Brain Research, 103 (1976) 381–385

Decreased conduction velocity in the proximal projections of myelinated dorsal root ganglion cells in the cat

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(Accepted October 23rd, 1975)

The myelinated primary afferent fibers arising from cells of the spinal dorsal root ganglia (DRG) have been thought to have generally constant fiber diameter and, hence, constant conduction velocity over their entire course[6] except for branching terminally within the spinal cord[17] and peripherally near the receptors.

A similar assessment for motor neuron axons has recently been challenged by physiologic data showing a 25% decrease in conduction velocity for the segment between brachial plexus and spinal cord in the baboon[1]. The same authors further claimed to have evidence for similar proximal slowing in myelinated afferents from evoked potential recordings in dorsal roots, although they presented no data on the subject.

In this study, conduction velocities were measured in the distal and proximal processes of individual DRG cells. Eleven adult male and female cats were surgically prepared by L4–S1 laminectomy under deep pentobarbital anesthesia while positioned in a stereotaxic frame. During the experiment, the animal was paralyzed with Flaxedil and artificially ventilated; the temperature of the body and the mineral oil-filled spinal pool were maintained automatically at 36–38 °C. Bipolar stimulating electrodes (pairs of platinum hooks) were placed on the distal stump of the cut right L7 dorsal root and on the sciatic nerve which was dissected free but left intact in the posterior groove between the hamstrings. Monophasic electrical pulses (0.1 or 0.3 msec duration) from isolated bipolar constant current stimulators were always delivered using the hook closest to the ganglion as cathode. Conduction distances were measured *in situ* at the end of each experiment by laying a piece of string from the cathode to the center of the ganglion. Dorsal root distances varied from 15 to 22 mm and sciatic nerve varied from 91 to 133 mm. The methods are described in greater detail elsewhere[13].

Extracellular single unit records were obtained with glass insulated platinum–iridium[21] or Parylene insulated tungsten[14] microelectrodes which were inserted in pairs into the intact L7 DRG. Filtering and differential recording were used to cancel the mass potential evoked by synchronous electrical activation of the DRG cells, and single ganglion cell soma potentials were clearly discernible at threshold as all-or-

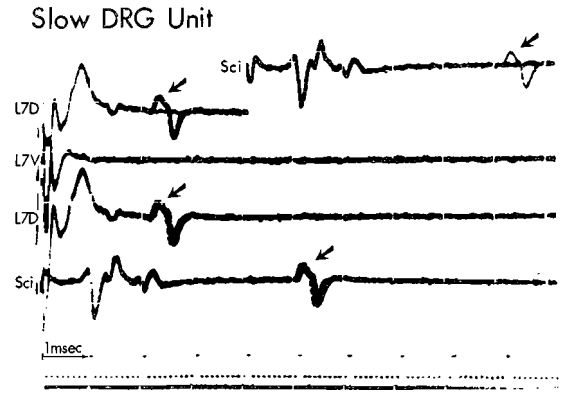

Fig. 1. Multiple superimposed trace recording of a slowly conducting myelinated afferent physiologically driven by hair movement on the medial toe. The bottom trace (Sci) shows the ganglion cell action potential (arrow) beginning 4.9 msec after the end of the 0.1 msec duration sciatic nerve stimulating pulse triggering the sweep (conduction distance = 114 mm from proximal, cathodal electrode; distal conduction velocity = 23 m/sec). The L7D traces show the all-or-none cell responses to a threshold electrical stimulus to the L7 dorsal root (latency = 2.1 msec, conduction distance = 22 mm; proximal conduction velocity = 10.5 m/sec, or 45% of the distal velocity). The baseline deflection in the top trace 4 msec after the initial L7D stimulus indicates a repeat sciatic nerve stimulus which evokes a response in the ganglion cell only on the one sweep when the threshold stimulus to L7D fails to propagate along the fiber. Trace L7V indicates failure to drive this ganglion cell with supramaximal stimuli to the L7 ventral root.

none events with 100–500 μV amplitude. Units were searched for by either physiologic (manual manipulation of the leg) or electrical (supramaximal sciatic) stimuli. Conduction latencies in the proximal (L7 dorsal root) and distal (sciatic nerve) branches of each ganglion cell were taken as the time between the end of the stimulus pulse at threshold amplitude and the beginning of the ganglion cell action potential (see below). Continuity of the two branches was always demonstrated by collision (see Fig. 1). Units were characterized as proprioceptive, cutaneous, or unknown modality based on response to manual manipulation of the leg; noxious, thermal, and vibratory stimuli were not employed.

A total of 124 DRG cells were isolated and electrically characterized antidromically and orthodromically. Fig. 2 shows the scattergram of the 59 proprioceptive and 50 cutaneous afferents plotted by proximal *versus* distal conduction velocities (the 15 unknown modality units fall within the scatter). The regression line (least squares fit, intercept fixed to zero) calculated for all 124 points indicates a typical proximal velocity about 43% of the distal velocity, with considerable scatter from about 20 to 70%. Only 3 points (one not shown) lie conspicuously outside this scatter and all were obtained from one preparation. Distal conduction velocities cover the range 10–120 m/sec, with sparse representation of Aδ fibers and no C-fibers.

The conduction velocities were calculated directly from the distances and latencies without allowance for 'utilization time' or other correcting factors. This would appear to be justified by several aspects of the data. First, the slowing observed appears to be a consistent process for all myelinated fibers, whereas apparent slowing

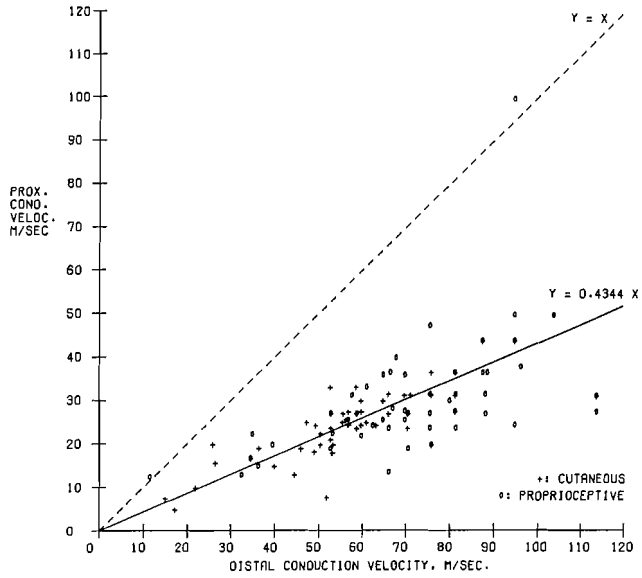

Fig. 2. Scattergram of the proximal *versus* the distal conduction velocities of 59 proprioceptive (○) and 50 cutaneous (+) units. The 45° line for equal velocity is compared to the regression line calculated from the data (intercept fixed to origin, slope = 0.4344).

caused by a constant additive factor reflecting utilization time should be heavily weighted to the faster fibers. Second, there is no difference in the distribution of points obtained with 0.3 msec and 0.1 msec stimulus durations. Third, thresholds were abrupt, with less than 0.1 msec jitter or change in latency with increasing amplitude for 0.1 msec duration stimuli. Finally, other investigators have found such additive delays insignificantly small for DRG cells (0.05 msec)[17]. Sources of experimental error include variability in position of the cell body with respect to the center of the ganglion (approximately 2 mm, with 10% possible error in proximal velocity) and difficulty fixing the onset of the polyphasic action potentials (estimated at 0.1 msec, with 5–20% error for slow to fast fibers, respectively).

The disagreement between these data and predictions of equal velocity on both sides of the ganglion[6] is explained by two previous assumptions. First, the data suggesting that the primary afferent fibers are the same diameter on both sides of the ganglia comes from Dale's 1899 survey in which the distal branch calibers were calculated by subtracting the ventral root population from the spinal nerve totals[3]. Dale realized that his conclusion depended on the constancy of ventral root fiber diameters, and in the same paper, he showed a small increase in caliber from proximal to distal along the ventral root. Larger changes from ventral root to periphery have since been demonstrated histologically[20] and may be inferred from physiologic data[1]. In the DRG itself, the well known proximal decrease in conduction velocity of unmyelinated fibers[6] correlates nicely with a change in axon caliber immediately histologically apparent at the bifurcation[9]. Electron microscopy of the bifurcation sites of myelinated axons shows no comparable dichotomy in either caliber or myelin thick-

ness[9], but this does not rule out such changes beyond the immediate electron microscopy field.

Second, conduction velocity was assumed to be linearly related to myelinated fiber outside diameter. Such a relation is both theoretically sound[8,16] and experimentally demonstrable[12] in the peripheral nervous system, where the ratio of axon diameter to myelin sheath outside diameter is a constant (0.69)[7] nearly equal to the theoretical optimum for maximizing speed for a given fiber size (0.7) (ref. 10). However, marked departures from this optimum have been described; in particular, motor fibers in the ventral root have larger axon diameters but thinner myelin sheaths than in the periphery[20]. Since most of the action current in mammalian myelinated fibers is spent discharging the capacitance across the myelin[15], such structural variation would be expected to compound the problem of inferring conduction velocities from fiber diameters measured in the transition zone from central to peripheral nervous system.

The change in conduction velocity observed here is only a lower bound to the inhomogeneities that may actually be present along any given length of myelinated afferent fiber, since the data yield only the average conduction velocity in two long lengths of fiber. It is, therefore, difficult to speculate on whether such changes represent axonal tapering, changing myelination patterns, differing membrane properties, or fiber branching. Of these possibilities, definite exclusion of even the latter remains elusive. Light microscopy counts concluded that the numbers of dorsal root fibers and ganglion cells were equal[4,11]. However, recent electron microscopy counts have revealed large errors in the unmyelinated fiber counts and also suggest a significant number of DRG cells projecting to the cord via the ventral root[2].

If there is, in fact, no significant degree of branching, then differences in the properties of the myelin producing cells and/or changes in the axon itself seem likely. The former would make an interesting case in which to test recent models of myelin development[5]. The latter could support Tennyson's hypothesis that the two projections of DRG cells have different cytoplasmic origins which are retained after unipolar fusion, with a dendrite-like peripheral process and axon-like central process[19]. The difference in conduction velocity noted here may be another result of such a dichotomy manifested as an axon caliber change and/or differing trophic action on Schwann cells. Failure to see an immediate separation of myelin or cytoplasmic characteristics in the region of the bifurcation[9] does not rule out such transition zones which might have migrated some distance from the bifurcation during maturation when myelination is rapidly changing[18].

Note added in proof. It has been called to this author's attention that proximal and distal conduction velocities of certain L7 DRG fibers may be inferred from some figures in F. J. Clark's Central projection of sensory fibers from the cat knee joint, *J. Neurobiol.*, 3 (1972) 101–110. In those cases, there appears to be no appreciable slowing until entering the spinal cord. Whether this reflects differences in technique (*e.g.*, lack of spinal pool temperature control) or a unique characteristic of this receptor pool (no knee joint afferents were identified in the present study) remains unclear.

The author expresses his deep appreciation to Dr. Karl Frank for advice and support, Dr. R. E. Burke for criticism of the manuscript, and Dr. Zev Rymer for helpful discussion.

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