The neurotoxicity of interferon-alpha

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Interferon-alpha (IFNα) is a pleiotropic cytokine expressed by a wide variety of cell types during inflammatory events, especially viral infections. In the central nervous system IFNα can be expressed by infiltrating leukocytes, glia and even neurons. When IFNα has been used as therapy for various diseases (e.g., hepatitis) and can be measured in the cerebrospinal fluid (CSF), it invariably causes cognitive dysfunction that is reversible when treatment is discontinued. IFNα has been measured in the CSF of people living with HIV and correlates with cognitive dysfunction. Both animal studies and in vitro investigations indicate that IFNα is toxic to neurons. We have shown that in a mouse model of HIV associated neurocognitive disorders (HAND), brain IFNα levels correlate with errors made in maze testing. Furthermore, behavioral abnormalities and histopathology can be ameliorated by treating these mice with neutralizing antibody to IFNα. In vitro studies using rat neurons reveal that IFNα exposure leads to dendritic simplification, which is likely a cellular correlate to memory loss. This dendritic simplification is not only mediated through the Type I IFN receptor, but also through the GluN2A subunit of the N-methyl-D-aspartate receptor. Preliminary studies in the HAND mouse model suggest that combined antiretroviral therapy (cART) plus an IFNα binding protein, B18R, are superior to cART alone in improving neuropathological markers. Our most recent unpublished data show that B18R can reverse abnormal behavioral seen with object recognition testing in HAND mice. Treatment of IFNα neurotoxicity may not only be effective in humans with HAND, but in other neurological disorders associated with cognitive dysfunction.

Recent Publications


Biography

William Tyor is a Professor of Neurology at the Emory University School of Medicine and the Atlanta VA Medical Center. He is the Co-Director of the Emory/Atlanta VA MS Center and the Emory Center for AIDS Research NeuroAIDS Scientific Work Group. His research has focused on basic and translational investigations of neuro-inflammatory diseases of the central nervous system including clinical trials in multiple sclerosis (MS) and translational studies in MS and HIV associated neurocognitive disorders (HAND). His NIH and VA grant funding has focused primarily on the pathogenesis and treatment of HAND using a mouse model and neuronal culture systems. He attends outpatient clinics in his subspecialty of CNS inflammatory disorders at the Atlanta VA and Emory Clinic as well as General Neurology Patient Management in the VA Residents’ Clinic and VA Inpatient Consult Service.

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