Reprint Brain, Behavior and Evolution, Vol. 7, No. 1 (pp. 34-83), 1973

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A Review

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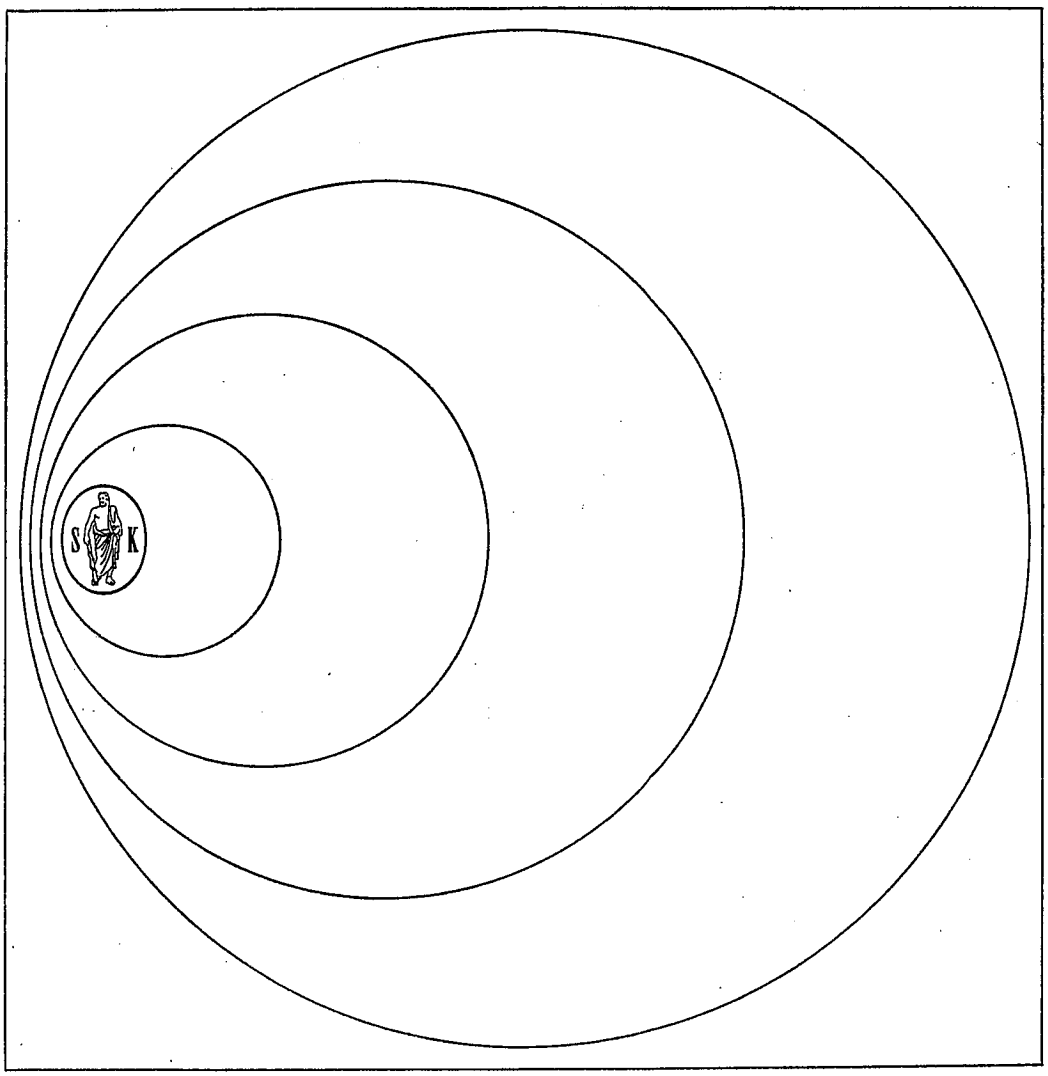

Printed in Switzerland

S. Karger Basel Arnold-Böcklin-Strasse 25 CH-4000 Basel 11
München Angerhofstrasse 9 D-8034 Germering/München
New York P.O. Box 352 White Plains, NY 10602

Brain, Behav. Evol. 7: 34–83 (1973)

Clarke's Column and the Dorsal Spinocerebellar Tract: A Review

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Abstract. The cellular structure of Clarke's column is reviewed with respect to the organization of cell types and their afferent and efferent connections. What is known about the physiology of the spinocerebellar system in the cat is summarized with a critical review of current notions of its function. The paucity of comparative physiological work on the system is indicated.

Key Words
Spinocerebellar pathways
Dorsal spinocerebellar tract
Clarke's column
Spinocerebellar physiology

I. Introduction

The dorsal spinocerebellar tract (DSCT) and the nucleus which gives rise to it, Clarke's nucleus, are perhaps the most studied ascending system of the spinal cord. They have received the attention of anatomists for well over 100 years, and of physiologists for over two decades. Recent emphasis on the importance of specifying the source and pattern of activity in the mossy fibers, the form in which the DSCT fibers terminate, as the key to understanding cerebellar function [105], make a review of the DSCT particularly timely.

A mere listing of all investigations into this system would require a small volume. Accordingly, a complete review of the literature would be exceedingly long. A shorter treatment is in order because it is possible to

[1] The author was supported during part of the preparation of this work by USPHS grant GM00223 to the Department of Physical Biology, Cornell University, and by USPHS grant NS05082 to the Department of Physiology and Biophysics, University of Washington. The author is indebted to Dr. DANIEL N. TAPPER for advice during the preparation of the manuscript, and to Dr. ARNOLD L. TOWE for reading an earlier draft. Gratitude is expressed to HANNA ATKINS for making illustrations.

ascertain the general principles of structure and function of the system from the selected investigations to be cited here. These comprise a substantial amount of the work published previous to and nearly all work published since 1956. OSCARSSON [106] has reviewed the spinocerebellar pathways with an emphasis on a comparison of information transmitted by each one. In so doing, he treated the structure and function of each pathway only superficially. I propose to deal with only one pathway, the DSCT, in detail.

Of first consideration is the anatomy of the system, specifically of Clarke's nucleus, the DSCT and its cerebellar terminations. Having the anatomy firmly in hand, we will then consider the physiological properties of the system that have been deduced from studies at each of these levels. All of the investigations reviewed here are of the DSCT in the cat with the exception of a few in primates [103, 122, 137], and other animals as indicated in the text. Although the system probably exists in a number of vertebrates other than mammals, there has been little physiological work done on species other than the cat.

The following abbreviations will be used throughout this review: DSCT, dorsal spinocerebellar tract; DLC, dorsolateral column; CC, Clarke's column; SCT, spinocervical tract; VSCT, ventral spinocerebellar tract; CCT, cuneocerebellar tract; EPSP, excitatory postsynaptic potential; u-EPSP, unitary excitatory postsynaptic potential; IPSP, inhibitory postsynaptic potential; and FRA, flexor reflex afferents.

II. Anatomical Structures of the Dorsal Spinocerebellar System

A. The Anatomy of Clarke's Column

In 1851, CLARKE [18] described to the Royal Society of London two structures in the gray matter of the spinal cord of the calf, sheep, pig, dog, cat, rabbit, guinea pig, frog and man. He called these structures the 'posterior vesicular columns' and described them as follows:

'two considerable columns of caudate vesicles in intimate connections with the posterior roots of the nerves extend through the whole length of the chord: commencing small at its lower extremity, increasing in size in the lumbar and cervical enlargements, and terminating at the upper part of the medulla oblongata.'

The columns lay just dorsolateral to the central canal in the medial part of the gray matter corresponding to part of REXED's [114] lamina VII and were composed of oval, pyriform, stellate and more or less fusi-

form cells of large size that were in intimate contact with collaterals of the dorsal root fibers [19]. CLARKE [19] expressed surprise that some longitudinal processes of the large cells extend some distance within the column intermingling with the processes of other large cells and the numerous small cells also located within the column.

In some of the later anatomical literature, the columns described by CLARKE were referred to as the nucleus dorsalis, yet in most anatomical and all physiological studies the columns are called Clarke's columns.

CLARKE's original description was of a column of cells extending through the whole length of the spinal cord to the upper part of the medulla; however, it has been clearly shown that the column does not extend through the whole length of the cord. REXED [114] limited CC to the first thoracic through the fourth lumbar spinal segments, in disagreement with BECK [4], but in agreement with the majority of investigators [23, 44, 84, 106, 123].

BOEHME [7] described the fine structure of the column in detail. The larger cells (30–40 μm in diameter) of the column occur in isolated groupings in upper thoracic segments, but are more evenly distributed in other regions. Smaller cells (20 μm or less) are most numerous at upper thoracic levels and least numerous at midthoracic levels. In the lower thoracic and lumbar segments, the larger cells are less densely packed, but there are more cells per unit of cord length. Spaces between these less densely packed cells are occupied by the rich dendritic arborizations of the large cells themselves.

The cells with somata located in the periphery of the circular cross-sectional nucleus send their dendrites toward the center of the nucleus and longitudinally along it. Cells with somata located in the center of the nucleus send dendrites in all directions, but their processes, like the processes of the peripheral cells, do not leave the nucleus. The preceding description holds for the smaller cells and for one class of large cells. There is another class of large cells that possesses the same characteristics and also sends dendritic arbors ventrally into the intermediate nucleus [7]. The connections established in the latter nucleus are unknown. Some dendrites have been observed to extend more than 500 μm in a longitudinal direction within the nucleus. In cross-section, it is the large size of the dendrites and the density of the dendritic plexus that distinguishes CC [85].

LOEWY [85] divided the cells of the column into three classes on the basis of soma size: small cells ($\leqslant$15 μm diameter), medium cells

(20 ⩽ width ⩽ 30 μm, 20 ⩽ length ⩽ 50 μm) and large cells (width ⩽ 55 μm, length 140 μm). The small cells usually were oval in shape, and the medium, oval or triangular, while the large cells usually were lenticular. The cells also differed in the extent to which their dendritic arbors could be traced. Dendrites of large cells were traced for more than 200 μm, those of medium cells up to 80 μm and those of smaller cells only up to 10 μm. The dendritic arbors of some of these medium and small cells were oriented mediolaterally, leading LOEWY [85] to speculate that they might receive different afferent connections than the longitudinally oriented dendrites of the larger cells.

B. Afferent Fibers to CC

The principal afferent fibers to Clarke's nucleus are collaterals of primary afferent fibers that are observed to descend directly from the dorsal columns as illustrated in figure 1 [83, 110, 120, 124]. After entering the nucleus, the afferent fibers (pa in fig. 1) run in a longitudinal direction paralleling the dendrites of the large cells upon which each, after losing its myelin sheath, makes a series of knob-like synaptic terminals, the last one being near the base of the dendrite [7, 113, 124]. SZENTÁGOTHAI and ALBERT [124] termed the last of these synapses of passage 'giant synapses' because of their huge surface area relative to synapses observed on motoneurons. While motoneuron synapses measure 1 or 2 μm in diameter [25], the gigantic terminal endbulbs of CC cells often reach 15 by 8 μm and usually are half-buried in a notch near the soma. The synapses contain relatively large, 400–600 Å, spherical vesicles accumulated on the presynaptic side and a thickened membrane on the postsynaptic side.

Collaterals of group Ia primary afferent fibers run a lateral-to-medial course within the nucleus as they ascend, thus affecting a slice of nucleus oriented obliquely in the cord [44, 123]. In this manner, afferent fibers originating from lower segments contact cells located more medially than do fibers originating more cranially. RETHELYI [112] observed that collaterals of presumed Ib fibers are not somatotopically arranged and tend to be restricted to a much smaller ventrolateral part of the column. This classification of collaterals is based on differing sites of origin of collaterals within the dorsal columns, as well as sites of termination within the nucleus. The group of collaterals termed Ib by RETHELYI

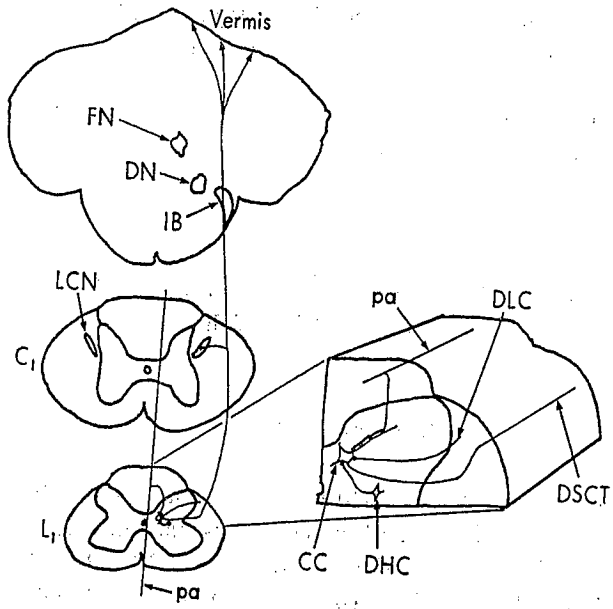

Fig. 1. Schematic drawing of the organization of the DSCT adapted from ECCLES *et al.* [30]. The levels indicated are the first lumbar segment, L_1, the first cervical segment, C_1, and the medullary level. DSCT axons arise from the dorsal horn and traverse the dorsolateral column; giving off collaterals to the lateral cervical nucleus, LCN; passing through the inferior brachium of the cerebellum, IB; and reaching the cerebellar cortex in the vermis. In the medullary section two subcortical nuclei, fastigial (FN) and Deiter's (DN) nuclei, are shown. The enlargement at the right shows the organization of afferents to Clarke's column cells, CC. Collaterals of dorsal column fibers, pa, drop down and make 'giant synapses' on dendrites, while collaterals of cells of the dorsal gray matter, DHC, and axons of the dorsolateral column, DLC, end in synapses on CC somata.

[112] terminate on about one third of Clarke cells, and they are the first to be given off within any segment. Both these observations are in accord with physiological observations [86, 104]. Clearly the separation on these bases is tenuous. Within the nucleus, some collaterals pass more than 2 cm before they end on a Clarke cell. In addition, a single primary afferent gives off preterminal branches that run a longitudinal course paralleling dendrites of a Clarke cell. RETHELYI [112] has estimated that a single primary afferent fiber may have 50 or more bouton contacts on the same dendrite, or several dendrites of a single cell. Sec-

tion of the dorsal roots leads to terminal degeneration in CC so dense 'as to defy minute analysis' [120]. However, section of a single dorsal root yields dense degeneration on some dendrites of a given Clarke cell, while other dendrites are free of degeneration. This leads to the conclusion that afferents from different roots make synaptic contacts on the same cell [124].

After section of a given dorsal root, degeneration is always found to be most dense in the segment into which the severed root entered, and the amount of degeneration decreases gradually, distributing both rostrally and caudally from the entry zone [83]. The phenomenon is illustrated in the histograms of figure 2 constructed from data presented by LIU [83]. Such degeneration is found only ipsilateral to the cut root [44, 83].

There is considerable overlap in the distribution of the dorsal roots to CC. LIU [83] showed degeneration of afferent fibers from the hindlimb in Clarke's nucleus from L_3 to T_7 with the degeneration located more medially in the more rostral segments. Afferent fibers from the trunk were found degenerated throughout the nucleus (indicated in schematic drawing of CC at the bottom of figure 2). In fact, section of sacral and lower lumbar dorsal roots yields degeneration in CC six segments more rostral than the most rostral dorsal root severed [110]. GRANT and REXED [44] severed the L_1 and L_3 dorsal roots and found degeneration in all seven segments rostral to the corresponding entry segments.

In addition to dorsal root collaterals, BOEHME [7] observed that fibers emerging from the DLC and collaterals of cells at the base of the dorsal horn also end in Clarke's nucleus. The significance and any synaptic specializations of the DLC collaterals have not received any attention to date; in contrast, the other afferent source has received considerable attention.

SZENTÁGOTHAI and ALBERT [124] described two sorts of synapses other than giant synapses that are located on the somata of CC cells. Ordinary boutons terminaux were often found on the somata of the cells; however, they were never seen on the dendrites. These boutons did not degenerate following dorsal root section, nor was there degeneration of the third type, the coiled fiber terminals. The investigators speculated that the ordinary boutons are terminations of recurrent collaterals, but LUNDBERG and OSCARSSON [86] demonstrated conclusively that DSCT axons do not give off recurrent collaterals. SZENTÁGOTHAI [123] suggested that the ordinary boutons probably belong to axons of cells of the

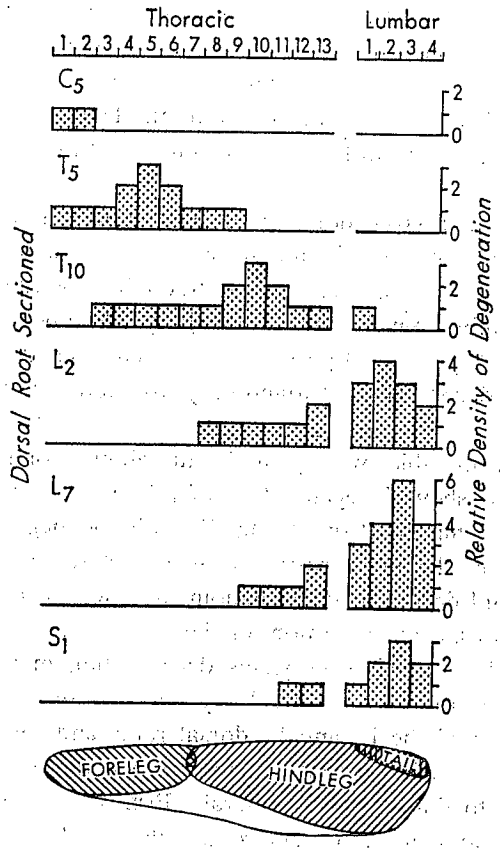

Fig. 2. The relative amount of degeneration within Clarke's nucleus at various levels above and below the level of transection of a single dorsal root are shown for C_8, T_5, T_{10}, L_2, L_7, and S_1 dorsal roots. The transected root is indicated at the left of each histogram. Note that the maximum degeneration for roots entering the segments containing CC (i.e., T_5, T_{10}, and L_2) is in the segment of entry. The lower diagram indicates the roughly topographical organization of CC. The outside perimeter indicates both the boundary of the nucleus and the boundary of the termination areas for afferents originating in the trunk area. Data for the figure are taken from LIU [83].

dorsal horn. These boutons contain smaller spherical vesicles than the 'giant synapses' and probably are excitatory [113]. Perhaps they are terminals of the excitatory interneurons whose presence in the pathways to Clarke cells has been demonstrated [88], or of the border cells of RE-

THELYI [112], for which a role in transmission in CC has been suggested by KOSTYUK [73].

SZENTÁGOTHAI and ALBERT [124] suggested that the coiled fibers were also collaterals of dorsal horn cells, and RETHELYI [113] confirmed their local character by showing that they do not degenerate after deafferentation or cord hemisection below the caudal end of CC, at L_4. On the basis of the flattened vesicles in these synapses, RETHELYI suggested that they may represent inhibitory interneuron terminals mediating postsynaptic inhibition [7]. It must be borne in mind, however, that separation of synaptic effects based upon vesicle structure is purely speculative at present [79, 128].

RETHELYI [113] also described synaptic contacts between small boutons with flattened vesicles and the giant synaptic terminals. From structural considerations he concluded that the giant synapses were postsynaptic in this axo-axonic synaptic complex. It seems plausible that this structural interrelation mediates presynaptic inhibition; however, the existence of this inhibition is disputed [35, 65]. Nevertheless, these axo-axonic contacts occur frequently in Clarke's nucleus [113].

C. Efferent Fibers from CC

The major efferent outflow of the large cells of CC goes into the homolateral cerebellar vermis via the DLC [23, 43, 82, 83, 117, 119, 122]. The route has been shown by tracing the axons into the DLC in microscopic preparations, by tracing degeneration following lesions in the column itself and by chromatolysis of Clarke neurons following section of the DLC in the thoracic segments. The small cells of the nucleus are not chromatolyzed after the same section of the DLC, implying that they have only local terminations or do not go into the DLC [81, 113, 117].

The DSCT axons, 7,000–10,000 of which traverse the length of the cord in the DLC [5], are seen to be rather coarse [39, 43]; in fact, 36% of the fibers at the L_1 segment are larger than 5 μm in diameter [5].

Counts and measurements made by VON BEUSEKOM [5] required the assumption of homogeneity of the DLC in a localized region where the DSCT was supposed to be (described below). MANN [95] showed that the DLC is inhomogeneous at nearly every point [89] and that DSCT axons may be located throughout the DLC, with the exception of the

most dorsomedial part. Most of the DSCT axons probably are of large diameter since the somata of CC cells that project into the DLC are relatively large. There is no physiological evidence that fibers in the DSCT are smaller than 3 μm in diameter [88, 95].

As the axons ascend the spinal cord, they shift their position dorsally and toward the periphery [92, 110, 117, 137]. This suggests that new fibers are added to the tract in its medial and ventral parts and that there is a segmentotopic organization in the dorsolateral funiculus.

The DSCT axons may give off collaterals in the cervical segments of the spinal cord, since chromatolysis in Clarke's nucleus is much less severe following transection of the DLC above this level than after an equally extensive transection below this level [82]. The severity of the chromatolysis of Clarke cells is less, following the higher transection, than would be expected just on the basis that more axoplasm is spared [6]. SPRAGUE and CHAMBERS [quoted by 47] also found no retrograde changes in Clarke's nucleus following cerebellectomy. These results suggest that collaterals of DSCT fibers are sustaining the cell; they suggest also that the fibers that degenerate in the lateral cervical nucleus following lesion of Clarke's nucleus [5, 46, 47] are true collaterals and not merely propriospinal fibers originating in or around CC (fig. 1). Cells of the lateral cervical nucleus send collaterals into the inferior olive and thus could be part of a DSCT-lateral cervical nucleus-olivo-cerebellar pathway [102].

From its beginning in the lumbar segments of the spinal cord, the DSCT occupies the dorsal portion of the lateral funiculus, especially a crescent-shaped zone along the dorsal and lateral edges of the funiculus [16]. There is some disagreement about the most dorsomedial portion, where the SCT is said to lie. Most investigators have restricted the DSCT from this area [105]; however, some anatomists show degenerating fibers there [16]. The fibers in this area probably are SCT fibers that terminate in the lateral cervical nucleus and not DSCT fibers [95, 136].

At the level of the gracile and cuneate nuclei, the DSCT occupies a dorsolateral position in the posterolateral funiculus just ventral to the descending root of the trigeminal nerve. More rostrally the tract occupies a crescent-shaped region located along the dorsal and lateral edge of the restiform body, much as in the spinal cord. At the level of Horsley-Clarke coordinate P8, the DSCT has moved into a more dorsomedial position in the restiform body in preparation for its entry into the cer-

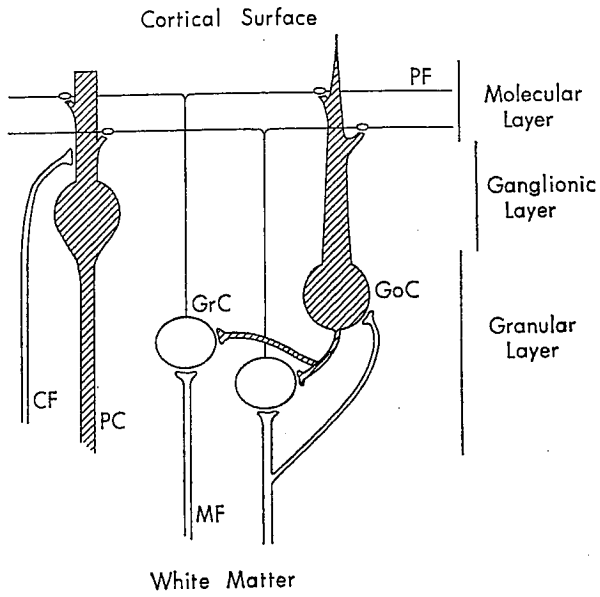

Fig. 3. Schematic drawing of a transverse section through the cerebellar cortex. Afferent fibers are indicated as MF, mossy fibers, and CF, climbing fibers. The primary termination of MF is on granule cells (GrC) whose axons are the parallel fibers (PF). The Golgi cells (GoC) are inhibitory interneurons in a feedforward inhibitory system in which MF activity inhibits the MF-GrC relay and in a feedback inhibitory system in which PF activity inhibits the MF-GrC delay. Both PF and CF are excitatory to Purkinje cells (PC), the only cerebellar efferents that have only inhibitory effects. Another cortical interneuron, the basket cell, has been omitted for simplicity.

ebellar white matter [5, 16]. At this point, the tract is a small, tightly packed, circular bundle adjacent to the lateral vestibular nucleus [4].

The tract fibers then course through the white matter of the cerebellum, giving off collaterals to the folia and narrowing along the way [129]. Some investigators have suggested that the fibers also send collaterals into the cerebellar nuclei [30, 92, 98]; however, others suggest that they proceed directly to the cerebellar cortex [4, 43, 131]. Responses attributable to DSCT activity have been recorded from these nuclei [30]. Despite this disagreement, there is complete agreement that the final termination of DSCT fibers is as cerebellar mossy fibers [10]. The relationship between mossy fibers and neurons of the cortex has been demonstrated by ECCLES *et al.* [30], and is summarized in figure 3.

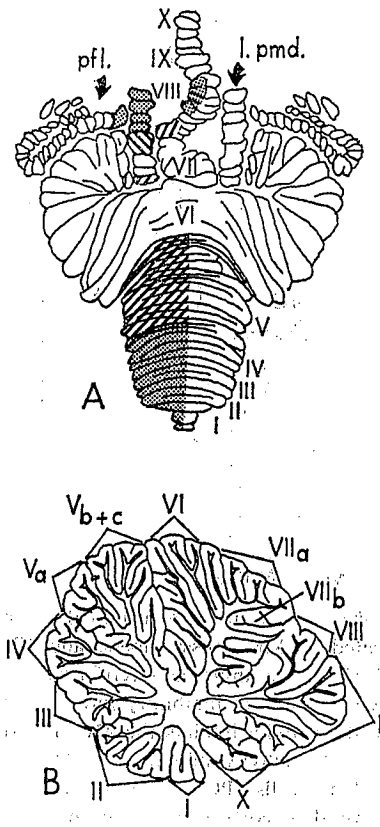

Fig. 4. Termination of DSCT and CCT in the vermis and LARSELL's terminology. *A* Termination of DSCT (stippled areas) and CCT (hatched areas) in the vermis as discussed in text. In diagram, cerebellum has been unfolded to show all lobules; rostral direction is downward. *B* Midsagittal section through cerebellum with lobules indicated according to the terminology of LARSELL [81]. Abbreviations employed: pfl., paraflocculus; l.pmd., paramedian lobule. Termination sites from GRANT [43].

D. Cerebellar Termination of DSCT

Degeneration of DSCT fibers has been observed at one time or another in practically every region of the cerebellum except the cerebellar hemispheres. Recently the termination sites have become more restricted as techniques for creating lesions and staining degenerated fibers have

improved. Part of the confusion over termination sites is perhaps the result of the old terminology applied to regions of the cerebellum. Not long ago, LARSELL [81] developed a system for numbering the lobules, helping to eliminate some of the confusion. The general features of his scheme are illustrated in figure 4B.

Fibers of the DSCT have been traced to LARSELL's [81] lobules VI, VIII, and IX [4, 43, 137] into lobule VII and the paramedian lobule [4], but not into X [4, 137]. The major site of termination is considered to be the anterior lobe, particularly lobules II–IV and the rostral part of V [129]. GRANT [43] noted two major areas of termination: one anterior, in lobules I–V, and one posterior, in lobule VIII, in the pars copularis of the paramedian lobule, and in the most medial part of the paraflocculus, but not lobule IX (fig. 4A).

The majority of DSCT fibers terminate ipsilaterally; however, a few fibers are found to terminate contralaterally. The course taken by the fibers in reaching the contralateral cortex is unknown. Ipsilateral fibers terminate most densely in a strip of cortex just lateral to a sagittal plane through the lateral extremity of lobule I; degeneration more medially is sparse [43]. ECCLES *et al.* [30] showed that the mossy fiber projection from the spinal cord (including the ventral spinocerebellar tract, VSCT) is mainly to the deeper regions of the granular layer of the cortex, while mossy fibers originating in the brain stem project to more superficial layers. As yet, there is dispute as to whether such a difference in cortical effects exists on electrophysiological grounds [3, 115].

Recently, the organization of spinocerebellar terminations within the anterior lobe has received considerable attention. VOOGD *et al.* [131] observed degeneration resulting from hemichordotomy at C_1 or C_3, thus including the DSCT, the rostral spinocerebellar tract and the VSCT. The termination pattern ipsilateral to the transection probably represents DSCT fibers in the main, since only a few VSCT fibers terminate ipsilateral to the section [106]. The amount of degeneration due to transection of the rostral spinocerebellar tract is unknown, but may not be insignificant since the tract is known to terminate in the hindlimb as well as the forelimb zone [108]. These authors examined both the white and gray matters of the cerebellum and found in both rostrocaudal bands consisting of alternating very dense and very sparse regions of degenerating fibers. Six maxima of degeneration were clearly seen in lobules III and IV and less clearly seen, but present, in lobule II and the rostral part of lobule V. The lack of clarity of the pattern in lobule II is due to

the greater amount of degeneration in the troughs between maxima. In lobule V, these troughs are filled with degenerated CCT fibers, provided suitable lesions have been made. The CCT is the forelimb equivalent of the DSCT, and it may be interrupted by lesion of the external cuneate nucleus [20].

The separation between DSCT and CCT terminations was described in less detail by GRANT [43]. It appears that the cortex is organized topographically into transverse zones of hindlimb and forelimb activity (fig. 4A), but within each larger division there is a distribution of DSCT fiber terminations that is longitudinal. Such longitudinal organization may be related to the destination of the output of those regions. CHAMBERS and SPRAGUE [17] have shown that the cerebellum is organized into longitudinal zones from which Purkinje cells project to different cerebellar nuclei. Five such zones have been described by VOOGD [130] that are roughly in correspondence with some of the six maxima of DSCT degeneration observed by VOOGD *et al.* [131].

No evidence exists for a differential distribution of fibers in the cerebellar cortex from different segments above the caudal end of CC [43]. As yet there is no anatomical tool that allows further refinement of topographical organization. Electrophysiology offers such a tool.

E. Comparative Studies

Though it has been known for a considerable time that many species other than cats possess a DSCT or some analogous pathway [18, 19], curiously, few physiological studies have been performed in other animals. Anatomical studies indicate that the DSCT is very large in ungulates compared with other mammals [134], yet these animals have received no attention from neurophysiologists interested in the spinocerebellar tracts.

A pathway analogous to the DSCT is present in plagiostomes, at least in sharks. Fibers originating in the ipsilateral upper cervical cord, maintain a lateral position as they course through the medulla and terminate in the central part of the cerebellum [2]. In teleosts, a fairly large spinocerebellar tract has been observed for *Prionotus* [48] and *Gadus* [9]. In *Prionotus,* the tract consists of heavily myelinated fibers that travel near the spinal trigeminal tract and probably contains fibers homologous to the DSCT. In the alligator *(Alligator mississippiensis),*

HUBER and CROSBY [56] have described a large spinocerebellar tract that lies in the cord just under the dorsal horn, runs a course in the medulla near the trigeminal nucleus and enters the cerebellum. This tract carries crossed and uncrossed fibers that probably originate in the homologue of Clarke's nucleus. LARSELL [80] has described a dorsal spinocerebellar system in the lizards, *Anniella, Scleroporus, Phrynosoma, Gerrhonotus,* and *Thamnophis,* but the origin of this tract within the cord is unknown. In the chameleon, SHANKLIN [116] found a DSCT containing crossed and uncrossed components, but with an emphasis on the crossed. None of these species has been examined electrophysiologically, as far as this writer knows.

In some avian species, the DSCT has been studied more extensively, with some electrophysiology that will be described later. In the pigeon, dusky horned owl, hummingbird and chicken, the pathway is seen in the superficial part of the lateral white matter and it proceeds rostrally along the lateral surface of the medulla. It enters the cerebellum quite abruptly after passing through the rootlets of the VIIIth nerve. Degenerating fibers have been followed into lobules II–V, VIa, VIII and IX [135].

III. Electrophysiology of the Dorsal Spinocerebellar System

Electrophysiological studies of the dorsal spinocerebellar system are many, making it perhaps the most well-known of the ascending systems, and certainly the best known of the cerebellar afferent systems. These studies have focused on three different areas: Clarke's nucleus, the DSCT, and the cerebellar cortex itself.

A. Physiological Cell Types in the DSCT

Interest in the electrophysiology of the dorsal spinocerebellar system antedates the beginning of widespread usage of microelectrodes for intracellular recording in the central nervous system. Many important features of the system have been studied without resorting to intracellular recording, but instead, using mass discharge or single axon recordings.

GRUNDFEST and CAMPBELL [45] performed the first significant electrophysiological study of the mass discharge in the DLC. They concluded that the tract was activated only from muscle proprioceptors; howev-

er, this notion is incorrect, even for mass discharges [91]. Stimulation of muscle nerves yields a well-synchronized DLC volley, while stimulation of cutaneous nerves leads to a longer-latency, less-well synchronized DLC volley with a prominent delayed discharge. The stylized traces of figures 5A–D demonstrate this difference. The longer latency of the cutaneous response is accounted for by the lower conduction velocity of cutaneous peripheral nerves [77, 91]. The latency of cutaneous discharges in the DLC is probably obscured by the presence of a SCT response, since LUNDBERG and OSCARSSON [88] showed that there is no cerebellar cortical potential corresponding to the first component of the mass discharge in the DLC. Figures 5E–H show typical responses recorded from the cerebellar cortex (E, G) and the DLC (F, H) due to stimulation of hamstring (E, F) and superficial peroneal (G, H) nerves. Note the lack of an early discharge in G corresponding to the early discharge in H. The dispersion of the discharge evoked by cutaneous nerve stimulation is presumably related to the dispersion reported for cutaneous volleys in the dorsal columns [84].

Dorsal root fibers of all thresholds make excitatory connections on DSCT neurons, as judged from the increasing response in the DLC with each increment in the dorsal root discharge, with the reservation that fibers other than those of DSCT (e.g. SCT) may contribute to the responses. The input-output relation for group I volleys is approximately linear, while that for cutaneous volleys is curvilinear, rising more steeply than that for group I and reaching a 100-per cent response plateau at about 60% of the maximal cutaneous volley. It appears that little summation is required to secure a postsynaptic discharge [45, 84, 91], in agreement with the suggestion of EIDE *et al.* [38] and MANN [95].

There is little reduction in the mass response amplitude when stimuli are applied at or in excess of 100/sec, except in the delayed discharge of the cutaneous response [91]. Post-tetanic potentiation is present in the DLC, but it is less than one tenth of the amount observed in the ventral roots [51, 91]. Apparently there is only a small subliminal fringe in the DSCT cell population compared with that in motoneuron pools.

Verifying the existence of a subliminal fringe, HOLMQVIST *et al.* [51] noted that some cells that failed to discharge upon single or double stimulation were discharged post-tetanically.

While recording the mass discharge in the DLC is a useful method in preliminary examination of the DSCT, it is not sensitive enough to detect small changes that are accessible to single fiber recording (intracel-

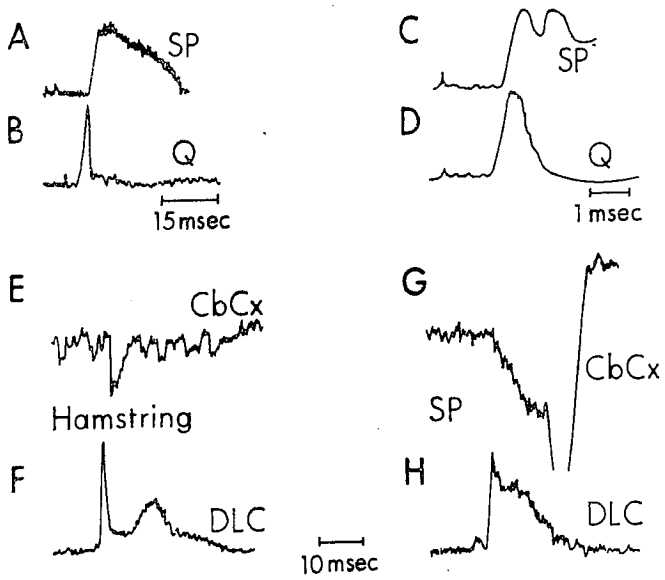

Fig. 5. Typical responses that can be recorded from the dissected dorsolateral column following stimulation of superficial peroneal (A, C) and quadriceps nerves (B, D), illustrating differences in latency and duration of responses as discussed in text. Simultaneous recordings from the cerebellar cortex and the intact dorsolateral column are shown in E, G and F, H, respectively. There is no discharge in the cerebellar cortex (G) corresponding to the early discharge in the dorsolateral column (H) following cutaneous stimulation, but there is a corresponding potential in the cortex for the first discharge following hamstring stimulation (E, F). Traces adapted from HOLMQVIST *et al.* [51].

lular or extracellular). For determining which sorts of peripheral receptors activate DSCT axons, single unit recording is necessary.

The receptive field and discharge properties of the cells of the DSCT were illuminated by a series of experiments performed in the laboratories of LUNDBERG and OSCARSSON [51, 76–78, 86–88, 90]. A method for identifying DSCT axons was developed using the properties of the direct passage to the cerebellar cortex and the lack of DSCT axons caudal to CC. Fibers that were activated antidromically from the cerebellar cortex, but which were not activated by stimulation of the DLC at L_5, were classed as DSCT axons. The importance of this verification is emphasized by the demonstration of three non-DSCT pathways in the DLC [89].

Table I. Characteristics of DSCT axons

Subdivision	Class	Adequate stimulus	DSCT, %	Conduction velocity[1] m/sec	Spontaneous activity[1] spikes/sec
A. Proprioceptive[2]			53	63 (21–100)	17.8 (0–09)
	1. Group Ia	muscle stretch			10[3]
	Group II	muscle stretch			–
	2. Group Ib	muscle twitch			20[3]
B. Exteroceptive				66 (21–110)	9.6 (0–75)
	1. Footpad	pressure on footpads[4]	19	–	–
	2. Mechanoreceptors			63 (21–110)	8.2 (0–75)
	a. Hair	hair displ. (h)		63 (36–85)	6.4 (0–30)
	b. Skin	touch (t)		70 (41–95)	1.2 (0–5)
	c. Hair and skin	h+t		66 (21–110)	6.7 (0–20)
	3. Skin and muscle[5]	h, t and muscle stimulation	8	71 (21–95)	12.2 (0.45)

[1] Values given are means and ranges (parentheses).
[2] Defined by response to adequate stimulation [67, 90].
[3] Data taken from JANSEN and RUDJORD [67].
[4] Including toepads and skin between, in some cases.
[5] Muscle component activated by muscle squeeze only.

1. Proprioceptive Subdivision

Five classes of the DSCT (table I) were recognized by LUNDBERG and OSCARSSON [88] and by OSCARSSON [105]. One class of DSCT axons was caused to discharge by activation of groups Ia and II primary afferent fibers from muscle spindle receptors. Natural and selective activation of Golgi tendon organs demonstrates conclusively that no propagated discharge is elicited in this group of DSCT cells by activity in Ib fibers [90].

A second class of DSCT axons is activated by group Ib fibers. This group comprises about 36% of the group I-activated axons [86].

JANSEN and RUDJORD [67] further divided the first class, Ia and II DSCT cells, into two groups on the basis of the similarity of their responses and the responses of different spindle receptors to muscle stretch. Group Ia-activated cells respond with increasing frequency to increasing

length of the muscle, but when the stretch is completed, the frequency falls rapidly to a lower rate (fig. 6B, a). Group II-activated cells respond in the same manner to dynamic stretch, but there is a more gradual and less pronounced decrease in frequency when the dynamic phase is ended (fig. 6B, b). The threshold for electrical stimulation is lower for the former group than for the latter, and the firing during stretch is more irregular. Group Ia-activated units tend to respond to electrical nerve stimulation with a single spike; however, group II-activated units respond repetitively to single shock stimulation [78]. Neither group responds to twitch contractions as do the class Ib DSCT cells (fig. 6A, a–c). Group Ib-activated DSCT axons do not show high-frequency discharges during passive extension, but do respond with a high-frequency discharge to twitch contractions (fig. 6A, c). With electrical nerve stimulation, the units respond at thresholds characteristic of the group Ib afferent fibers with which they are presumed to be associated [67, 90].

Though the extracellular record of the discharge of muscle afferent-associated DSCT cells allows them to be classified into three groups, it is not so easy to distinguish them on the basis of intracellular records of postsynaptic potentials. The large size of the cells of Clarke's nucleus have made them tempting targets for intracellular recording, but despite the size of the somata, many investigators have emphasized the difficulty of recording intracellular potentials from these cells [24, 31, 53]. When such penetrations are done successfully, the cells are found to be damaged, as suggested by their rather low membrane potentials. Some properties may still be studied in partly damaged cells and in the few cells that are apparently viable.

Increasing the size of an afferent volley causes an increase in the slope of the EPSP observed in Clarke cells [24]. In addition, one third of the DSCT cells studied by ECCLES *et al.* [31] responded to stimulation of more than one muscle nerve. These observations imply convergence of several afferents onto each Clarke cell, corroborating the anatomical observations of SZENTÁGOTHAI and ALBERT [124]. Convergence of activity from more than one muscle is common for Ia and II DSCT units, but not for Ib DSCT units. The full significance of this difference has not been explained as yet, but perhaps the cerebellum recovers information about tension in individual muscles from Ib DSCT cell discharges and joint angle from the discharges of Ia and II DSCT cells. Some of the latter groups do respond to stimulation of only one muscle, and those cells may be adequate to signal muscle length.

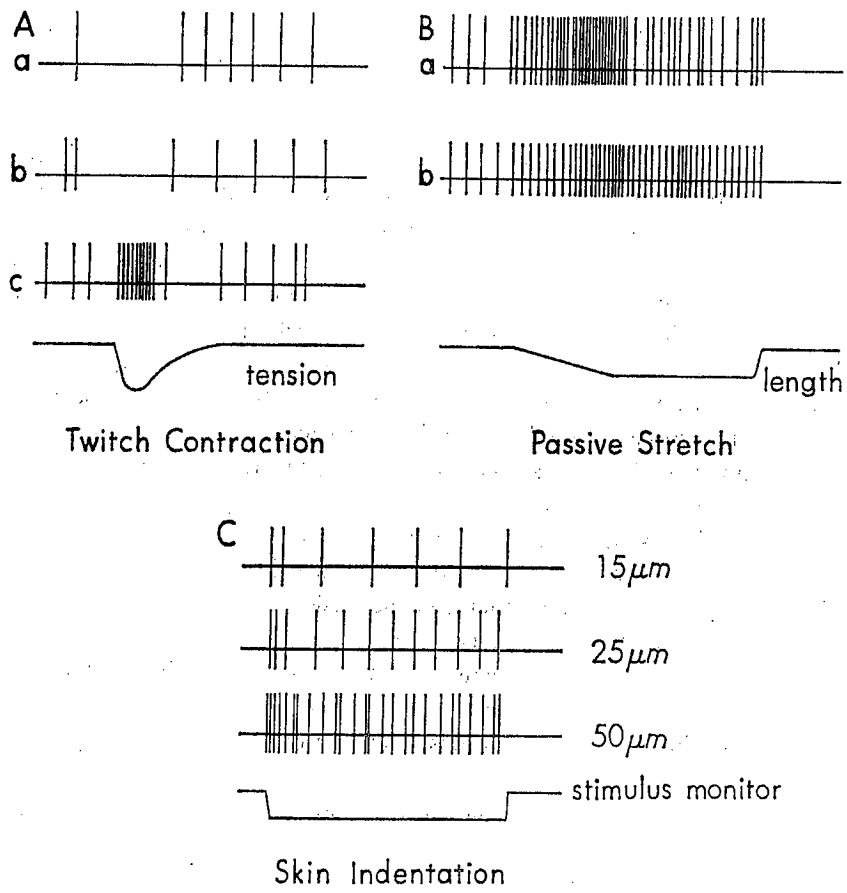

Fig. 6. Responses typical of various classes of DSCT axons are illustrated. Aa, Ba are typical responses of a group Ia DSCT axon to twitch contraction and passive stretch of the appropriate muscle. Similar responses of a group II DSCT axon are shown in Ab, Bb. No response or a slight depression of ongoing activity was observed in these units during twitch contraction, but not in a group Ib DSCT unit (Ac). In C are shown typical responses of a cutaneous DSCT axon (one responding to displacement of slowly adapting receptors) to controlled steady indentation of the skin to indicated depths. The lower trace is the stimulus monitor throughout the illustration. All responses are diagrammatic and do not represent actual cell discharges. Approximate times for the illustrated events are 0.1 sec for the duration of twitch contraction (A), 0.8–1.0 sec for the duration of the dynamic phase of the passive stretch (B), and 2 sec for the duration of maintained displacement (C). Data for the figure taken from JANSEN and RUDJORD [67] and unpublished observations.

In addition to the convergence of different muscle groups, there is convergence of activity from different types of afferent fibers as well. ECCLES *et al.* [31] located about equal numbers of Clarke cells in which they could evoke monosynaptic EPSPs by stimulation of either group Ia or Ib afferents or both group Ia and Ib afferents. In addition, they observed convergence of excitatory action from groups Ia and II, groups Ib and II, and groups Ia and Ib and II in a small, but significant number of cells. It will be recalled that LUNDBERG and WINSBURY [90] demonstrated a complete separation of Ia and Ib activity in Clarke cells. Apparently only one of these afferent fiber types is capable of evoking a propagated discharge in each cell, despite the fact that both evoke EPSPs, thus the difficulty in identifying cell types in terms of EPSPs.

LAPORTE and LUNDBERG [76] showed that some neurons excited by electrical stimulation of a certain muscle nerve failed to respond on adequate activation of the stretch receptors. Activity from this muscle must summate to evoke a discharge, but the asynchrony of stretch-evoked discharges is too great to allow such summation.

IPSPs also were observed in Clarke cells, but their latencies were on the order of 0.8 msec longer than the latencies for EPSPs in the same cell, suggesting that conduction is disynaptic, i.e. an internuncial is interposed between the primary afferent terminal and the Clarke cell [24]. IPSPs evoked by group I stimulation had rise times of 2–3 msec and durations of 10–20 msec, while those evoked by FRA stimulation had a somewhat slower time course, with rise times of 3–10 msec and durations of 15–50 msec [53]. The reversal of the IPSP to a depolarizing potential by use of a KCl electrode suggests that the mechanism of production is the same as in motoneurons [24].

In group I-activated neurons, disynaptic IPSPs were observed following stimulation of group I afferents of antagonist muscles, but also upon stimulation of group I afferents of other muscles [24, 31]. Additional IPSPs were produced in group I-activated neurons by stimulation of cutaneous and high-threshold muscle afferents.

ECCLES *et al.* [31] observed that a large proportion of Clarke cells show no IPSP from any source. In fact, the number that do show IPSPs is not great enough to account for the inhibition of the mass discharge observed in the DSCT [31, 35]. Inhibition of the mass discharge has a time course much like that for presynaptic inhibition elsewhere in the central nervous system. The maximum depression of the group I test re-

sponse occurs at 20 msec and the total duration is more than 100 msec following volleys in other group I fibers [35]. Using WALL's [132] method, ECCLES *et al.* [35] showed an increase in the excitability of the group I primary afferent terminals in CC during trains of impulses in group I fibers from both flexor and extensor muscles and in cutaneous nerves. The time course of the increased excitability was a mirror-image of the time course of inhibition of the mass discharge in the DSCT. This analysis has been extended to show that both Ia and Ib primary afferents are depolarized by conditioning volleys in Ib fibers and FRA, but not by volleys in Ia fibers [61].

The effectiveness and duration of the inhibition of the group I test response are potentiated by administration of nembutal and strychnine in a manner similar to that shown for presynaptic inhibition of the monosynaptic reflex. The result is the same whether the inhibition is produced by Ib volleys or cutaneous volleys [60]. This can be considered further evidence that the inhibition is presynaptic, but one must keep in mind the work of KELLERTH [70] demonstrating that effects of pharmacological agents cannot be used reliably to distinguish between pre- and postsynaptic inhibition.

There is yet some disagreement about the existence of presynaptic inhibition in this system. On the basis of changes (and lack of changes) in discharge characteristics of DSCT cells during inhibition, JANSEN *et al.* [65] concluded that there is either a mixture of pre- and postsynaptic inhibition in variable proportions on various units, or a purely postsynaptic inhibition with a variable degree of shunting of excitatory currents. These authors prefer the second possibility because (1) it is simpler, (2) it explains the inhibitory effect on spontaneous activity, (3) it explains the rebound after inhibition, (4) it explains the similarity of muscle-evoked and cortex-evoked effects, and (5) it corresponds with the anatomy in which synaptic contacts are distributed over the dendrites. These points also are easily explained by invoking a mixture of pre- and postsynaptic inhibition that, in addition, can explain the observed increase in the excitability of the primary afferent terminals and the axo-axonic synapses described by RETHELYI [113]. A mixture of pre- and postsynaptic inhibition is, in the final analysis, a postsynaptic inhibition with a variable shunt of excitation, and it has the advantage that the nature of the shunting mechanism is known.

The foregoing discussion of inhibitory potentials in CC lacked a specification of the influences of such potentials on the discharges propagat-

ed along the DSCT axon. This information has emerged from the studies of single axons in the DSCT.

Convergence of inhibition is common for muscle-activated DSCT units. Stretching muscles that do not supply excitation often leads to inhibition, especially if the muscle is antagonistic to the muscles producing excitation [95, 105]. JANSEN *et al.* [64] showed that gastrocnemius and soleus tendon organ activity inhibits ankle flexor Ia DSCT units, while gastrocnemius and soleus primary spindle activity inhibits digit flexor Ia DSCT units at muscle lengths that would be encountered during physiological activities [61]. This specificity and the specificity of excitatory effects [88] suggest that signals mediated by DSCT Ia units are not simply a function of length and rate of change of length of a certain muscle, but rather a more complex function of these parameters, and tension in a number of interrelated muscles [64]. Signals of the length of the appropriate muscle must be submerged in this complex function, leading one to question the ability of the granule cells to decode the signal. WALLØE [133] suggested that this is possible only if the DSCT signals are read by granule cells from single DSCT axons. This may be the case (as he suggested), for a mossy fiber is observed to make only one contact with the dendrite of a granule cell in each glomerulus, but, on the other hand, a single granule cell usually contributes dendrites to 4–5 glomeruli [30]. It would appear that activity in more than one mossy fiber may be necessary to bring a granule cell to discharge [34].

2. Exteroceptive Subdivision

The Swedish investigators distinguished a third class of DSCT neurons activated by pressure on footpads [76, 88]. This class responded to light pressure on one or two pads and sometimes only a part of one pad, with only moderate adaptation during sustained stimulation. Usually these units did not respond to stimulation of hairs or other structures around the pads. In another study [95], few such units were found, but units activated by stimulation of pads were also activated by stimulation of skin and hairs surrounding the pad or between toe- and footpads when both were sensitive.

The fourth class of the DSCT is activated by mechanoreceptors in the hairy skin. The neurons are activated from relatively restricted cutaneous receptive fields ranging in size from a few square centimeters to about one half of a limb. Many units were activated by light touch in the center of the receptive field, but only responded to pressure or pinch

on the periphery [105]. These units responded to movement of hairs, to displacement of slowly adapting mechanoreceptors and to both hair movement and mechanoreceptor displacement [95]. Many of the units (especially those with larger receptive fields) activated by both kinds of stimulation had heterogeneous receptive fields, i.e. a given receptor type was not sensitive over the whole of the field. This partially accounts for the differences in sensitivity across fields as demonstrated by the Swedish group [105], but in addition, stimulation of the same receptor type in different areas of the field often elicited a quite different response [95]. Characteristics of the discharges of the different types of primary afferent fibers [12, 14] from the skin were observed in the DSCT discharges to a variable extent, depending upon where in the field the associated receptor structure was located [95]. Hair-associated units usually responded with a single impulse or a short burst when a hair was bent in one direction and a similar discharge was often observed when the hair was released. Cells responded to sustained stimulation of slowly adapting receptors with a slowly adapting response if the receptors were in the center of the area of the field in which they were sensitive. In the other areas, the response was often more attenuated, even to the point where it sometimes became phasic at extreme distances from the center [95]. In response to electrical nerve stimulation, there were as many as 16 impulses initiated in these units per volley, occurring at frequencies up to 1,000/sec. Sometimes there were only one or two spikes per volley, occurring 2–6 msec later than the repetitive responses in other fibers. Probably these late responses were polysynaptically evoked [78]. Inhibitory effects from other areas of skin were occasionally found, but these areas had no consistent spatial relationship to the excitatory field [95].

DSCT neurons of the fifth class were activated by cutaneous and high-threshold muscle activity. Some cutaneous afferents were connected to DSCT neurons monosynaptically, but excitation from high-threshold muscle was mediated by interneurons [105], or, at least, the excitation occurred with longer latency. The activity of these units was dominated by the cutaneous component of the receptive field, as might be expected from its monosynaptic connection to the cell. Response to cutaneous stimulation was much like that of the purely cutaneous class, and the receptor types in the fields were similar. The receptive fields were observed by OSCARSSON [105] to be larger than those of purely cutaneous cells; however, MANN [95] was unable to distinguish these cells on the