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Characteristics and Formation of the Peripheral Myelinated Nerve Fiber Paranodes

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The paranodes restrict bilaterally the nodal axolemma abundant of sodium channels. The glial paranodal loops build together with the axolemma the heterotypic axo-glial septate-like junctions. Unique autotypic adherent junctions, named desmosome-like junctions, attach the membranes of the loops to each other. Developing myelinated fibers of rabbit spinal roots were examinated by conventional electron microscopy. As a rule, the axo-glial junctions appear after beginning of compact myelin formation. The adnodal loops form first their septate junctions. The process continues to the internode. At the same time, develop the autotypic adherens junctions. The interrelated development of both junctions is obviously of significance for achievement of the regular organization of the myelinated fibers. The findings put the question about the developmental priority of the axo-glial junctions or the desmosome-like junctions, i.e. about the leading role of the neuron or the glial Schwann cell in the formation of the mature paranodes.

Key words: nerve fibers development, paranode, axo-glial junctions, desmosome-like junctions.

Introduction

The myelin sheath is a unique and fundamental adaptation of vertebrates. The physiological end product of myelination is saltatory conduction where the nerve impulse rapidly "jumps" from node to node. The myelinated axon can be divided into three domains: the internodal axon covered by compact myelin; the paranodal axon connected to the terminal ends or paranodal loops of the myelin internode; and the nodal axon which is apposed by Schwann cell finger-like processes in the peripheral nerves. The paranodal loops tightly adhere to the axon through a continuous spiral of axo-glial or septate-like junctions [1]. They form a physical barrier that prevents diffusion of nodal Na+ channels and juxtaparanodal K+ channels [6]. The adherent or desmosome-like (D-L) junctions [2, 4, 8] connect multiple layers of paranodal loops in their middle region. The single tight junctions [3, 5] appear between the paranodal loops in their adaxonal area of. The interrelated development of all these contacts of the paranode was not investigated.

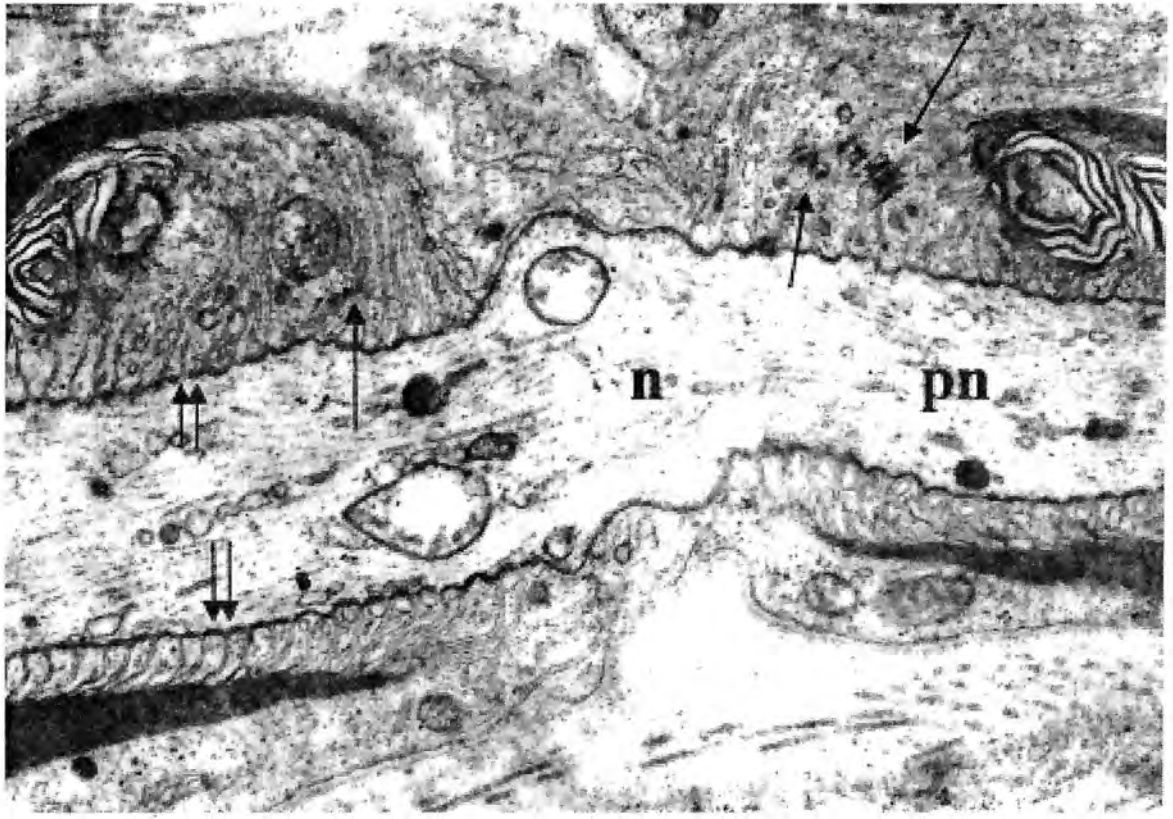

Fig. 1. Newborn rabbit. A longitudinal section through the ventral root. Axo-glial junctions of paranode pn (double arrows). D-L junctions between the membranes of neighboring paranodal loops (arrows). At the right paranodal zone, the D-L junctions are disposed in two rows, n — node. EM Siemens I × 24 000

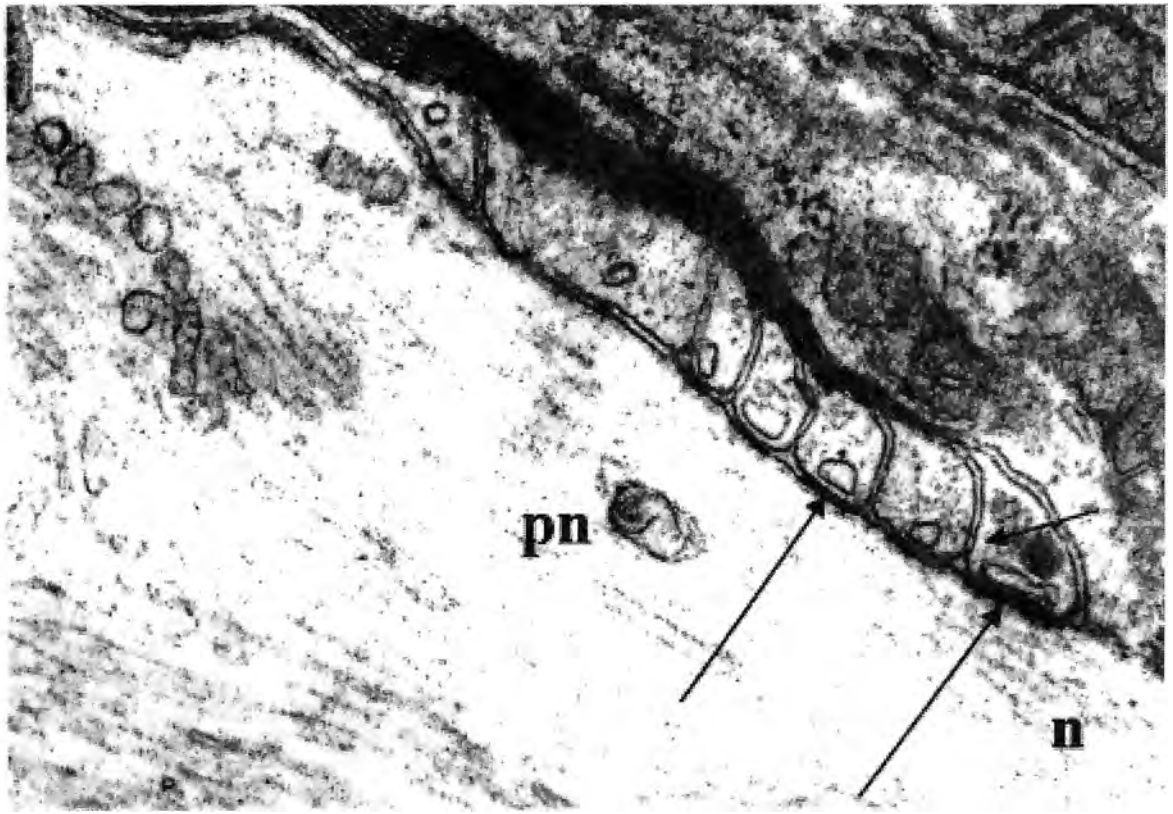

Fig. 2. Newborn rabbit. A longitudinal section through the dorsal root. Adnodal axo-glial junctions (long arrows). Tight junction between membranes of two neighboring paranodal loops (short arrow), n — node, pn — paranode. EM Siemens I × 70 000

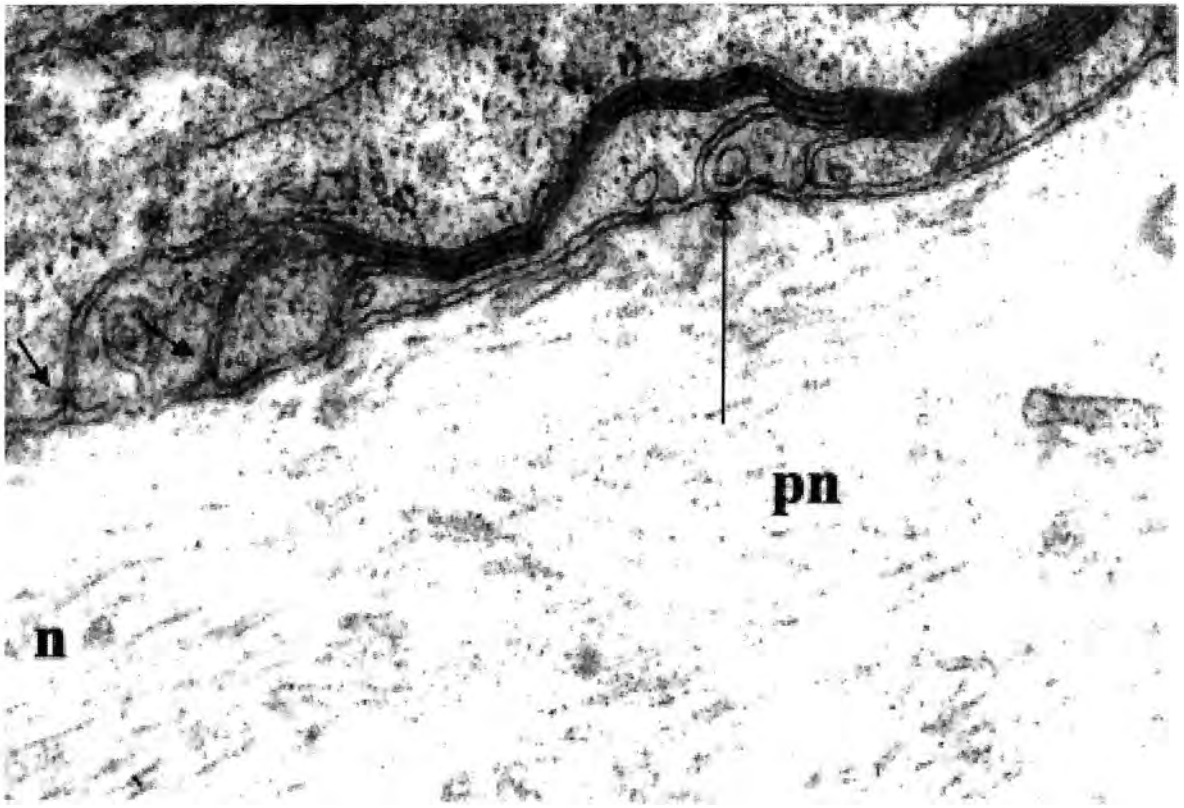

Fig. 3. Newborn rabbit. A longitudinal section through the dorsal root. An initial formation of axo-glial junction in the middle of the paranode **pn** (long arrow). Tight junctions between the adaxonal paranodal membranes (short arrows), **n** — node. EM Siemens I × 60 000

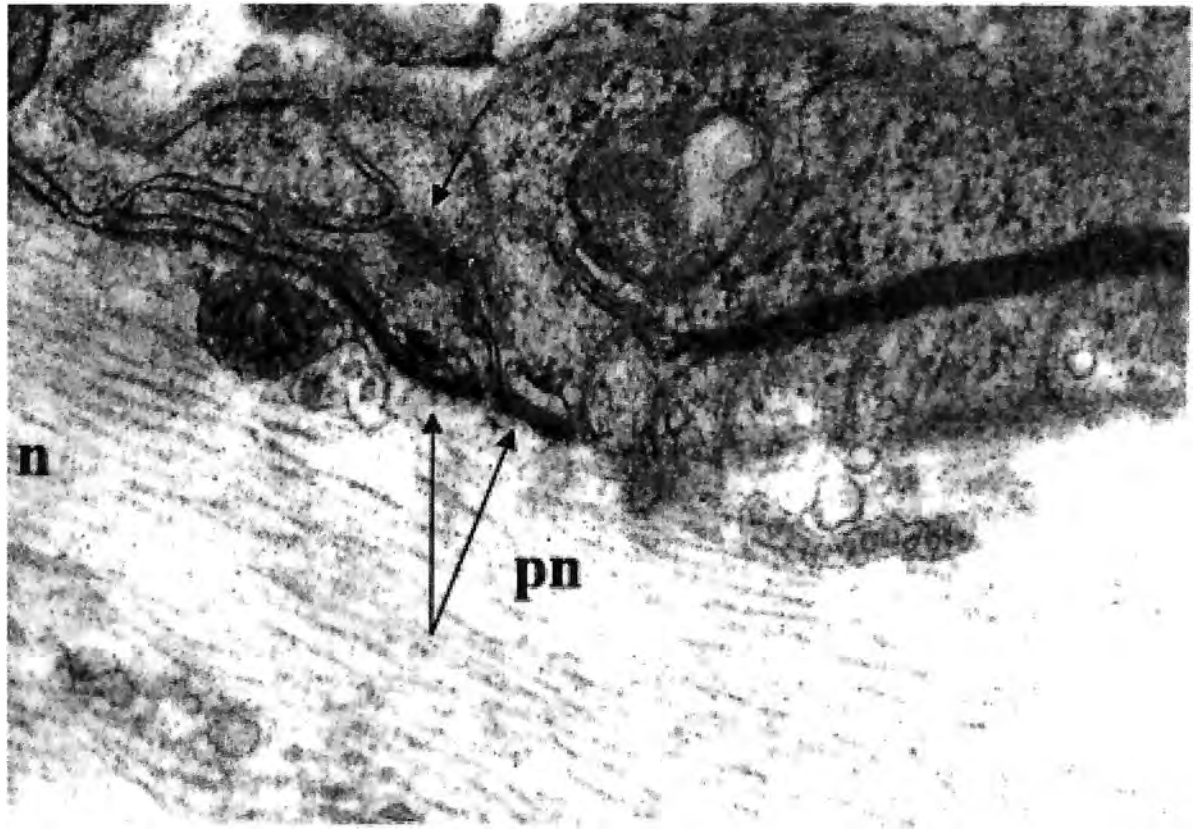

Fig. 4. Newborn rabbit. A longitudinal section through the dorsal root. Axo-glial junctions of two adnodal loops of the paranode **pn** (long arrows). Formation of D-L junctions (short arrow), **n** — node. EM Siemens I × 70 000

Material and Methods

Rabbits of 9 age groups (newborn — 8 months) were used. Segments of ventral and dorsal spinal roots were removed and prepared for EM according to the routine protocol. Longitudinal sections were examined under Siemens I EM.

Results

In well-developed myelin sheaths, the axo-glial junctions appeared as uniform thickenings between axolemma and all paranodal loops (Fig. 1). In appropriate sections, D-L junctions appeared in one or two rows between the neighboring membranes of the paranodal loops (Fig. 1). In nonmature myelin sheaths, the axo-glial junctions have first appeared at the adnodal loops of the paranode (Figs. 2, 4). Short tight junctions were visualized between adaxonal segments of neighboring paranodal loops (Figs. 2, 3). In a single case, we have seen an initial formation of axo-glial junction in the middle of the paranode, constituting of three dense particles (Fig. 3). In appropriate sections, it could be observed a simultaneous development of the first adnodal axo-glial junctions and D-L junctions, belonging to the same paranodal loop membranes (Fig. 4).

Discussion

Our findings have supported the data of Yamamoto et al. [7] that the axo-glial junctions develop from the node to the internode. However, we have shown that the rule is not absolute. In some cases, first develops axo-glial junction at a loop in the middle zone of the paranode (Fig. 3). During the formation of axo-glial junctions, in the paranode develop also tight junctions. Similarly to the D-L junctions, they connect the membranes of the paranodal loops. That connection, however, is limited to the membranes. The outer layers of both contacting unit membranes only fuse to each other. Hence, the tight junctions are not able to draw together the neighboring loops. The adherens, D-L junctions, develop simultaneously with the axo-glial junctions, also from the node to the internode. The D-L junctions are able to draw together the paranodal loops owing of their solid cytoplasm densities, which fuse to each other and build a complete spiral on the length of the paranode. At the other hand, the first D-L junctions develop in close interrelation with the adjacent D-L structure of the outer mesaxon (Fig. 4). The mesaxons are often associated with such structures, before and during the myelinization [8]. I.e., the D-L junctions as a whole have a priority in their genesis and formation. Taking into account all these findings, we may suppose that the adherent junctions have developmental priority in comparison to the axo-glial junctions. Nevertheless, additional studies in this aspect are necessary.

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