Brain Behav Immun. 2013 Oct;33:164-72. doi: 10.1016/j.bbi.2013.07.003. Epub 2013 Jul 22.

Altered cognitive-emotional behavior in early experimental autoimmune encephalitis--cytokine and hormonal correlates.

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Abstract

Multiple sclerosis (MS) is often associated with co-morbid behavioural and cognitive impairments; however the presence of these symptoms does not necessarily correlate with neurological damage. This suggests that an alternate mechanism may subserve these impairments relative to motor deficits. We investigated whether these abnormalities could be studied in experimental autoimmune encephalomyelitis (EAE), an animal model of MS. In myelin oligodendrocyte glycoprotein peptide (MOG35-55)-induced EAE mice, no motor deficits were observed until d9 after immunization. This enabled us to carry out a series of neurobehavioral tests during the presymptomatic stage, between d6 and d8 post-immunization. EAE mice spent more time in the outer zone in an open field test and in the closed arms of an elevated plus maze and, showed decreased latency for immobility in the tail suspension and forced swim tests and reduced social interaction compared with controls. These results are indicative of anxiety- and depression- like behavior. In addition, EAE mice appeared to exhibit memory impairment compared to controls based on their reduced time spent in the target quadrant in the Morris water maze and their faster memory extinction in the fear conditioning test. No demyelination, microglial activation or astrogliosis was observed in the brain at this early stage. Transcript analysis by RT-PCR from d6 to d8 brain revealed elevated interleukin (IL)-1β and TNF-α in the hypothalamus but not in the amygdala or hippocampus of EAE mice. Lastly, plasma corticosterone levels increased in EAE mice compared to controls. In conclusion, emotional and cognitive deficits are observed in EAE prior to demyelination and are associated with elevated IL-1β and TNF-α in the hypothalamus and changes in the hypothalamic-pituitary-adrenal axis.

KEYWORDS:

Anxiety; Cytokines; Depression; EAE; HPA axis; Multiple sclerosis

PMID:

23886782

DOI:

10.1016/j.bbi.2013.07.003