The Pathophysiology of Acute Experimental Allergic Encephalomyelitis Induced by Whole Spinal Cord in the Lewis Rat

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Abstract

Histological and electrophysiological studies were performed on Lewis rats with acute experimental allergic encephalomyelitis (EAE) induced by inoculation with guinea-pig spinal cord and Freund's adjuvants, in order to determine the cause of the neurological signs. These studies demonstrated demyelination-induced nerve conduction block in the large and also the smaller diameter fibres at the ventral root exit zone (VREZ) of the lumbar spinal cord. The demyelination at the VREZ affected both centrally and peripherally myelinated internodes, but predominantly the former. Studies on the H reflex recorded from a hindfoot muscle indicated normal peripheral nerve motor conduction but interruption of the monosynaptic reflex arc, as would be anticipated from this efferent conduction block and previously reported afferent conduction abnormalities. It is concluded that conduction block in α, β and γ motor fibres at the VREZ is an important cause of hindlimb weakness in whole spinal cord-induced acute EAE.

Keywords: conduction block; demyelination; experimental allergic encephalomyelitis; fusimotor fibres; h reflex; small myelinated fibres; ventral root exit zone; whole spinal cord

Introduction

Experimental allergic encephalomyelitis (EAE) is an autoimmune disease of the nervous system induced by inoculation with whole central nervous system (CNS) tissue, CNS myelin, purified myelin basic protein or proteolipid protein, and adjuvants (Raine 1984; Yamamura et al. 1986). It is widely studied as an animal model of multiple sclerosis. In multiple sclerosis, CNS demyelination contributes significantly to the production of neurological signs (McDonald 1974). However, because of reports of absent or minimal demyelination in some animals with neurological signs of acute EAE or the first attack of chronic relapsing EAE, it has been suggested that the signs of EAE are not due to demyelination (Hoffman et al. 1973; Lassmann and Wisniewski 1979; Panitch and Ciccone 1981; Raine et al. 1981; Simmons et al. 1981, 1983; Kerlero de Rosbo et al. 1985). Furthermore, it has been stated that the recovery of function in rats with EAE is too rapid to be accounted for by remyelination, and that demyelination is therefore not responsible for the neurological signs (Panitch and
Ciccone 1981; Simmons et al. 1981). Thus the neurological signs of EAE have been attributed to oedema (Paterson 1976; Simmons et al. 1982, 1983) or an impairment of monoaminergic neurotransmission (Carnegie 1971; White 1984).

We have recently shown that, in rabbits with whole spinal cord-induced acute EAE, nerve conduction block due to demyelination of large diameter fibres in the dorsal root ganglia is an important cause of hindlimb motor dysfunction (Pender and Sears 1982, 1984). In rats with whole spinal cord-induced acute EAE, the dorsal root ganglion involvement does not contribute significantly to the hindlimb motor dysfunction (Pender and Sears 1986) but does result in an impairment of tail nociception which is probably due to conduction block in small diameter myelinated fibres (Pender 1986b). I now report that in rats with this form of EAE there is demyelination-induced nerve conduction block in the large and also the smaller diameter fibres at the ventral root exit zone (VREZ) of the spinal cord and that this is an important cause of hindlimb weakness. A brief preliminary report of some aspects of this work has already been published (Pender 1986a).

Materials And Methods

Induction of EAE

Lewis rats (JC strain) were kept in cages of 5 and were fed rat and mouse cubes and water ad libitum. The inoculum was a homogenate of equal volumes of a 30% suspension of guinea-pig spinal cord (the spinal roots having been stripped away) in 0.9% saline and a suspension of 4 mg of killed and dried *Mycobacterium butyricum* (Difco) per ml of incomplete Freund’s adjuvant (Commonwealth Serum Laboratories, Melbourne, Australia). Under ether anaesthesia 8-10-week-old rats were inoculated with 0.05 ml of inoculum in the footpad of each of the 4 feet or with 0.1 ml in a footpad of each hindfoot. They were examined daily from the 7th day post-inoculation. Histological studies were carried out on 4 rats (2 male and 2 female) with EAE, 2-3 days after onset of tail weakness and 1 day after onset of hindlimb weakness. In terminal experiments electrophysiological studies were performed on 11 male rats with EAE, 1-4 days after onset of tail weakness and 0-2 days after onset of hindlimb weakness.

Controls

Two and 9 normal male Lewis rats, 10-12 weeks old, served as controls for the histological and electrophysiological studies respectively. As these studies were performed on the animals with EAE about 2 weeks after inoculation, the control animals were the same age as the animals with EAE at the time of the studies.

Histological studies

Histological studies were performed on the brain, spinal cord, dorsal and ventral roots, dorsal root ganglia, spinal nerves and the sciatic and tail nerves as previously described (Pender 1985; Pender and Sears 1986).
Electrophysiological studies

(a) Ventral root and ventral root exit zone recordings. Under urethane and pentobarbitone anaesthesia a T12-L4 laminectomy was performed and the left sciatic nerve was exposed in the posterior thigh as previously described (Pender and Sears 1986). Radiant heat maintained the laminectomy and sciatic nerve pools at 37 °C. The left L2-L6 dorsal roots were cut close to the spinal cord and displaced laterally. By freeing the two most caudal left denticulate ligaments from the dura and tying them to right paravertebral tendons, the spinal cord was rotated through 90° so that its ventral surface faced laterally to the left. The freed left sciatic nerve was lifted away from the volume conductor and stimulated in continuity with platinum electrodes 3mm apart delivering 0.1msec square-wave voltage pulses at 1.0 Hz. Volume conductor recordings were made with a 0.5mm diameter silver ball electrode over one or more, in turn, of the left L4, L5 and L6 ventral roots, 1-3mm distal to the respective ventral root exit zones (VREZs), and over the rostral parts of these VREZs. A reference electrode was placed on the right paravertebral region at the same level. Monophasic ventral root recordings were made as previously described (Pender and Sears 1984). At the end of each experiment the dissection was extended to confirm that the L4 and L5 spinal nerves always gave large contributions to the sciatic nerve and that the L3 and L6 spinal nerves gave small contributions.

(b) M wave and H reflex recordings. The rats were mounted in a frame and the sciatic nerve was prepared as described above. An adequate depth of anaesthesia was maintained without depressing the corneal reflex. The left sciatic nerve was stimulated in continuity as above except that the polarity of the electrodes was reversed. Recordings were made with a 25 gauge needle electrode in the belly of the fourth dorsal interosseus muscle and with a reference 25 gauge needle electrode subcutaneously in the plantar aspect of the distal fourth digit of the left hindfoot.

Results

Clinical findings

Tail weakness commenced 8-14 days after inoculation and was accompanied by an ascending impairment of tail nociception as previously described (Pender 1986b). Tail paralysis, hindlimb weakness and sometimes hindlimb paralysis followed. Forelimb weakness occurred occasionally. Most rats survived the acute episode and by 20 days after inoculation were clinically normal apart from mild tail weakness.

Histological findings

The histological findings have previously been described in detail (Pender and Sears 1986) and will be presented only briefly. There was subpial and perivascular inflammation and demyelination in the CNS, especially the lumbar, sacral and coccygeal segments of the spinal cord. There was also perivascular inflammation and demyelination in the peripheral nervous system (PNS), particularly the dorsal root ganglia but also the dorsal and ventral roots. There was minimal if any involvement of the spinal nerves and peripheral nerves. The spinal cord VREZ was a site of predilection for demyelination, which affected the CNS glial (oligodendrocyte-myelinated) part more than the PNS non-glial (Schwann cell-myelinated) part (Fig. 1).
**Fig. 1.** Transverse section through a ventral root exit zone (VREZ) of the sacral spinal cord of a Lewis rat with hindlimb and tail weakness due to whole spinal cord-induced acute EAE, 3 days after the onset of tail weakness. Demyelinated axons are present in the CNS part of the VREZ, both within the spinal cord (large arrows) and in the central tissue projection within the proximal ventral root (small arrows). Normal PNS myelinated proximal ventral root fibres can also be seen (arrowhead). Epok 812 section stained with toluidine blue. Bar = 25 µm.

**Fig. 2.** Monophasic compound action potentials recorded from the distal cut ends of the lumbar ventral roots of a normal control rat when the sciatic nerve was stimulated. (A) maximal L4 response; (B) maximal fast, low threshold, L5 response; (C) maximal slow, high threshold, L5 response; (D) maximal L6 response. The conduction distances were similar for each root.
**Electrophysiological findings**

(a) Monophasic ventral root recordings in normal controls. To accurately determine the spectrum of conduction velocities of sciatic nerve-directed fibres in each of the lumbar ventral roots, monophasic recordings were made from these roots. In the normal control rat the sciatic nerve-directed motor fibres formed a unimodally distributed fast conducting group in the L4 ventral root, a unimodally distributed slowly conducting group in the L6 ventral root and bimodally distributed groups of fast, low threshold, and slow, high threshold, fibres in the L5 ventral root (Fig. 2 and Table 1). The fast L5 group had velocities very similar to those of the L4 group while the slow L5 group had velocities similar to the L6 group.

<table>
<thead>
<tr>
<th></th>
<th>Cv\textsuperscript{a} onset (m/sec)</th>
<th>Cv peak (m/sec)</th>
<th>Cv end (m/sec)</th>
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<tbody>
<tr>
<td>L4 (n = 3)</td>
<td>76.7 ± 3.2</td>
<td>59.5 ± 2.7</td>
<td>41.7 ± 5.1</td>
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<tr>
<td>L5 fast (n = 3)</td>
<td>77.4 ± 2.5</td>
<td>61.0 ± 1.5</td>
<td>-</td>
</tr>
<tr>
<td>L5 slow (n = 3)</td>
<td>-</td>
<td>42.8 ± 2.0</td>
<td>29.6 ± 2.6</td>
</tr>
<tr>
<td>L6 (n = 2)</td>
<td>52.6 ± 1.0</td>
<td>39.8 ± 2.1</td>
<td>21.7 ± 8.6</td>
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\textsuperscript{a} Conduction velocity at 37 °C (mean ± SD) of the onset, peak, and end, respectively, of the maximal ventral root monophasic compound action potential elicited by stimulation of the sciatic nerve.

**Fig. 3.** Volume conductor recordings of the maximal L4 ventral root (VR) and L4 ventral root exit zone (VREZ) responses to sciatic nerve stimulation in a normal control rat (A) and in a rat with hindlimb weakness due to whole spinal cord-induced acute EAE, 4 days after the onset of tail weakness and 2 days after the onset of hindlimb weakness (B).
In the normal control rats the L4 ventral root response, recorded in the volume conductor, to sciatic nerve stimulation was a biphasic wave (positive, negative), the amplitude of the negativity being greater than that of the initial positivity (Fig. 3A). The positivity is due to passive outward current driven by the approaching impulses, and the negativity is due to active inward current occurring during the rising phase of the action potential under the active recording electrode. The L4 VREZ response is very similar. In the rats with hindlimb weakness due to EAE, the L4 ventral root response was normal (Fig. 3B) apart from a slight reduction in the conduction velocity of the peak negativity (mean ± SD for controls = 60.5 ± 0.6 m/s and for rats with EAE = 56.6 ± 2.4 m/s; P < 0.05) indicating conduction block and/or slowing in a small proportion of these fibres between the ventral root and sciatic nerve. However, the L4 VREZ response showed a marked reduction in the amplitude of the negativity, without temporal dispersion, indicating conduction block in a high proportion of the fast conducting large diameter myelinated fibres in the region of the VREZ (Fig. 3B). The ratio of the amplitude of the negativity to that of the initial positivity serves as a useful indicator of the proportion of fibres undergoing conduction block at the VREZ (Table 2). For simplicity, the term "fast conducting large diameter" or "slowly conducting smaller diameter" will be used for fibres whose normal conduction velocities are greater or less than 50 m/sec.

In normal control rats, the L5 ventral root and VREZ responses, recorded in the volume conductor, had an initial low threshold fast conducting negative peak followed by a high threshold slowly conducting negative peak (Fig. 4A). Rats with hindlimb weakness due to acute EAE had normal L5 ventral root responses (Fig. 4B) except for a slight reduction in the conduction velocity of the first negative peak (mean ± SD for controls = 59.6 ± 1.4 m/sec and for rats with EAE = 54.9 ± 2.3 m/sec; P < 0.05) indicating conduction block and/or slowing in a small proportion of these fibres between the ventral root and sciatic nerve. However, the L5 VREZ response showed a reduction in the amplitude of the initial negativity, without temporal dispersion, and an even greater reduction in the amplitude of the second negativity (Fig. 4B). These findings indicate conduction block in a significant proportion of the fast conducting large diameter myelinated fibres and in an even higher proportion of the slowly conducting smaller diameter myelinated fibres at the L5 VREZ. Recordings over the L6 ventral root and VREZ in rats with hindlimb weakness due to EAE demonstrated normal conduction between the sciatic nerve and ventral root, but conduction block in a high proportion of the slowly conducting smaller diameter myelinated fibres at the L6 VREZ (Fig. 5). Conduction block was demonstrated at each of the 14 lumbar VREZs studied in the 6 rats with hindlimb weakness due to EAE. The results are summarized in Table 2.
### Table 2
Lumbar VREZ Responses To Sciatic Nerve Stimulation In Normal Control Rats And In Rats With Hindlimb Weakness Due To Whole Spinal Cord-Induced Acute EAE

Each response was recorded at the stimulus intensity giving the maximal amplitude of the respective ventral root response. Values are the mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 3)</th>
<th>EAE (n = 5)</th>
<th>P</th>
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<tbody>
<tr>
<td>L4 amplitude of negativity/amplitude of initial positivity</td>
<td>2.1 ± 0.2</td>
<td>0.6 ± 0.1</td>
<td>&lt;0.001</td>
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<tr>
<td>L5 amplitude of first negativity/amplitude of initial positivity</td>
<td>1.9 ± 0.3</td>
<td>1.0 ± 0.4</td>
<td>&lt;0.05</td>
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<tr>
<td>L5 amplitude of second negativity (µV)</td>
<td>94 ± 25</td>
<td>21 ± 26</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>L6 amplitude of negativity/amplitude of initial positivity</td>
<td>3.8 ± 3.0</td>
<td>0.5 ± 0.1</td>
<td>&lt;0.05</td>
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a n = 2 for L6.
b n = 4 for L4.
c Statistical significance of difference between groups (ANOVA).

### Table 3
Maximal M Wave And Maximal H Reflex In Fourth Dorsal Interosseus Muscle In Normal Control Rats And In Rats With Hindlimb Weakness Due To Whole Spinal Cord-Induced Acute EAE

Values are the mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 5)</th>
<th>EAE (n = 5)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>M peak-to-peak amplitude (mV)</td>
<td>4.6 ± 1.1</td>
<td>4.6± 1.6</td>
<td>NS</td>
</tr>
<tr>
<td>M latency to onset (msec)</td>
<td>2.23 ± 0.34</td>
<td>2.39 ± 0.28</td>
<td>NS</td>
</tr>
<tr>
<td>H peak-to-peak amplitude/M peak-to-peak amplitude</td>
<td>0.50 ± 0.09</td>
<td>0.29 ± 0.07</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>M-H latency b (msec)</td>
<td>4.62 ± 0.28</td>
<td>4.87 ± 0.26</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = not significant (P > 0.05).
a Statistical significance of difference between groups (ANOVA).
b Difference between latency to onset of maximal M wave and latency to onset of maximal H reflex.
Fig. 4. Volume conductor recordings of the maximal low threshold fast conducting and high threshold slowly conducting L5 ventral root (VR) and L5 ventral root exit zone (VREZ) responses to sciatic nerve stimulation in a normal control rat (A) and in a rat with hindlimb weakness due to whole spinal cord-induced acute EAE, 2 days after the onset of tail weakness and 1 day after the onset of hindlimb weakness (B).

Fig. 5. Volume conductor recordings of the maximal L6 ventral root (VR) and L6 ventral root exit zone (VREZ) responses to sciatic nerve stimulation in a normal control rat (A) and in a rat with hindlimb weakness due to whole spinal cord-induced acute EAE, 1 day after the onset of tail weakness and on the day of onset of hindlimb weakness (B).

(c) M wave and H reflex recordings. Although it would be anticipated that these efferent conduction abnormalities and the previously reported afferent conduction abnormalities (Pender and Sears 1986) would interrupt the monosynaptic reflex arc, other workers have reported the preservation of the lumbar monosynaptic reflex in rats with hindlimb paralysis due to acute EAE (White and Barnes 1975; White 1979). It was therefore important to assess this reflex pathway in the present study. In normal control rats a H reflex and M wave could be recorded in the fourth dorsal interosseus muscle when the sciatic nerve was stimulated in continuity (Fig. 6A). The H reflex is a monosynaptic reflex while the M wave is due to direct activation of motor fibres in the sciatic nerve. The H reflex was maximal at a lower stimulus intensity than that giving the maximal M wave. As the stimulus intensity was increased above that giving the maximal H reflex, the amplitude of the H reflex declined as a result of collision, in the ventral root, between the orthodromic impulses of the H reflex and antidromic impulses evoked by direct activation of sciatic nerve motor fibres. As the amplitude of the H reflex was greater after a period of no stimulation for several seconds, the maximal H reflex was usually recorded as the
response to the first stimulus after a 5-sec period of no stimulation. The ratio of the peak-to-peak amplitude of the maximal H reflex to that of the maximal M wave serves as a reliable indicator of the integrity of the monosynaptic reflex arc. It was established that the H reflex of the fourth dorsal interosseus muscle is mediated through the L5 dorsal and ventral roots and to a lesser extent the L6 ventral root. The conduction velocity of the fastest L5 ventral root fibres destined for this muscle was 49.5 m/sec, which was slightly faster than the velocity for the corresponding L6 ventral root fibres (46.6 m/sec). It would appear that the motor fibres mediating the H reflex in this muscle belong to the higher threshold slowly conducting fibre groups in the L5 and L6 ventral roots. As reported by Bessou et al. (1965) for the cat, the conduction velocity of motor fibres to this distal muscle is slower than the corresponding velocity of L5 ventral root fibres to the more proximal anterior tibial muscle (61.9 m/sec).

In rats with hindlimb weakness due to EAE, the M wave was normal in configuration, amplitude and latency but the H reflex was reduced in amplitude (Fig. 6B and Table 3). This indicates normal motor conduction in the peripheral nerve but interruption of the monosynaptic reflex arc, which is partly accounted for by demyelination-induced nerve conduction block in the slowly conducting smaller diameter myelinated fibres at the L5 and L6 VREZs. The difference between the latency to onset of the M wave and latency to the onset of the H reflex represents the time for transmission through the monosynaptic reflex arc from sciatic nerve back to sciatic nerve at 37°C and was normal in rats with EAE (Table 3).

**Discussion**

The present study demonstrates that in whole spinal cord-induced acute EAE in the Lewis rat there is nerve conduction block in both large and smaller diameter myelinated fibres at the ventral root exit zone of the lumbar spinal cord. The L4 ventral root fibres and the fast group of L5 ventral root fibres activated by sciatic nerve
stimulation are predominantly $\alpha$ (skeletomotor) axons with possibly some $\beta$
(skeletofusimotor) axons; the slow group of L5 ventral root fibres and the L6 ventral
root fibres are probably composed of slow $\alpha$ axons, a considerable number of $\beta$ axons
and some of the faster $\gamma$ (fusimotor) axons. $\beta$ axons have velocities intermediate
between $\alpha$ and $\gamma$ axons, innervate both extrafusal and intrafusal muscle fibres and
have been shown to be abundant in the nerves innervating the cat hindlimb muscles
(Bessou et al. 1965; Emonet-Denand and Laporte 1975) and rat tail muscles (Steg
1964; Kidd 1964). Conduction block of $\alpha$ and $\beta$ axons obviously causes muscle
weakness. Furthermore, $\gamma$ axon conduction block may also contribute to the muscle
weakness as there is evidence that the $\gamma$ fibres are necessary for maximal muscle
contraction (Hagbarth et al. 1986).

As the VREZ was both a site of predilection for demyelination and a site of
localized nerve conduction block, demyelination readily accounts for the conduction
block. Furthermore, demyelination-induced nerve conduction block at the
sacroccocygeal VREZs is likely to be an important cause of tail weakness. The
involvement of smaller diameter fibres may assume an even greater role here because
of the predominance of such fibres in tail muscle innervation (Steg 1964; Thompson
1970). Demyelination of the ventral roots and of the intramedullary portion of the
lower motor neurone axon between the cell body and the VREZ probably also
contributes to the limb and tail paralysis. Demyelination of descending motor pathways
in the spinal cord may also have a role in producing limb and tail weakness. Demyelination
of the VREZ, intramedullary and extramedullary ventral roots and
afferent pathway to the spinal cord (see Pender and Sears 1986) accounts for the
reduced H reflex. Such demyelination could also explain the reported failure to elicit
reflex contraction of the anterior tibial muscle by posterior tibial nerve stimulation in
rats with EAE (Baum and Rosenthal 1966). On the other hand, White and Barnes
(1975) and White (1979) were able to elicit monosynaptic responses in the lumbar
ventral roots of rats with hindlimb paralysis due to EAE; however, as the response
amplitudes were relatively low in normal rats and in rats with EAE and as inter-animal
variability was high, the sensitivity of this method for detecting conduction block is
likely to be low. Furthermore, the technique employed would not have detected
conduction abnormalities in the dorsal root ganglia and distal dorsal and ventral roots.

It is often stated that the recovery of function in EAE and in some episodes of
multiple sclerosis is too rapid to be accounted for by remyelination and therefore that
demyelination is not responsible for the neurological signs (Halliday and McDonald
1977; Panitch and Ciccone 1981; Simmons et al. 1981). However, such rapid
recovery could be due to the restoration of nerve conduction by the development of
electrical excitability in demyelinated internodal axolemma, as has been observed to
occur as early as 4 days after the induction of demyelination by diphtheria toxin or
lysophosphatidylcholine (Bostock and Sears 1978; Smith et al. 1982). Rapid recovery
could also be due to repair of structurally minor, yet functionally significant, damage
to the myelin sheath, for example loosening of the paranodal axoglial junction (Hirano
and Dembitzer 1978). Thus demyelination readily accounts for the neurological signs
of whole spinal cord-induced acute EAE and there is no need to invoke other factors
such as oedema. Axonal degeneration also occurs in EAE (Lampert and Kies 1967);
however, this would not be responsible for the rapidly reversible neurological signs
of ordinary acute EAE, although it may contribute to any persistent neurological deficit. On the other hand, axonal damage may have an important role in the production of the neurological signs of hyperacute EAE where there is substantial vascular damage in the nervous system (Levine and Wenk 1965).

The L5 VREZ recordings suggest that the smaller diameter myelinated fibres may be more susceptible to conduction block than the large fibres. Such a susceptibility of smaller diameter myelinated fibres in the sacrococcygeal dorsal roots and dorsal root ganglia (Aδ fibres) may account for the almost invariable impairment of tail nociception in rats with acute EAE (Pender 1986b). A differential susceptibility of smaller fibres to demyelination-induced conduction block has been observed in rat ventral root fibres demyelinated with anti-galactocerebroside serum (Lafontaine et al. 1982). A susceptibility of smaller diameter myelinated fibres in EAE could be due to (1) susceptibility to the demyelinating process per se, or (2) a susceptibility to the pathophysiological consequences of demyelination. In the present study there was no obvious difference in the relative proportions of large and smaller diameter fibres demyelinated but morphometric studies would be needed to confirm this. However, other studies have indicated that smaller fibres may be more readily demyelinated than larger ones (Jacobs 1967; Brown et al. 1980; Saida et al. 1983). Alternatively, the smaller diameter fibres may be more vulnerable to the pathophysiological consequences of demyelination because of a lower safety factor (see Nathan and Sears 1963) or because the increase in the ratio of nodal to internodal capacitance and conductance would be much greater in smaller fibres for a given degree of demyelination (see Lafontaine et al. 1982).

The vulnerability of the VREZ in EAE is probably due to a number of factors. Firstly, the blood-brain barrier may be reduced at this point of transition between the CNS and PNS, as there is a lesser blood-tissue barrier in the roots than in the CNS proper (Olsson 1968). Secondly, there is a concentration of astrocytes at the transitional zone (Gamble 1976). As astrocytes may act as antigen-presenting cells (Fontana et al. 1984), this concentration of astrocytes may focus the inflammatory response in the region of the VREZ. Thirdly, the myelin at this transitional zone is much thinner, at least in rats of the age studied, than along the same fibres in either the PNS or CNS proper (Pender, unpublished observations). There may be an important parallel between the VREZ and the retina-optic nerve junction, a site of predilection for optic nerve involvement in EAE (Rao 1981). Like the VREZ the retina-optic nerve junction is a transitional zone and has a reduced blood-tissue barrier (Tso et al. 1975), a concentration of astrocytes and disproportionately thin myelin sheaths (Hildebrand et al. 1985).

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References


