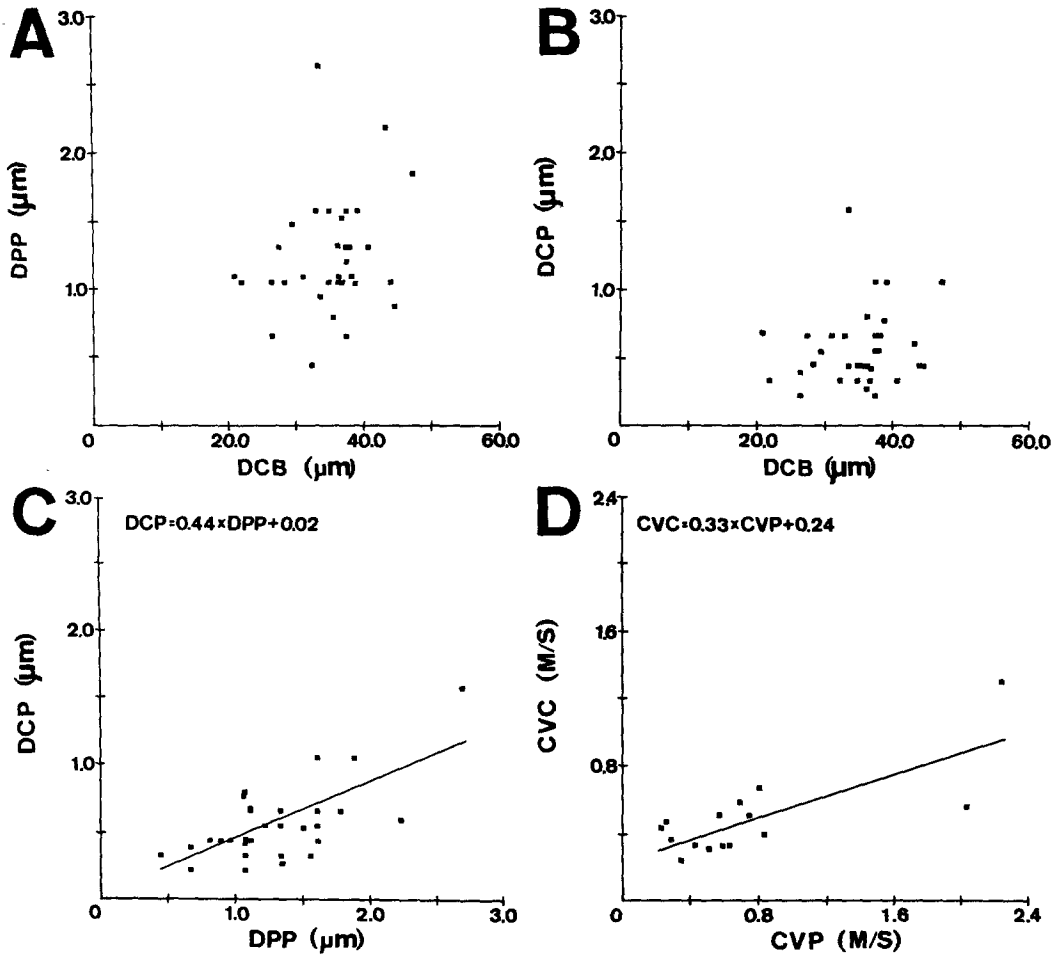

Fig. 7. A. Plot of the relation between conduction velocity of impulses carried by the peripheral process (CVP) and the diameter of the peripheral process (DPP) for A cells. B. Plot of the relation between conduction velocity of the central process (CVP) and the diameter of the cell body (DCB) for A cells.

than the peripheral process for sensory cells with unmyelinated processes but that the two processes are of equal size for those with myelinated processes (Lieberman, 1976).[30] The present paper disagrees with this last statement.

In the present study, the average diameter of myelinated (as defined by conduction velocity) central dorsal root ganglion cell processes is 3.98 μm and the diameter of the peripheral processes of the same cells is 5.34 μm, a 33% difference. In addition, in a recent electron microscopic study it was found that the average diameter of sensory axons in the dorsal root is 30% less than that of sensory axons in the mixed nerve of the same segment (Suh et al., 1984),[40] and several physiological studies

showed that the myelinated central processes conducted action potentials more slowly than the peripheral processes of the same cells (Loeb, 1976; Czeh et al., 1977; Kirkwood & Sears, 1982).[31,10,26] Finally, as mentioned above, almost every classic study on dorsal root ganglion cells showed finer central than peripheral processes for all cells, large and small alike. Thus, even though there is dispute, we believe that the bulk of the evidence shows that myelinated central processes are considerably finer than myelinated peripheral processes for mammalian dorsal root ganglion cells.

A partial explanation for the above disagreement might be that the size differential is proportionately greater for smaller sensory fibers. Thus in the present study, the central processes of C cells have an average diameter of 0.57 μm and the peripheral processes of these same cells have an average diameter of 1.27 μm, a difference of 55%. Similarly in an electron microscopic study, the difference in diameters between central and peripheral unmyelinated sensory processes was 50% (Suh et al., 1984).[40] These are larger differences than for the myelinated fibers (see preceding paragraph). Thus our data supports earlier work showing that the central processes of all dorsal root ganglion cells are finer than the peripheral processes, but we also point out that this discrepancy is greater for cells with unmyelinated processes than for cells with myelinated processes.

The Question of Separate Size Populations of Dorsal Root Ganglion Cells

It is generally agreed that there are 2 categories by size of dorsal root ganglion cells (e.g., Ranson, 1912; Lieberman, 1976; Lawson, 1979; Harper & Lawson, 1985).[34,30,28,20] It might be asked, however, whether this way of categorizing dorsal root ganglion cells indicates 2 separate populations or whether attention is focussing on examples from 2 ends of a spectrum. Most investigators favor the former because : 1) histograms of cell sizes often show 2 populations (Lawson, 1979; Szarijanni & Rethelyi, 1979),[28,42] 2) the cytology of the cell types is different (large light cells and small dark cells)(Andres, 1961; Lawson, 1979)[3,28] and 3) the large cells are thought to give rise to myelinated fibers, the small to unmyelinated fibers (Ranson, 1912; Lieberman, 1976).[34,30] In the present study, we cannot comment on the cytology of dorsal root ganglion cells, but our histograms show 2 populations of cells which we call large and small cells. There is considerable overlap of these populations in our material, but we do confirm that there are more small and large cells than intermediate sized cells. Whether only large cells give rise to myelinated fibers and only small cells to unmyelinated fibers will be considered below.

A cells and C cells. A subsidary issue to the above concerns our use of the terms "A cells" and "C cells". It is accepted in sensory physiology that A fibers conduct impulses at more than 2.5 m/sec and are myelinated whereas C fibers conduct impulses at less 2.5 m/sec and are unmyelinated (Gasser, 1950; Douglas & Ritchie, 1962).[16,14] Thus in this study the sensory cells that give rise to processes that conduct impulses more rapidly than 2.5 m/sec are referred to as "A cells" and those whose processes conduct impulses at less than 2.5 m/sec as "C cells". The relation of these 2 categories with the common subdivision of dorsal root ganglion cells into large cells and small cells will be discussed below. As a final point, it is

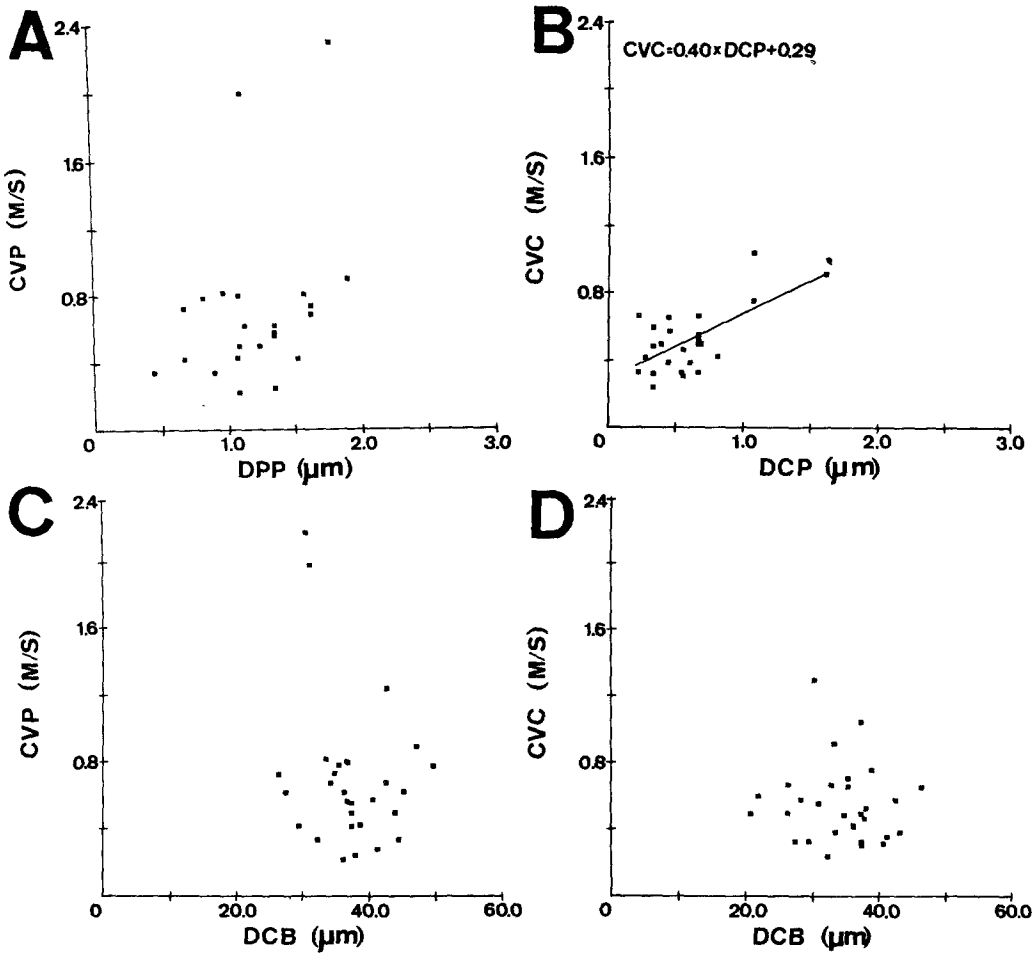

Fig. 8. A. Plot of the relation between the dimeter of the peripheral process (DPP) and diameter ofthe cell body (DCB) for C cells. No linear relationship between these variables could be demonstrated. B. Plot of the relation between the diameter of the central process (DCP) and the dimeter of the cell body (DCB) for C cells. No linear relationship between these varibles could be demonstrated. C. Plot of the relation between dimeter of the central process (DCP) and dimeter of the peripheral process (DPP) for C cells. D. Plot relation between the conduction velocity of impulses carried by the central process (CVC) and the conduction velocity of the impulses carried by the peripheral process (CVP) of C cells.

interesting that our data show a "break" or absence of conduction velocities between 1.5 and 2 m/sec rather than the 2.5 m/sec suggested by Gasser (1950).[16] To establish the exact relation between conduction velocity and myelination, however, will require measuring conduction velocities and demonstrating the presence or absence of myelin for individually identified ax-

ons, an experiment that is now technically feasible.

Lack of cells with rapidly conducting action potentials. One feature of the present study and that of Lawson and Harper (1985)[28] is that there are only a few cells whose peripheral axons carry impulses at more than 60 m/sec. This might seem surprising given the predominance of fast fibers in compound action potentials or in recordings from small filaments of dorsal roots and peripheral nerves Lawson and Harper (1985)[28] attributed this apparent lack to the youth of the animals they studied. This is not the case in our material, however, for our cats were clearly adult. In this regard, we noted in an earlier study (Suh et al., 1984)[40] that less than 2% of the peripheral myelinated sensory axons were 10 μm or more in diameter, as determined from axonal areas, for lumbosacral segments in the cat If Hursh's (1939)[23] factor of 6 is used (6X fiber diameter in μm equals conduction velocity in m/sec), this implies that less than 2% of the peripheral myelinated sensory axons would conduct at 60 m/sec or more. If the lesser correction factor of 5.4 for large fibers proposed by Boyd and Kalu (1979)[6] is used, less than 0.4% of the fibers would conduct at 60 m/sec or more. Thus the relative scarcity of cells whose processes conduct impulses at 60 m/sec or more is in our opinion not surprising. It simply reflects the relative paucity of such cells in comparison to the total for lumbosacral segments of the cat.

The Relation Between Axonal Size and the Conduction Velocity of the Signal Carried by the Axon

Myelinated fibers. For myelinated fibers, the first widely accepted formula relating conduction velocity to the size of myelinated axons is that the conduction velocity in m/sec is 6 times the fiber size in μm (Hursh, 1939).[23] Other studies agree that the relation of conduction velocity and diameter of fiber is linear, but the reported slopes or scaling factors vary (Tasaki et al., 1943; Hutchinson et al., 1970; Waxman & Bennett, 1972; Boyd & Kalu, 1979).[44,24,45,6] Several theoretical calculations also support the idea that the conduction velocity is linearly related to fiber diameter (Rushton, 1951; Goldman & Albers, 1968),[38,18] but non-linear relations have also been proposed (Coppin & Jack, 1971; Jack, 1975).[7,25] In our material, we find a linear relation between axon diameter and conduction velocity, but the formula has wide confidence limits. Thus a linear relation between conduction velocity and diameter is as good but not better than various power functions for our material, and the linear relationship is chosen only because of simplicity. In most other studies of this type, however, fiber diameter rather than axon diameter is measured. If the ratio of the diameter of the axon to the diameter of fiber for our fibers is assumed to be the same as the values reported in other studies (Williams & Wendell-Smith, 1971; Arbuthnott et al., 1980),[47,41] then our findings are more in accord with the lower correction factors reported by Bessou and Perl (1966)[5] and Boyd and Kalu (1979)[6] for small myelinated fibers than with the widely quoted factor of Hursh (1939).[23]

Unmyelinated fibers. There have been few studies relating conduction velocity to diameter of axon for unmyelinated fibers in mammals. There are theoretical studies, however, showing that if membrane and axoplasmic parameters are the same from axon to axon, conduction velocity should vary as the diameter of axon (Hodg-

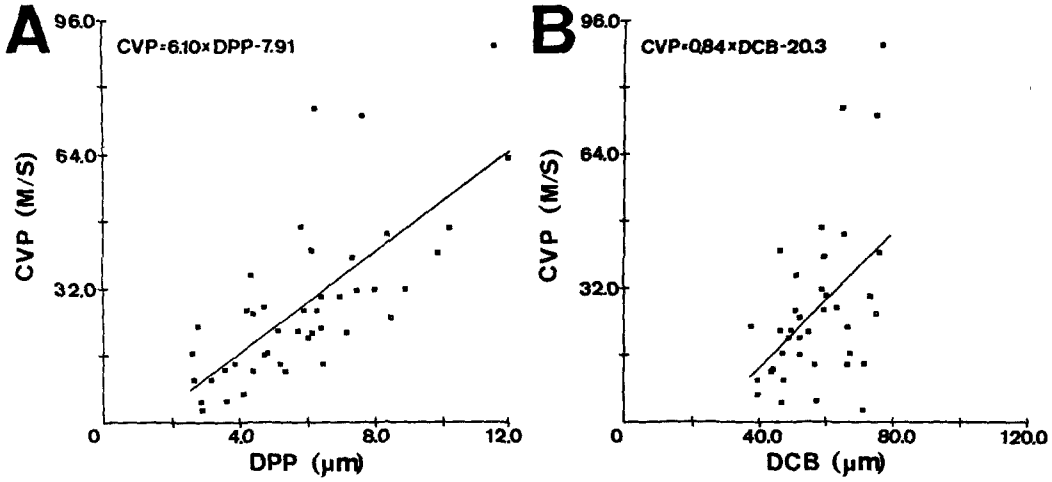

Fig. 9. A. Plot of the relation between the conduction velocity of the peripheral process (C VP) and the dimeter of the peripheral process (DPP) for C cells. No linear relationship between these variables could be demonstated. B. Plot of the relation between the conduction velocity of impulses carried by the central process (CVC) and diameter of the central process (D CP) for C cells. C. Plot of the relation between the conduction velocity of impulses carried by the peripheral process (CVP) and dimeter of the cell body (DCB) for C cells. No linear relationship between these varibles could be demonstrated. D. Plot of the relation between conduction velocity of impulses carried by the central process (CVC) and the dimeter of the cell body (DCB) for C cells. No linear relationships between these varibles could be demonstraated.

kin, 1954).[22] Some tests of this idea have been done on invertebrate axons and the results are variable (Jack, 1975).[25] For mammals, Gasser (1950; 1955)[16,17] attempted to reconstruct the compound action potential and reported that conduction velocity could be related to axon diameter, but this work was criticized, and even with Gasser's assumptions, the fit would equally well have been with a power function (Abott et al., 1958).[1] Finally a linear relation between conduction velocity and diameter of axon for small dorsal root ganglion cells of the mouse was claimed but a formula was not provided (Yoshida & Matsuda, 1979).[48] In our work we find moderately good linear correlations between 1) diameter of the central axon and conduction velocity, 2) central and peripheral axon diameter and 3) central and peripheral conduction velocities. There is no demonstrable correlation between diameter of the peripheral axon and peripheral conduction velocity, but if 2 aberrant points (Fig. 9A) are eliminated, a linear correlation is also obtained here. Thus axon size and conduction velocity are moderately well correlated for these fine axons, but it must be remembered that there is enough scatter in the data that it is difficult to choose between a linear function and a power function as

the best representation of this relationship.

The Relation of Cell Body Size to Axon Size and the Conduction Velocity of the Signals Carried by the Axon of the Cell

It has long been suggested that the size of a cell body is proportional to the size of its axon (e.g, Deiters, 1865, Ramon y Cajal, 1909).[12,33] The evidence is that large cells tend to have large axons and small cells, small axons. It was not until recently, however, that axon and cell body sizes for the same neurons were determined thus allowing more precise correlations to be made. When this was done, a linear relation between cell body size and axon size was reported for mouse dorsal root ganglion cells and cat spinal motoneurons (Cullheim, 1978; Cullheim & Ulfhake, 1979; Yoshida & Matsuda, 1979),[8,9,48] but actual formulae were not provided. In our material the correlations of cell size with axonal size and conduction velocity are different for A as opposed to C cells. For A cells (cells whose peripheral processes conduct potentials more rapidly than 2.5 m/sec), there are linear correlations between cell body size and axonal size or axonal conduction velocities even though the confidence levels of these correlations are wide. By contrast, for those ganglion cells whose processes conduct potentials at less than 2.5 m/sec, there are no demonstrable correlations between cell size on the one hand and size of processes or conduction velocity of potentials carried by these processes on the other. This means that there is so much variability that there is no value in knowing the size of a C cell for predicting the size of its processes and the conduction velocity of the potentials carried by its processes. These results are somewhat different than those of Harper and Lawson (1985)[20] who found better correlations between cell body size and axonal conduction velocity for slowly conducting axons. We are unable to explain the different conclusions.

The Questions Whether Large Dorsal Root Cells Give Rise to Myelinated Axons and Small Dorsal Root Ganglion Cells to Unmyelinated Axons

A common suggestion is that large cells give rise to myelinated axons and small cells to unmyelinated axons (e.g., Ranson, 1931; Lieberman, 1976).[35,30] In our material, however, there is considerable overlap of the large and small cell populations, and for the cells whose diameters are intermediate in size, it is not possible to predict whether impulses carried by the processes of the cells will conduct more or less than 2.5 m/sec. This is seen most clearly if we split our cells into 3 groups, those with cell bodies less than 35 μm in diameter, those with cell bodies 35 ~ 50 μm in diameter and those with cell bodies greater than 50 μm in diameter. If we do this, the 18 cells in the less than 35 μm group give rise to processes that conduct impulses at less than 2.5 m/sec and the 47 cells in the more than 50 μm group give rise to processes that conduct at greater than 2.5 m/sec. For the 55 cells in the 35 ~ 50 μm range, however, 25 give rise to processes that conduct at less than 2.5 m/sec and 30 carry potentials at more than 2.5 m/sec. Furthermore this difficulty is not simply that conduction velocities for these intermediate cells cluster around 2.5 m/sec, because our conduction velocities split into 2 relatively separate groups, the first being 0.25 ~ 1.0 m/sec and the second being 10 ~ 60 m/sec. Thus even though the

clearly small cells give rise to processes that conduct impulses at less than 2.5 m/sec and are thus presumably unmyelinated (Gasser, 1955)[17] and the clearly large cells give rise to processes that conduct at more than 2.5 m/sec and are thus presumably myelinated (Gasser, 1955),[17] there is an intermediate group with many cells where such predictions cannot be made. There are enough exceptions that it seems to us an oversimplification to say that large cells give rise to myelinated axons and small cells to unmyelinated axons

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