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Functional and Anatomical Features of the Dorsal Column Nuclei in Mammals and Lower Animals

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Abstract The dorsal fasciculi of the spinal cord are known as the chief pathways for the conduction of impulses underlying deep sensibility and tactile discrimination from limbs which reach the thalamus and ultimately the cerebral cortex after a relay at a bulbar level, the dorsal column nuclei. It is believed that the development of the dorsal fasciculi and their nuclei in the mammalian and primate series is correlated with increasing sensory discrimination in the skin and the increased development of proprioceptive sense in the limb musculature. In this review we will discuss the reflection of the development of limbs and sensory discrimination in lower animals and mammals on the organization and some functional aspects of these nuclei.

Keywords: *Gracile, Cuneate, Neurons, Development*

1. Introduction

The dorsal column nuclei (DCN) are interested part of the central nervous system for studying the somatosensory pathways [1]. These nuclei receive primary afferent fibers from the trunk and limbs and give rise to the medial lemniscus that ascends upward and terminate in the thalamus. The fibers then reach the primary somatosensory area in the cerebral cortex. It is commonly known that the term DCN refers to the gracile nucleus (Gr) and cuneate nucleus (Cu). Actually, the tailed-animals often possess an accessory cell group called nucleus of Bischoff (Bi) situated in the median plane between the two gracile nuclei of each side and is considered as a part of DCN [2,3]. The external cuneate nucleus and nucleus Z (a rostrolateral extension of Gr) are sometimes considered as a DCN [4,5], but they will be out of the focus of this review.

2. First Appearance of the DCN

The rostral extension of the dorsal fasciculi of the spinal cord is studied in different vertebrate species. The first appearance of the DCN have been found in reptiles [6]. Some authors denied the presence of the DCN and medial lemniscus system in subreptilian vertebrates [6,7]. Others suggested that a primordial DCN are present in the obex region (the junction between the open medulla and closed medulla) of amphibians [8,9,10].

3. Amphibians

The first vertebrates known to have developed sensory fibers projecting to supraspinal levels are the amphibians [11,12]. Loosely packed neurons are collected at the rostral end of the dorsal spinal column in the frog medulla extending from the second spinal root to the obex [10] (Figure 1). Although not divided into Gr and Cu, this neuronal collection would appear as a homologue of the DCN in mammals [13]. Three different neuronal populations have been described based on the size of the nerve soma [10]. The most frequent neurons (>70 %) were medium-sized, measured 10-20 µm in diameter, and were homogeneously distributed throughout the nucleus. Neurons which were less than 10 µm in diameter comprised 15 % of the nucleus and were more frequent in the rostral portions. Neurons which were over 20 µm in diameter represented the remainder and were more prominent in the caudal parts of the nucleus.

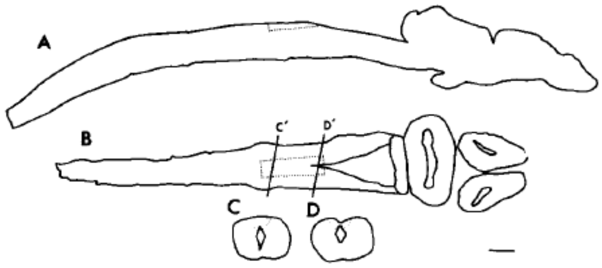

Figure 1. The approximate location of the dorsal column nucleus in the frog brain. Figure from Silvey et al. [10].

4. Reptiles

Reptiles showed the first definite appearance of the DCN with Gr and Cu subdivisions [6]. The appearance of these nuclei in reptiles might be associated with the development of limbs which is necessary for the terrestrial life. These nuclei have been found in limbed lizards [14,15,16,17], iguana [18], turtle [19] and alligator

[6,20,21]. However, the snakes, which do not have limbs, have also DCN [6,11,19,22,23,24].

The DCN in some tailed-reptiles was divided into large lateral part, considered as the main DCN, and small medial part, referred as the Bi in either side of the midline (e.g., Tegu lizard [15], garter snake [22] and Python [19,23,24]) (Figure. 2). However, Bi is not described in other tailed-reptiles such as some types of lizards [16], turtles [19] and boas [11].

The DCN of the *Python reticulates*, the world's longest snake and longest reptile, has been studied ultra-structurally [25]. On the basis of the size of the nerve somata, nuclear morphology and cytoplasmic organelles features, three neuronal types have been described in both the main DCN and the Bi.

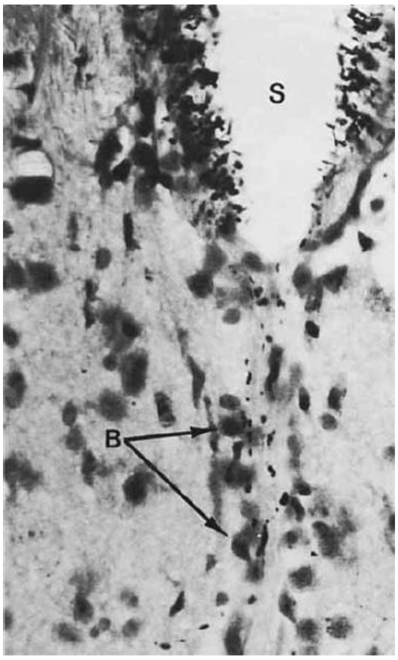

Figure 2. Bischoff nucleus the (B) in snake. Figure from Jacobs and Sis [22].

5. Birds

The dorsal column system of birds is of a primitive type presumably due in part to the lack of discriminative sensibility of skin covered with feathers. In pigeon for instance, the DCN are not well developed as are in mammals, but somehow separable into two components [26] (Figure 3) with broad outline resembling some mammalian projections [27]. No classification of the DCN neurons in any bird species has been reported in literature.

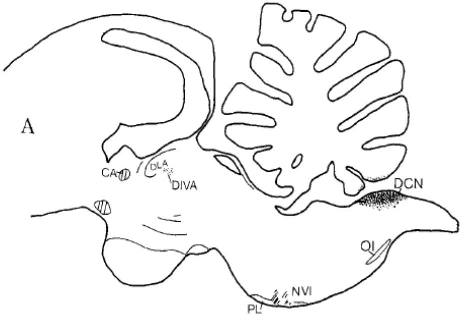

Figure 3. The approximate location of the DCN in the pigeon brain. Figure from Wild [26].

6. Sea Mammals

Sea mammals, whose mode of life places no premium on a detailed knowledge of the surrounding objects and who lack prehensile and manipulative ability, have a poorly developed dorsal-column system [28].

7. Mammals

It is believed that the development of the dorsal fasciculi and their nuclei in the mammalian and primate series is correlated with increasing sensory discrimination in the skin and the increased development of proprioceptive sense in the limb musculature [28]. The DCN can be divided clearly into Cu, which receives afferents from the forelimb (upper limb) [29] and Gr, which receives afferents the hindlimb (lower limb) [30]. A third nucleus known as Bi, is present between the gracile nuclei of both sides in some tailed-mammals such as raccoon [31] and opossum [32]. The Bi in tailed-mammals resembles those described in some tailed-reptiles and receives afferents from the tail [2,6]. As the case in some tailed-reptiles, Bi is not described in other mammalian species with well-developed tails such as the spider monkey [28], the rat [33,34,35] and the cat [30,36,37].

Golgi and/or Nissl studies of the DCN in rat [33,38], cat, [29,30,36,39] monkey [40] and camel [41,42] showed that it contain a heterogeneous neuronal population of various shapes and somata diameters (7 µm - 74 µm). Using horseradish peroxidase (HRP) injection into ventro-postero-lateral nucleus in the cat thalamus, gracilo-thalamic projection neurons identified as large cells (≥18 µm in diameter) confined to a region known as the "cell nest region" [43,44]. Based on their retrograde response to upper mesencephalon lesions in the cat, the DCN neurons projecting into the medial lemniscus were identified as large round cells located at the dorsal part of the cell nest region [36].

Anatomical studies showed that a series of collaterals immerge from dorsal column afferents into several rostrocaudal levels of the Cu and Gr [37]. These collaterals might be related with the multiple representation of receptive areas. However, the neuronal connections of afferent, efferent, and intranuclear fibers may vary greatly at different rostrocaudal levels [36]. Based on anatomical and physiological studies in several mammalian species such as monkey [45] and cat [27,46,47], the DCN have been divided into three regions: caudal, middle and rostral.

7.1. Rats

In the rat, The Gr lies close to the midline at the dorsal surface of the medulla oblongata extending from C1 level of the spinal cord to 300 µ rostral to the obex [33] (Figure 4). Cytoarchitecturally, the Gr zones are less well defined than those in cat and monkey (described on 7.2 and 7.3). Nissl-stained preparations confirmed the presence of two distinct regions [33]. The first region extends from C1 level of the spinal cord to 200-300µ caudal to the obex and is characterized by a heterogeneous neuronal population with diameters ranging from 8 to 24µ. The second region extends more rostrally and its neurons show fewer large neurons (> 18µ). Golgi-stained preparations showed that caudal part of the Gr contains neurons with vertically oriented dendrites known as the “dendritic column”; while the rostral part contains various neuronal types with transversely or vertically oriented dendrites [33].

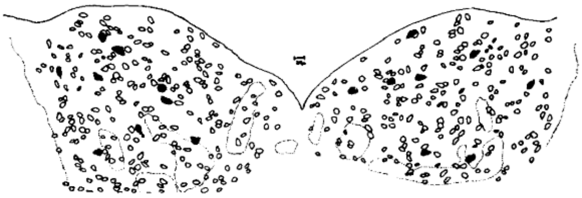

Figure 4. Camera lucida drawing of a transverse section from adult rat brain stained with cresyl violet demonstrating the area occupied by Gr at the level 250 μ caudal to the obex. Figure from Gulley [33].

An early study of the rat Cu using Nissl and Golgi staining methods revealed no rostrocaudal divisions [35]. In other later Nissl study, however, the preparations showed that the rat Cu is separable into two rostrocaudal regions [38] as the case in the rat Gr. Moreover, studies of primary afferent projections to the rat Cu [48] found a region located caudal to the obex expected to be functionally homologue to the middle region in cats and the pars rotunda in primates (described on 7.2 and 7.3) [49]. Other studies using HRP, histochemistry and immunohistochemistry techniques also confirmed the presence of a middle region in the rat Cu [48,50,51,52] in spite of its unclear identification using Nissl and Golgi staining methods.

7.2. Cats

Based on the Nissl preparations of the Gr of the cat, the longitudinal axis of the nucleus is divided into three distinct regions [30] (Figure 5): (1) the “reticular region” rostrally is characterized by small scattered neurons, (2) the “cell nest region” in the middle region contained clusters of larger round neurons, (3) the “caudal region” contained much larger neurons. The afferent fibers carrying vibration, hair stimulation and foot pad stimulation are somatotopically arranged and terminated mainly by synapsing with the neurons of the middle region “cell nest region” [30,31,36,53]. The neurons of the cell nest region have restricted receptive fields, small cortical input and, most of them, project to the medial lemniscus [30,31]. There are also neurons which are responsive to hair stimulation, light pressure and touch located at the rostral region “reticular region” of the Gr [30,31,53]. The neurons of this region are loosely organized homogeneous triangular or fusiform cells [36,37,39,54]. Comparing with the neurons of the cell nest region, the receptive fields of the hair stimulation in the reticular region are larger, the dorsal column input to this region is lesser and not arranged somatotopically, the neurons of this region have large cortical input and a small proportion of its neurons contribute to the medial lemniscus fibers [30]. The physiological studies of the Gr in the cat showed also that the terminal ends of the nerve fibers which carry the sensation from the distal parts of the hindlimb ”the foot” have more extensive representation at the Gr and are a located dorsomedial to those of the nerve fibers which carry the sensation from the proximal parts of the hinlimb [21,55].

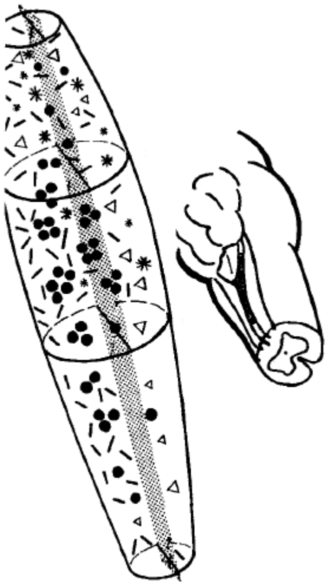

Figure 5. Heterogeneity of Gr of the cat. Figure from Berkley [43].

7.3. Monkeys

The location and distribution of the DCN in rhesus monkey have been studied [59] (Figure 6). The physiological studies of the Cu in galagos [56] and New and Old World monkeys [57,58,59,60,61,62,63] showed that the cell clusters in the main part of the nucleus (pars rotunda) is related to specific inputs from the hand. These cell clusters, identified as cytochrome oxidase (CO)-patches, receive inputs from digits 1–5 in a lateromedial sequence. The major portions of both the Cu and Gr in the primates are well differentiated into ovals CO-patches reflecting cell clusters. The arrangement of these CO patches in the Gr is less regular in arrangement and more spread out along the rostrocaudal length of the nucleus. The differentiation of these nuclei in other mammals is often less pronounced [64].

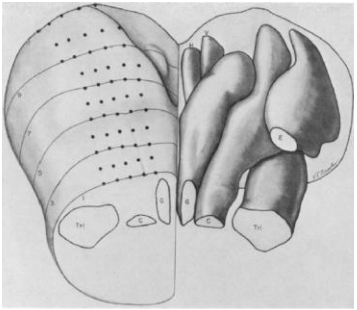

Figure 6. DCN in rhesus monkey. Figure from Biedenbach [40].

The Cu of the Macaca fascicularis has been studied ultra-structurally [65]. The neurons somata were varied in shape and size with short axes ranged from 4 to 22 μm and long axes ranged from 9 to 37 μm. The neurons were classified into three groups according to their nuclear morphology, the arrangement of the rough endoplasmic reticulum (RER) and the appearance of the Golgi complexes.

7.4. Camels

The camel is one of the largest animals on earth. It has adapted to live in desert in several ways. It has long, strong legs. Powerful muscles in the upper part of the legs allow the animal to carry heavy loads for long distances. The large size and heavy duties of the camel may create need to develop sophisticated balance system including well developed DCN (Figure 7). Recent Golgi studies on the camel Gr [41] and Cu [42] revealed the presence of a wide variety of neurons comprising a broad spectrum of sizes, shapes, dendritic density, dendritic branching pattern, somatic spines and appendages and dendritic spines and appendages. These studies demonstrated certain complex morphological features of neurons in the camel DCN such as wide variation of somatic and dendritic spines and appendages, flower-like dendritic ends, spiny axons and profusely branched axons. Most of these neuronal characterizations are not described in the previous studied species. This may reflect a part of relationship between the special characteristic camel's limbs and the diversity of the DCN neurons.

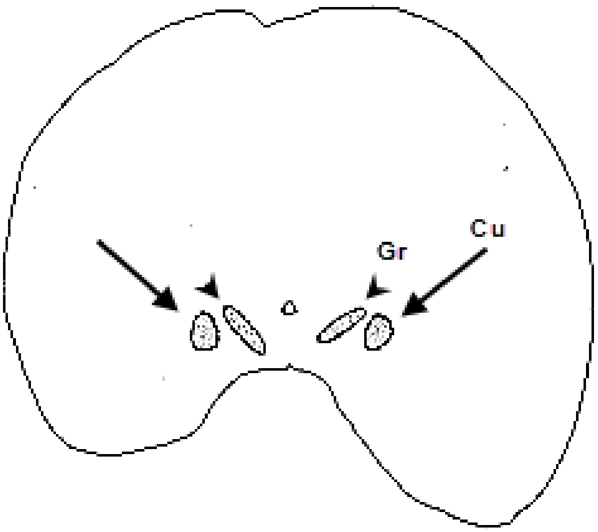

Figure 7. Camera lucida drawing of a transverse section from adult camel brain stained with H&E demonstrating the area occupied by Gr at the level of 200 µ caudal to the obex.

Conclusion

The first vertebrates known to have developed sensory fibers projecting to supraspinal levels are the amphibians. However, reptiles showed the first definite appearance of the DCN with Gr and Cu subdivisions. A third nucleus known as Bi, is present between the gracile nuclei of both sides in some tailed-reptiles and -mammals. Based on anatomical and physiological studies in several mammalian species, the DCN have been divided into three regions: caudal, middle and rostral. Several neuronal types have been described in the DCN of mammals and lower animals. Neurons in the DCN of the camel seem to have the most complex features among the species studied so far by Golgi impregnation. It seems that the complexity of neurons in these nuclei is correlated with increasing the importance of sensations such as discriminative touch in the skin and proprioception (sense of position and sense of movements) in the muscles and joints. This review may shed a light on the subdivisions of these nuclei and the importance for further physiological and molecular studies to reveal their specific functional rules.

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