Mesaxonal Membrane Junction of Myelinated Nerve in the Central and Peripheral Nervous System

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Summary. Cell junction of the myelinated nerve mesaxon in the sciatic nerve and spinal posterior funiculus of rabbits and rats was examined by the freeze-fracture method. In replicas of fractured specimens, the cell junctions were the tight junction which was composed of parallel arrays of membrane particles. The rows of particles were straight or gently undulating along the long axis of the fibers. Occasional interconnections were formed among these rows. In the external mesaxon, the tight junctional particles in the central nerve were arranged in 3 to 6 lines and well developed more than those of the peripheral nerve consisting of 1 to 2 linear arrangement of particles. “Intramyelinic” tight junctions were well developed as well as some arrays of linear arrangement of particles in the central nerve. However, the junctions were poor and fragmental in the peripheral nerve.

Functional meanings of the difference of the mesaxonal and intramyelinic tight junctions between the central and peripheral myelinated nerve are discussed.

The tight junction of the myelinated nerve mesaxon was demonstrated in the thin section (Robertson, 1958) and on the freeze-fractured specimens (Dermietzel, 1974; Schnapp and Mugnaini 1975; Shivers, 1979). The existence of the tight junction was reconfirmed in both the central and peripheral myelinated nerve (Refer to the review by Peters et al., 1976a). These tight junctions are thought as sealing of the “intraperiod gap” ( Peterson and Pease, 1972) which is an intramyelinic extracellular space (Schnapp and Mugnaini, 1975, 1976; Tetzlaff, 1978).

On the other hand, some structural differences are known between the central and peripheral myelinated nerve. The intraperiod gap of peripheral myelin is wider than that of central myelin (Karlsson, 1966; Bischoff and Moor, 1967; Napolitano and Scallen, 1969). The experimentally administered lanthanum penetrates easily into the peripheral myelin sheath (Revel and Hamilton, 1969). Furthermore, the extracellular fluid condition, which is known to modify the tight junctional structure (Wade et al., 1973; Wade and Karnovsky, 1974; Humbert et al., 1975; Bouchaud and Bouvier, 1978), is different in the perifascicular space between the central and peripheral nerve (Davson, 1972; Harreveld, 1972; Van Lis and Jennekens, 1977).

These data suggest the difference of sealing structure at the mesaxon. However, no available information has been presented as far as we know. The present
study was undertaken to compare the tight junction structure of the mesaxon between the central and the peripheral myelinated nerves.

**MATERIALS AND METHODS**

Mature albino rabbits and rats were used in this study. The animals were anesthetized with sodium pentobarbital or ketamine hydrochloride, and were systemically perfused through the aortic arch with saline at room temperature and then with 2.0% paraformaldehyde in 0.1 M cacodylate buffer (pH 7.4). Portions of spinal cords (posterior funiculus) and sciatic nerves were dissected out and immersed in the same fixative. Small pieces of the fixed tissue were transferred into 40% glycerol. The specimens were quickly frozen in liquid nitrogen, and fractured in a JEOL EE-FED-B freeze-etching apparatus at -130 to -150°C. Replicas of the fracture faces were made by evaporation of platinum-palladium and carbon, and examined with a Hitachi H-500 electron microscope.

**RESULTS**

Longitudinally fractured surfaces of myelinated nerves revealed the mesaxonal region as a furrow (Fig. 1, 2) which runs parallel or obliquely to the course of the nerve fiber. A linear edge of the mesaxon was traced by linear rows of particles on the fractured membrane (Fig. 3-6). These rows of particles represent the tight junctional structure which is classified as type II by Suzuki and Nagano (1978). These rows were mostly parallel to each other and followed a straight or gently

![Fig. 1. A diagram showing the tight junctional rows (dotted line) of particles at the external mesaxon (M) of peripheral myelinated nerves. Chain lines indicate fracture planes. A axon, C pinocytotic caveolae.](image)
Fig. 2. P-face of fractured Schwann cell membrane in rat sciatic nerve. The fractured plane is through the W-X-Y of Figure 1. The external mesaxon is seen as a furrow, and no junctional structure is observed. My myelin lamellae. ×29,000

Fig. 3. P-face of fractured Schwann cell membrane in rat sciatic nerve. The fracture face is through W-X-Z of Figure 1. Arrow indicates a tight junctional row of membrane particles at the external mesaxon. ×43,000
Fig. 4. E-face of fractured Schwann cell membrane in rabbit sciatic nerve. Two parallel rows of junctional particles (arrows) extend along the mesaxon. C pinocytotic caveolae. × 64,000

Fig. 5. A longitudinally fractured surface of the external mesaxon of rabbit spinal cord. The tight junction can be seen as rows of membrane particles. N nucleus of a nerve cell. × 14,000

Fig. 6. The boxed area in Figure 5 is closed up. × 57,000
Fig. 7. Longitudinally fractured myelinated nerve of rabbit spinal cord. Three rows of junctional particles are oriented along the long axis of the fiber. ×19,000

Fig. 8. A closer view of the squared area in Figure 7. The rows of junctional particles are seen in the fractured membranes of consecutive myelin lamellae (arrows). ×42,000

Fig. 9. Fractured surface of a myelin lamella in the rat sciatic nerve. Intramyelinic junctions are fragmental rows of membrane particles, extending diversely. Arrow indicates a gap junction. ×68,000
undulating course along the long axis of the nerve. Occasional interconnections were observed between neighboring rows of particles, but there was no formation of a wide-spread "network" as seen in a typical epithelial tight junction (Friend and Gilula, 1972; Staehelin, 1974).

The tight junctional rows of particles at the external mesaxon of the central myelinated nerves (Fig. 5-8) numbered 3 to 6, or occasionally more. In the peripheral nerves the junctional rows of particles formed only 1 to 2 arrays (Fig. 3, 4).

In addition to the tight junction at the mesaxon, continuous rows of membrane particles were evident in the compact myelin lamellae of the central nerves (Fig. 7, 8). Those structures represent the intramyelinic junctions (Dermietzel, 1974; Reale et al., 1975; Schnapp and Muggiani, 1976) being identical to the so-called "radial components" (Honjin, 1959; Peters, 1961). The intramyelinic junctions in the peripheral nerve were fragmental segments of various lengths and extensions (Fig. 9). Some gap junctions were observed in the vicinity of the junctional rows (Fig. 9).

DISCUSSION

Compared with the tight junction of various kinds of epithelia (Friend and Gilula, 1972; Staehelin, 1973; Claude and Goodenough, 1973), the junction of the myelinated nerve mesaxon was very simple. No obvious junctional strands and their networks could be found in the myelinated nerve. The linear arrangement of junctional particles observed in the present study was reminiscent of the intermediate stage of a developing tight junction of embryonic epithelial and mesothelial cells in various species (Revel et al., 1973; Montesano, 1975; Tice et al., 1977; Nagano and Suzuki, 1976a; Suzuki and Nagano, 1979), and also of the tight junctions in some vascular endothelia (Yee and Revel, 1975; Smionescu et al., 1975, 1976) Sertoli cells (Gilula et al., 1976; Nagano and Suzuki, 1976b) and the proximal convoluted tubule of the kidney (Claude and Goodenough, 1973) of adult animals. Thus, the mesaxonal tight junction is generally leaky or loose in structure. The mesaxonal tight junction of the peripheral myelin was poorer in development than that in the central one. The leaky structurc of the peripheral external mesaxon is compatible with the evidence that the experimentally administered lanthanum permeated to the intramyelinic space in peripheral nerves (Revel and Hamilton, 1969).

High concentration of ions and high osmotic pressure in the extracellular space have been known to induce a leaky structure of the tight junction in many kinds of epithelia (Wade et al., 1973; Wade and Karnovsky, 1974; Humbert et al., 1975; Boucaud and Bouvier, 1978). Therefore, the relatively high concentration of plasma proteins in the endoneurial interstitial fluid of peripheral myelinated nerves (Olsson, 1975; Van Lis and Jennekens, 1977) well reflects the leaky structure of the mesaxonal tight junction of the nerves. It is suggested that the leaky mesaxonal tight junction in periperal peripheral nerves is induced by not only the high concentration of plasma proteins, but also other ionic components. The condition of interstitial fluid is based on the different transport regulation of vascular walls for the plasma components in peripheral and central myelinated nerves (Reviews by Davson, 1972; Harreveld, 1972; Peters et al., 1976b).

In addition, it is possible that the loose structure of the intramyelinic tight
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junction in peripheral myelinated nerves may easily facilitate the lamellar “slipping” which occurs in some physiological and pathological conditions (HIRANO and DEMBITZER, 1967; FRIEDE and MIYAGISHI, 1972).

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