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Influenza vaccine and learning in C57BL mice with an acute experimental autoimmune encephalomyelitis

Research Article

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Abstract: Literature data suggest possible link between influenza vaccination and development of autoimmune processes. Therefore, the aim of the study was to investigate the effect of influenza vaccination on spatial learning in mice with experimental autoimmune encephalomyelitis (EAE). EAE was induced in eight-week-old C57BL/6J female mice by subcutaneous immunization (MOG_{35-55} in complete Freund's adjuvant) and Pertussis vaccine injected intraperitoneally. Mice were vaccinated with influenza vaccine three days before MOG immunization. The hippocampal-dependent spatial learning test, Morris Water Maze test (MWM), was performed before and after EAE induction. Significant difference ($P < 0.05$) in the time for completing the Morris Water Maze task was found between mice with mild clinical signs of EAE when compared to other mice. However no significant difference was observed between mice with EAE and mice with EAE that were vaccinated with influenza vaccine. Hippocampal tissue lesions in EAE mice are in correlation with memory impairment. Study shows no influence of influenza vaccine on progression of clinical signs of EAE, spatial learning and memory impairment.

Keywords: *Autoimmunity • EAE • Morris water maze • Spatial learning • Memory impairment*

1. Introduction

Some autoimmune diseases have been associated with vaccinations. It is estimated that influenza vaccination may have an impact on the development of autoimmune diseases such as Guillain-Barré syndrome [1,2]. Conflicting data exist regarding the connection between vaccines and multiple sclerosis [1]. Recent data suggest that peripheral infection with influenza virus elicits a central inflammatory response and impacts hippocampal structure and function, leading to cognitive dysfunction [3]. Cognitive dysfunction in infected mice was related to their failure to update the search strategy for the platform when the platform location changed. Impaired ability to efficiently navigate to the new location was shown by an increase in time and path length to the new platform location of the infected mice compared to controls [3]. However, there is insufficient data regarding influenza vaccination and its impact on hippocampal structure.

Experimental autoimmune encephalomyelitis (EAE), an autoimmune disease directed against myelin protein in the brain, is still the most commonly used animal model of multiple sclerosis (MS) [4,5]. Multiple sclerosis affects motor, sensory as well as behavioral and cognitive functions. Cognitive deficits are considered an early manifestation of the disease in MS patients. Similar memory impairment in EAE-induced mice is shown in many other studies [6-9]. EAE causes deficits in hippocampal-dependent learning and memory sight that is associated with early microglial activation, synaptic loss and neurodegeneration [7]. Studies in humans and animal models with hippocampal damage and lesions have provided evidence that this region of the brain plays a critical role in spatial memory; the part of memory responsible for regulating and encoding information about the surroundings and orientation in space [10,11]. Hippocampal formation is closely related to spatial learning because it consists of cells signaling the position of animal in space. In addition, mechanical or chemical inactivation of the hippocampus and neighboring cortex has shown to

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