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BBB Disruption and Permeability of Brain Tissues in MBP Induced Experimental Autoimmune Encephalomyelitis (EAE) Model in Rats

Isaac Levi

MD Biosciences Innovalora, Israel

Abstract

In spite of differences between the pathophysiology of EAE and the human Multiple Sclerosis (MS), EAE has become a common animal model in the development therapies for treatment of MS. The Myelin Basic Protein (MBP) induced EAE in rat consists of inflammatory cells infiltration into the spinal cord, cerebellum and brainstem. The paralytic episodes that in this model are thought to be the result of blood–brain barrier breakdown, inflammation, and edema, but not from demyelination. This paralysis initiates approximately 10 days post induction, followed by spontaneously recovers in 5–7 days. Therefore, the therapeutic window is very short. Blood-brain barrier (BBB) disruption and permeability in MBP-EAE animals was assessed by culling animals on study days 2, 6, 9, 11 and 13 for brain harvest, 2 hours following an intrajugular injection of 4% Evan's blue solution. Following collection, brains were sliced and immersed in formamide at 55°C overnight to extract the Evan's blue dye. The Evans blue dye content was quantified as µg/g brain tissue. Our data show that while the first clinical signs of the disease were seen on study day 9 following induction with MBP, the Evan's blue dye was observed in the brain already 2 days following induction (17.80±3.29 µg/g). The dye content in the brain tissue remained high until study day 9 (18.40±2.16 µg/g). Its level markedly decreased on study day 11, and was similar to the level in the naïve brain tissue Mono-nuclear and T-cells infiltration to the brain was observed early following induction with MBP, before the initiation of the first clinical symptoms of the disease. These data show dissociation between BBB permeability and the pick of the disease questioning the therapeutic vs. prophylactic traditional approach.

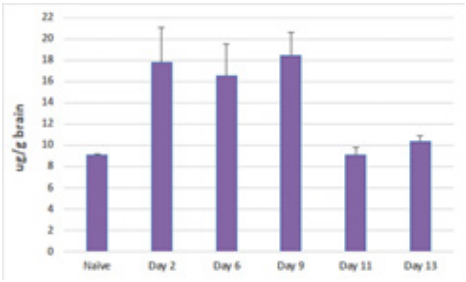

Figure 1: Blood-Brain Barrier Penetration in the MBP-induced EAE model in rat. Evans Blue staining, indicating of BBB disruption, is present in the brain already on study day 2.

Biography

Levi is the pre-Clinical department manager at MD Biosciences Ltd. MD Biosciences is a global industry-leading provider of preclinical services include efficacy and mode of action studies in the inflammation, immunology and CNS therapeutics areas. Dr. Levi holds a Ph.D. in Medical Science from the department of Immunology and Microbiology, Faculty of Medicine, in Ben Gurion University, Israel

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