

DEVELOPMENT OF A MODEL OF DEMYELINATION THAT PERMITS THE STUDY OF EARLY PHASES OF LESION DEVELOPMENT

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ABSTRACT

The ability to study the immediate, early events in the demyelinating process has been difficult and hampered by the lack of suitable models. The most commonly studied murine models of multiple sclerosis (MS) – experimental autoimmune encephalomyelitis (EAE) and Theiler's murine encephalomyelitis virus (TMEV) – provide researchers with excellent models to study demyelination caused by autoimmune responses or virus infection, respectively. However, these models suffer from a significant shortcoming in that it is not possible to determine the precise age of any particular lesion in the animal. To address this deficiency, we have modified the currently used TMEV-induced model of demyelinating disease. Following surgical exposure of the spinal cord, we directly injected TMEV with Hoechst dye (as a marker of the injection site) into the spinal cord of female SJL/J mice. Immunohistochemical staining with a polyclonal antisera to TMEV demonstrated virus localization in the spinal cord white matter of virus-injected mice. Replicating virus can be detected by viral plaque assay. By 3 to 5 days post-injection, immune cells can be detected at the lesion site. Real time PCR for myelin proteolipid protein (PLP) was performed on spinal cord tissue from the injection site and compared with tissue from mock-infected animals. PLP transcript levels were markedly increased in virus-injected animals compared to controls. This model will allow us to define the initial events following virus-mediated insult to the spinal cord white matter.

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