Letter

Neurological Signs in Inflammatory Demyelination

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Vass and colleagues [1] recently reported that interferon-\(\gamma\) potentiates antibody-mediated demyelination in the spinal cord in the rat. The rats developed prolongation of the latencies of somatosensory evoked potentials but no neurological signs. The authors stated that in this model there was more extended demyelination than is usually found in acute experimental allergic encephalomyelitis (EAE), and they concluded that their results contradicted the opinion that neurological dysfunction in rats with either actively induced or passively transferred EAE can be explained by demyelination alone [2, 3].

I wish to challenge their statement that there was more demyelination than usually present in acute EAE. In myelin basic protein-induced acute EAE (MBP-EAE) in the Lewis rat, there is substantial demyelination in the peripheral nervous system (PNS) randomly distributed along the lengths of the ventral and dorsal spinal roots [2-5]. Significant demyelination is also present in the PNS in whole spinal cord-induced acute EAE in the rat [2, 6]. Because myelin/oligodendrocyte glycoprotein (MOG) is confined to central nervous system (CNS) myelin, PNS demyelination would not be expected in the model described by Vass and colleagues. It is therefore invalid to extrapolate their findings to acute EAE, in which demyelination also occurs in the PNS, and in which, in some models, conduction block due to such PNS demyelination is likely to be the main cause of neurological signs [5, 7, 8]. In rabbits with acute EAE, demyelination-induced conduction block in the dorsal root ganglia is the major cause of ataxia [7, 8]. Intact conduction through unmyelinated C fibers in the same ganglia clearly indicated that demyelination alone was responsible for the conduction block, because other factors such as edema or cytokines should have also blocked unmyelinated axons [8].

In contrast to acute MBP-EAE, in which there is little CNS demyelination [5], there is substantial demyelination in the lumbosacral spinal cord in Lewis rats with acute EAE induced by inoculation with whole spinal cord, which contains additional antigens such as MOG [6]. In the latter model, focal conduction block occurs at the lumbar ventral root exit zone, which is a major site of the CNS demyelination; demyelination-induced conduction block in such a functionally critical region is likely to be an important cause of hindlimb weakness in these animals [9, 10]. The lack of neurological signs in the model of Vass and colleagues [1] is most likely explained by too few fibers in critical functional pathways undergoing demyelination simultaneously.

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References


