P02-202

AUTOIMMUNE-INDUCED PAIN ALTERS AFFECTIVE BEHAVIORS IN A MODEL OF NEUROPSYCHIATRIC LUPUS?

D. Ballok

Surgery (Neurosurgery, Neurobiology), McMaster University, Hamilton, Canada

As commonly seen in patients with neuropsychiatric systemic lupus erythematosus (NP-SLE), spontaneous disease onset in the MRL/MpJ-Fas^{lpr}/J (MRL-lpr) mouse model of NP-SLE is accompanied by increased autoantibodies, pro-inflammatory cytokines and behavioral dysfunction which precede neuroinflammation and structural brain lesions. Given that P2X purine receptors are important in peripheral "pain" signaling, the possibility that purinoception is involved in the development of aberrant affective behaviors was explored in the present study. Suramin, a P2X purinoceptor antagonist, was administered to lupus-prone mice from 5 to 14 weeks of age (60 mg/kg, i.p.). Novel object and sucrose preference tests were performed to examine behavior, and enzyme-linked immunosorbant assays for autoantibodies and pro-inflammatory cytokines were employed in immunopathological analyses. Suramin was found to attenuate markers of autoimmunity and inflammation, but was not immunosuppressive. Treatment did, however, prevent neophobic- and anhedonic-like deficits in MRL-lpr mice. More specifically, animals receiving the drug showed a profound 3-fold increase in their responsiveness to palatable solution (i.e. a reversal of anhedonia) and were less "distressed" by novelty. The present data supports the hypothesis that sustained activation of the peripheral immune system induces nociceptive-related behavioral symptomatology in lupus animals which is attenuated by the analgesic effects of suramin. It is proposed that anti-purine or cross-reactive autoantibodies cause neuronal hyperexcitability within "pain" pathways early in the disease process, which manifests as affective deficits. At a later stage of chronic lupus-like disease (following breakdown of the blood-brain barrier), fixed structural lesions in dopaminergic pathways likely account for and maintain impairments in emotionality.

https://doi.org/10.1016/S0924-9338(09)71125-3 Published online by Cambridge University Press