Dorsal–Ventral Differences in the Glia Limitans of the Spinal Cord: An Ultrastructural Study in Developing Normal and Irradiated Rats

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Abstract. The dorsal and ventral surfaces of the lumbosacral spinal cord were examined in normal and irradiated postnatal rats. In normal rats between three and 13 days postnatal (DP), the glia limitans (GL) of the ventral surface was a more complex structure than the dorsal GL. This greater degree of complexity was manifested in a greater number of subpial astrocytes, a greater number of radial glial processes and a more advanced state in differentiation of its constituents. In rats irradiated at three DP and examined at 13 DP, the ventral GL remained intact and relatively unaffected by the radiation. In contrast, the dorsal GL was disrupted, and Schwann cells were seen within the dorsal funiculus. The ventral GL of the rat lumbosacral spinal cord is a more substantial structure than the dorsal GL during normal development. This factor alone may account for the integrity of the barrier properties of the ventral GL following radiation. However, our observations suggest that subpial astrocytes of the dorsal GL are more susceptible to radiation damage at three DP than the subpial astrocytes and radial glia of the ventral GL.

Key Words: Astrocytes; Glia limitans; Radial glia; Radiation; Schwann cells; Spinal cord; Ultrastructure.

INTRODUCTION

It has been demonstrated that, under some conditions, Schwann cells can be introduced into the spinal cords of immature rats, where they develop in a consistent manner (1–8). This development occurs when the spinal cord is irradiated prior to normal myelination of its axons by oligodendrocytes. Studies of those irradiated spinal cords have shown that the Schwann cells are capable of invading the spinal cord, of undergoing cell division, and, subsequently, of myelinating or ensheathing intraspinal axons that have not previously acquired their normal central nervous system (CNS) myelin (3, 5). The extent of Schwann cell myelination differs with the amount of radiation administered (3) and with the region of spinal cord irradiated (4). Regardless of differing experimental conditions in studies carried out by Gilmore and co-workers (1–6), or by others (7, 8), a consistent characteristic of intraspinal Schwann cell development is that it exhibits a spatial gradient and that the cells do not occupy all regions of the irradiated spinal cord in a uniform fashion. Instead, these intraspinal Schwann cells occupy large portions of the dorsal funiculi and dorsal gray matter, while the ventral funiculi and ventral gray matter usually lack these...
cells. Similarly, pathological examination of the spinal cords of patients with multiple sclerosis (9) and of animals with experimental allergic encephalomyelitis (10) show a predilection for Schwann cells to enter the dorsal funiculi. In view of the potential role of myelin in facilitating impulse conduction (11, 12), it becomes important to examine the factors that influence Schwann cell invasion of the spinal cord.

It has recently been shown that the glia limitans (GL) on the dorsal surface of the spinal cord underwent marked structural changes following irradiation (5). Since the GL normally delimits the CNS from peripheral nervous system (PNS) tissue elements, radiation-induced changes in this structure could account for the initial invasion of Schwann cells into the dorsal funiculi. If this hypothesis is correct, there should be structural differences in the GL covering the ventral funiculi, as compared to the GL covering the dorsal funiculi, and the GL in these two areas should respond differently to radiation. The present ultrastructural study was undertaken (A) to compare the structure of the GL on the dorsal and the ventral surfaces of the spinal cords in normal immature rats and (B) to determine whether the GL on these two surfaces responds differently to exposure to ionizing radiation.

MATERIALS AND METHODS

Two litters of Charles River CD rats, each containing a maximum of ten pups, were used. On three DP, eight pups were x-irradiated with a single dose of 4,000 R. The irradiated area was restricted to a 5-mm length of lumbosacral spinal cord by a lead shield. A Philips Contact Therapy Apparatus was used to administer the radiation under the following conditions: 50 kVP; 2 mA; filter added, 0.25 mm Al; HVL, 0.16 mm Al.

Four normal pups were killed on three DP. Two additional groups, each consisting of four irradiated pups and two sham-irradiated littermate controls, were killed at eight and 13 DP (five and ten days post-irradiation respectively). The rats were anesthetized with chloral hydrate and perfused through the heart with a fixative containing 2% glutaraldehyde, 2% paraformaldehyde, 0.5% acrolein and 0.5% dimethyl sulfoxide in 0.12 M Sorensen's phosphate buffer at pH 7.2 to 7.4. The lumbosacral regions of the spinal cords were removed, cut into 2 mm segments and stored overnight in fixative at 4°C. The following day cord segments were post-fixed in 2% OsO₄ in buffer for two hours at 4°C. The tissue was then dehydrated and processed for ultrastructural examination as previously described (5). The dorsal and ventral surfaces of the spinal cords, between the respective roots and the midline (see Results and Figs. 1, 3) were examined by light microscopy and in a JEOLCO 100 CX electron microscope.

RESULTS

Observations on Normal Rats

Dorsal Glia Limitans: At three DP the GL on the dorsal surface of the cord appeared as a thin, darkly stained membrane when observed in 1 μm sections. The cell bodies of astrocytes forming this membrane were in locations adjacent to the surface and stained darkly as did their processes (Fig. 1). Ultrastructurally, these subpial astrocytes had a dense cytoplasmic matrix with numerous free ribosomes,

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Fig. 1. The dorsal spinal cord of a three-day-old normal rat. The glia limitans (large arrow) appears as a thin darkly stained membrane covering the dorsal funiculus (DF). Subpial astrocytes (small arrows) also stain darkly with toluidine blue. Sample area for electron microscopic examination in this study was limited to the portion of dorsal funiculus between vertical bars and did not include the root entry zone (RE). Myelinated axons are not present at this developmental stage. Compare the dorsal glia limitans (Fig. 1) with its ventral counterpart (Fig. 3). Toluidine blue. ×550.

Fig. 2. A subpial astrocyte (A) at the dorsal surface of the spinal cord in a three-day-old normal rat. Both dorsal and ventral subpial astrocytes are characterized by a dense cytoplasmic matrix, rich in free ribosomes and wide-bore rough endoplasmic reticulum (small arrows). Numerous Golgi apparatus (*) and mitochondria are seen in the perikarya. Axons in the dorsal funiculus (DF) are usually small diameter and unmyelinated. A continuous basal lamina (arrow-heads) covers the entire surface of the cord. ×13,500.
mitochondria, wide-bore rough endoplasmic reticulum and Golgi apparatus (Fig. 2). Other organelles observed less commonly were smooth endoplasmic reticulum and occasional glycogen granules. Filaments were not seen in these subpial astrocytes at this time. The extensions of the GL between the cell bodies of subpial astrocytes were composed of one to three flattened cytoplasmic sheets, with one or two sheets being most common. These sheet-like processes were almost entirely derived from subpial astrocytes and were similar to the perikarya with respect to cytoplasmic density due to the abundance of free ribosomes. Several radial glial processes were observed forming flattened cytoplasmic sheets at the dorsal surface of the cord. However, the contribution of these processes to the formation of the dorsal GL was limited due to the sparcity of their occurrence. Junctional complexes between the cytoplasmic sheets of the GL were not common and, when observed, took the form of small desmosomes. The dorsal funiculus was composed mostly of small unmyelinated axons (Fig. 2); however, a few large-caliber axons near the midline of the dorsal funiculi had thin myelin sheaths of up to three compact spirals. In general, the axons were uniformly packed, except where a few processes from subpial astrocytes encircled large bundles of axons.

At eight and 13 DP the thickness of the GL and number of subpial astrocytes was less than that observed at three days of age, and the GL was often composed of only a single flattened process. In spite of this arrangement, the GL was continuous, and no breaks or gaps were observed. The cytoplasm of some subpial astrocytes contained an occasional filament while maintaining a dense matrix of free ribosomes. Cytoplasmic glycogen granules were observed in several subpial astrocytes at eight DP; however, none were seen at 13 days. At this time, few radial glial processes were observed in the dorsal GL. When observed, they had dense, cytoplasmic matrices containing small bundles of filaments. Desmosomes between processes were more common at 13 DP than at three DP. Marked increases in the number of oligodendrocytes and of astrocytes not associated with the GL occurred throughout the dorsal funiculi. At eight and to a greater extent at 13 DP, many axons were myelinated or in the process of being myelinated. Typically, the cytoplasmic matrices of astrocytes scattered throughout the funiculi were paler than those of subpial astrocytes. At all periods examined, the dorsal GL was continuous and was covered externally by a distinct basal lamina.

Ventral Glia Limitans: At three DP the ventral GL was noticeably thicker than its dorsal counterpart, and the density of subpial astrocytes was much greater ventrally (Fig. 3). Between subpial astrocytes, the GL was composed of two to five layers of flattened glial processes. The processes arose either from subpial astrocytes or from radial glia located more deeply in the ventral funiculi. The latter type of processes was more common in the ventral GL than in the dorsal GL. With the exception of fewer glycogen granules and an occasional filament, the subpial astrocytes were similar to their dorsal counterparts in terms of their organelles and cytoplasmic density. In contrast, radial cytoplasmic processes from radial glia located within the funiculi contained more filaments than the few observed in the processes of ventral subpial astrocytes. Another notable dorsal–ventral difference in radial glia and subpial astrocytes of the ventral GL was the degree to which their processes extended through the associated funiculi. In the ventral funiculi, subpial astrocytic processes and radial glial processes often surrounded small bundles of axons or, in many instances, a single axon. Desmosomal junctions were observed, but, as in the dorsal GL at three DP, they were not common. At this time, the ventral funiculus
(Fig. 3) contained a greater number of myelinated axons or axons in the early stages of myelination than the dorsal funiculus (Fig. 1).

The ventral GL was thinner at eight and 13 DP than at three DP, and the subpial astrocytes were more widely spaced at these later intervals (Fig. 4). At 13 DP the GL between subpial astrocytes was generally composed of only two to three layers of flattened glial processes. Although an occasional small segment of the ventral GL was composed of a single subpial astrocytic process (Fig. 5) this process was two to three times thicker than its dorsal equivalent. Glycogen granules were not seen in ventral subpial astrocytes at eight or 13 DP. Cytoplasmic filaments and large mitochondria were common, especially in the radial processes at 13 DP. At eight DP and to a greater extent at 13 DP, the number of myelinated axons and the thickness of myelin sheaths (Fig. 4) was greater than observed earlier. In the VF, astrocytic processes with varying degrees of cytoplasmic density and filament content intermingled with the axons, but often could not be traced to their cell of origin. The surface of the ventral GL was continuous and was covered by a basal lamina on all postnatal days examined.

**Observations on Irradiated Rats**

*Eight-Day-Old Rats (five days post-irradiation):* Both dorsal and ventral funiculi in the irradiated cord still contained a few necrotic glial cells (Fig. 6) at eight DP. Although necrotic subpial astrocytes were seen occasionally in the dorsal and ventral GL, it was more common to observe the accumulation of dense cellular debris within the perikarya or processes of dorsal subpial astrocytes (Fig. 6). The dorsal GL was thin and was composed of a single subpial astrocytic process in most areas (Fig. 6). The ventral GL was similar in thickness to that seen in the eight DP normal rat. With the exception of a rare necrotic cell, the number of subpial astrocytes in ventral regions was similar to that seen in eight DP normal spinal cord. Both dorsal and ventral funiculi showed a marked hypcellularity and a reduction in myelin sheath formation as compared to controls. Portions of the dorsal funiculi were virtually devoid of myelin while the ventral funiculi usually contained a few larger-caliber axons with five to ten compact spirals of myelin. Despite the apparent radiation-induced glial changes, the processes of radial glia were observed in normal numbers and desmosomes were seen between in the dorsal and ventral GL. The basal lamina covering both cord surfaces was intact and normal in appearance (Fig. 6).

*Thirteen-Day-Old Rats (ten days post-irradiation):* Subpial astrocytes were reduced in number in the dorsal GL of irradiated rats as compared to normal rats. Gaps were observed between subpial astrocytic processes, so that the basal lamina, which remained continuous over the cord surface, was the only element intervening between axons of the dorsal funiculus and the extramedullary space (Fig. 7). Radial glial processes were observed at the same low frequency as seen in the normal 13 DP rat. In several instances, Schwann cells underlaid this basal lamina at the site of these gaps (Fig. 7). Although the majority of these Schwann cells were immature and had not yet formed compact myelin, several were in the process of myelin formation around large-caliber axons near the surface of the dorsal funiculi (Fig. 7).

As with their dorsal counterpart, the ventral funiculi (VF) were markedly depleted of their glial cell population (Fig. 8). Although far fewer than normal astrocytes were observed in the VF, the remaining astrocytes contained a greater density of filaments than astrocytes of the normal 13 day postnatal spinal cord. Despite the attrition of
Fig. 3. The ventral spinal cord of normal rat at three days of age. Compare the thickness of the glia limitans (large arrow) and density of subpial astrocytes (small arrows) to the glia limitans in the dorsal spinal cord (Fig. 1). A few myelinated axons (arrow-heads) are present in the ventral funiculus (VF). Area between vertical bars represents the portion of VF examined in this study. Toluidine blue. $\times550$.

Fig. 4. The ventral glia limitans (large arrow) of a 13-day-old rat does not stain as darkly and subpial astrocytes appear less frequently as compared to three-day-old spinal cord (Fig. 3). There are more myelinated axons in the normal ventral funiculus (VF) as compared to the irradiated spinal cord of the same age (Fig. 8). Toluidine blue. $\times600$. 

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Fig. 5. The ventral glia limitans (GL) of a 13-day-old normal rat. The glia limitans is usually composed of two or three flattened glial processes. However, in an occasional focal area it is composed of a single thick process (large arrow) derived from a subpial astrocyte (A) located a short distance away from the GL in the ventral funiculus (VF). Small processes (*) from this subpial astrocyte interdigitate between axons of the funiculus and form small desmosomal contacts (small arrows) with other processes. Large mitochondria are commonly seen within the processes of the glia limitans. A basal lamina (arrow-heads) covers the surface of the glia limitans. ×16,600.

Glial cells within the VF, the ventral GL appeared less affected by the radiation than the dorsal GL. Subpial astrocytes were present at the surface of the ventral cord (Fig. 9) in near normal frequency (Fig. 8). Dense radial processes still terminated in flattened cytoplasmic sheets at the ventral cord surface. The number of ventral radial glial processes appeared similar to normal spinal cord at 13 DP. However, because of the reduction of glia within the VF the ventral radial glial processes were highlighted against a background free of the normal complement of glial cells and myelin (Fig. 10). An intact basal lamina was present (Figs. 9, 10), and gaps were never observed in the ventral GL.
Fig. 6. Portion of the dorsal spinal cord of an eight-day-old irradiated rat (five days PI). The basal lamina (arrow-heads) covering the surface of the cord is normal in appearance. The glia limitans is thin and often composed of a single subpial process (large arrow). Subpial astrocytes (A) often have accumulations of dense flocculent material within their cytoplasm (small arrows). Necrotic glial cells (NG) are seen within deeper regions of the dorsal funiculus (DF). Axons within the irradiated dorsal funiculus are rarely myelinated at this time. ×13,000.
DISCUSSION

This study was undertaken to determine whether there are morphological differences in the GL covering the dorsal and ventral funiculi, and to investigate whether these two regions of GL respond differently to radiation in the postnatal period. Regional differences in structure of the GL are not unexpected; significant species differences have been reported. Human cortical GL is 15 to 25 μm thick and consists of multiple stacks of flat astrocytic processes (13). In contrast, the GL of the rat visual cortex often consists of a single astrocytic process less than 0.5 μm thick (14). Spinal cords from human beings (15, 16) and from rats (5, 17) reveal differences in the thickness of the GL, but previous studies have not examined differences in the ventral and dorsal funiculi.

This paper demonstrates distinct morphological differences between the GL of the ventral and dorsal funiculi. Moreover, structural differences in the GL can also be related to the developmental stage of the spinal cord. For example, the ventral GL of the three DP rats is thicker and contains a higher density of subpial astrocytes than the ventral GL of eight and 13 DP rats. The age-related reduction in both thickness and subpial astrocytic density may be explained by the continued development and expansion of the cord volume of the spinal cord with a concomitant increase in surface area, which is not compensated for by an increase in number of astrocytes. This development-related thinning of the GL may be explained by two other phenomena, neither of which is a strong possibility. One of these, death of subpial astrocytes, was not observed in normal tissue and this does not appear to play a significant role in the normal thinning process. The second possibility is that astrocytes migrate from a subpial location into the depths of the associated funiculus. Our observations, however, suggest that this is not a major factor since subpial astrocytes and radial processes, especially on the ventral cord surface, have large amounts of their volume in the GL where they form desmosomes with other processes, as well as having processes which interdigitate throughout the adjacent funiculus. Retraction of these interdigitating processes and migration to other locations is, therefore, not likely.

An additional observation related to regional differences of the GL in normal rat concerns the disparity in the distribution of radial processes forming this structure. At all periods examined, the dorsal GL consisted of substantially fewer radial glial processes than the ventral GL. At three days of age the dorsal GL was thinner than the ventral GL. As previously mentioned, the GL on both surfaces appears to become even thinner with increasing age, and subpial astrocytes tend to be more widely spaced. As a result, many areas of the dorsal GL are composed of a single flattened subpial astrocytic process by 13 DP. By three DP the GL on both surfaces of the cord has a full complement of subpial astrocytes and radial glial processes.

As reported previously (5), necrotic glial cells were observed in the dorsal funiculi in rats killed five days following irradiation. Our study extends these observations to glial populations in the ventral funiculi and to the subpial astrocytes on both dorsal and ventral surface of the cord. Earlier studies (18, 19) have shown that all regions of the irradiated spinal cord undergo a radiation-induced reduction in glial cells. However, evidence suggests that the immature cells are most affected by irradiation (20). At the time of irradiation a small number of axons in the ventral funiculi are myelinated. At five and at ten days following irradiation a small number of myelinated axons are still present, although their myelin sheaths have matured to eight to 12 compact spirals. These myelinated axons often appear in clusters.
Fig. 7. The surface of the dorsal funiculus (DF) in a 13-day-old irradiated rat (ten days PI). The basal lamina (arrow-heads) covering the spinal cord is intact although subpial astrocyte processes do not form a continuous glia limitans at this site. Schwann cells (SC) underly the basal lamina and reside in the spinal cord. A few large diameter axons (Ax) in this area are myelinated by Schwann cells while other smaller diameter axons (Ax) are surrounded by Schwann cell processes. A thin basal lamina (small arrows) covers the surface of Schwann cell processes. ×11,000.

Fig. 8. The ventral spinal cord of a 13-day-old irradiated rat (ten days PI). The glia limitans is intact (large arrows) and subpial astrocytes (small arrows) appear in near normal numbers.
Fig. 9. A subpial astrocyte (A) contributing to the ventral glia limitans (GL) of a 13-day-old irradiated rat (ten days PI). The subpial astrocytes appear relatively normal. However, there is an apparent increase in the density of filaments (small arrows) in these cells as well as in astrocytic processes within the ventral funiculus. The basal lamina (arrow-heads) covers the surface of the ventral cord. There is an absence of myelin sheaths as compared to normal (Fig. 5). ×10,000.

surrounding a common oligodendrocyte (21). In contrast to this small but persistent presence of advanced myelin sheaths ventrally, the dorsal funiculus at ten days post-irradiation is noticeably lacking in oligodendrocytes in the early stages of myelin formation. Thus, it might be suggested that if oligodendrocytes in the ventral funicu-

← as compared with normal spinal cord (Fig. 4). There is a lack of glial cells in the ventral funiculus (VF) and a sparsity of myelin sheaths as compared to normal (Fig. 4). Toluidine blue. ×560.
Fig. 10. A radial glial process (RP) in the ventral funiculus (VF) of a 13-day-old irradiated rat. Radial glial processes are a common constituent of the ventral glia limitans (GL), but are seen less frequently in the dorsal glia limitans. Radial glial processes of normal, and to a greater extent irradiated, spinal cord (this figure) contain bundles of filaments (arrows) at 13 days of age. Large mitochondria (m) are a distinguishing feature of glia limitans processes. A basal lamina (arrow-head) covers the surface of the cord, and there are no breaks in the continuity of the glia limitans. There is a relative absence of myelin in the ventral funiculus as compared to the control (Fig. 5). × 13,200.
lus have differentiated to the stage of myelin formation by the time of irradiation (three DP), they are less susceptible to its effects than are immature oligodendrocytes or their precursors. An apparent decrease in radiation sensitivity with maturation is also seen in the astrocytic population. Subpial astrocytes are more resistant to radiation effects than are immature astrocytes within the funiculi. One example of this maturation-dependent sensitivity of astrocytes was observed in rats killed 24 hours following irradiation (20), the greatest density of degenerating cells was observed in a cluster of immature astrocytes underlying the central canal. Ultrastructural observations have shown this cluster in the normal three DP rat to be a group of immature astrocytes that do not have filaments within their cytoplasm.

Exposure to radiation at three days affects the dorsal GL to a greater extent than the ventral GL. Several lines of evidence suggest that, at the time of irradiation, the subpial astrocyte population of the dorsal spinal cord may be less mature than its ventral counterpart. The slight, but notable, difference in the amounts of cytoplasmic filaments and glycogen granules and the extent of their processes suggest that subpial astrocytes of the ventral GL are in general more differentiated at three DP. With immunocytochemical staining there is an increase in glial fibrillary acidic protein (GFAP) associated with the maturation of the filamentous astrocytic population (22). The expression of immunoreactivity to GFAP is more pronounced during development in subpial astrocytes of the ventral cord than in those of the dorsal cord of postnatal rats (23, 24, and unpublished observations). If dorsal GL subpial astrocytes are less mature, they may be more sensitive to radiation effects than subpial astrocytes of the ventral GL. Furthermore, radial glial processes contained the greatest abundance of filaments of all the glial types observed and the numbers of these processes did not change due to the effect of radiation. It appears that the dorsal GL is a more fragile barrier to the invasion of Schwann cells than is the ventral GL. Following irradiation, Schwann cells have been observed penetrating the dorsal cord surface between the astrocytic processes of the GL (5). In instances where Schwann cells have been observed in human patients with no clinical or known neuropathological disease they occur frequently in the dorsal funiculi (9). There is a dorsal predilection in the location of Schwann cells in spinal cords of patients with multiple sclerosis (MS) (9). Observations on guinea pigs with experimental allergic encephalomyelitis also show that Schwann cells remyelinate axons in the dorsal funiculus to a greater extent than in the ventral funiculus (10).

A question that could be raised is whether the development of Schwann cells in the dorsum of the spinal cord in this study is related to the fact that the x-ray beam passed from dorsal to ventral through the animal. Although the beam used in this laboratory is of the soft type, the calibrations of the depth doses indicate that the ventral aspect of the three DP spinal cord receives essentially the same amount of radiation as the dorsal aspect of the spinal cord. Also, Beal and Hall (7) and Blake more and Patterson (8) used harder, more penetrating beams, and yet the Schwann cells were confined to the same area. Finally, in the studies by Blakemore and Patterson (8), the animal was placed on its side so that the beam passed laterally through the spinal cord. In spite of this, the Schwann cells developed in the dorsal aspect of that structure. Therefore, in view of these facts it is unlikely that the dorsal location of the Schwann cells in the spinal cord is related to technical aspects of the irradiation procedures.

One of the factors influencing the occurrence of Schwann cells within the spinal cord is presence of axons devoid of myelin (6). Similar observations in other myelinating systems suggests that unmyelinated or pre-myelinated axons provide instructive
or trophic (25) and mitogenic signals (26, 27) for myelin-forming cells. The presence of axons devoid of myelin may result from experimental procedures or demyelinating diseases or may be normal, as in the immature animal. Even if instructive or trophic signals for myelin-forming cells are present, a number of other factors influence the invasion of these cells. Data from this and a previous study (5) suggest that the astrocytic population is a major factor influencing Schwann cell invasion. The basal lamina covering the surface of the cord does not present a significant obstacle to Schwann cell invasion. The first CNS barrier to Schwann cell invasion is the GL. However, even if the GL is compromised, Schwann cells do not spread indiscriminately throughout the funiculi; astrocytes and their processes pervade areas of unmeylinated axons and create an effective barrier to Schwann cell invasion (5).

The route of entry of Schwann cells into the spinal cord in MS patients has been examined by other investigators. One principal source appears to be PNS root fibers at the root entry zone (9). Schwann cells are found in locations other than the dorsal root entry zone (9). Blood vessels may be another route of Schwann cell entry in MS and other demyelinating lesions (28–31). Recent studies in long-term irradiated rats have revealed isolated foci of Schwann cells adjacent to blood vessels in the spinal cord (3, 6). This observation, combined with those of a previous study which showed that many capillaries in the irradiated spinal cord lack the normal astrocyte covering (5), suggest that blood vessels may provide a migratory route for Schwann cells in certain pathological conditions. It appears that a common factor in the various routes of Schwann cell invasion is damage to the integrity of the astrocytic barrier. If the barrier-like properties of astrocytes and their processes are compromised, Schwann cells may enter the spinal cord and myelinate axons lacking normal CNS myelin. This Schwann cell myelination may have important implications with respect to conduction in axons that would otherwise remain devoid of myelin.

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