

Examination of the Blood Brain Barrier Integrity in a Mouse Model of the Neurodegenerative Canavan's Disease

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Description

The blood brain barrier (BBB) refers to the complex anatomical barrier in the brain composed of endothelial cells, astroglia, pericytes, perivascular macrophages and basal lamina. Its selectivity controls the entry of substances into the Central Nervous System (CNS) [1]. BBB disruption affects neurodegeneration [2] and in some cases can be harnessed to deliver intravenous therapeutics to the CNS. Canavan's disease (CD) is an autosomal recessive neurodegenerative disease caused by lack of aspartoacylase that causes extensive demyelination.

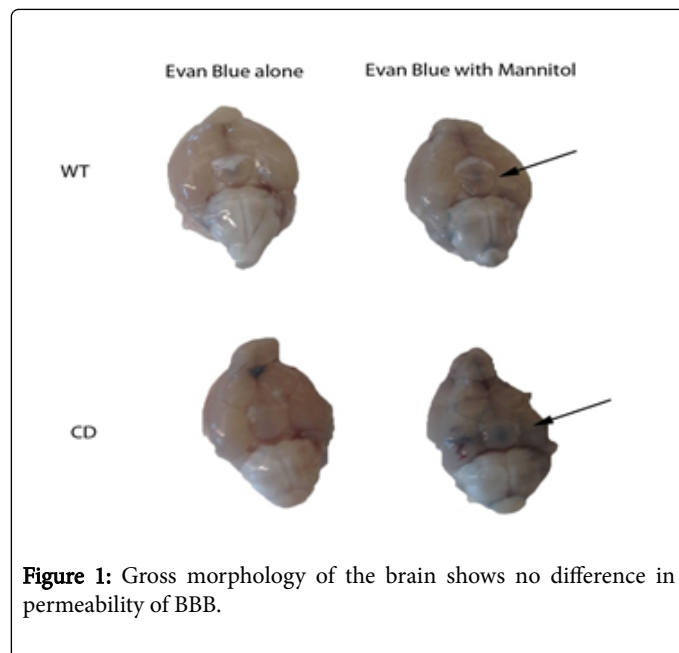


Figure 1: Gross morphology of the brain shows no difference in permeability of BBB.

The cause of neurodegeneration has not been conclusively determined. We investigated if BBB integrity is affected in the disease using an aspartoacylase knockout mouse [3]. Twenty one day old wild type and symptomatic diseased mice (n=3) were injected with Evans blue (EB) (4 ml/kg). Control mice were injected with saline or EB combined with mannitol pretreatment (3 ml/100 g) since mannitol reversibly opens the BBB. 30 minutes later, mice were perfused with PBS, and their brains homogenized. The supernatant was measured for absorbance at 610 nm to check the presence of EB using known concentrations as standard. Results showed no difference in the BBB of WT and diseased mice (Figure 1). All mice showed similar levels of EB retention in the blood and liver. Spectrophotometric readings showed no significant difference in BBB permeability between WT and diseased animals (Figure 2). As reported earlier [4], CD pathogenesis

sets in by 21 days of age and the results indicate that the BBB is not disrupted at least at this stage. Examination of EB retention in the brain with respect to body weight (Figure 3) because the amount of dye injected was irrespective of body weight and CD mice weigh one-third of their littermates. [4]. More animals and several time points along the progression of the disease need to be examined to conclusively establish the effect of the disease on the BBB or vice versa.

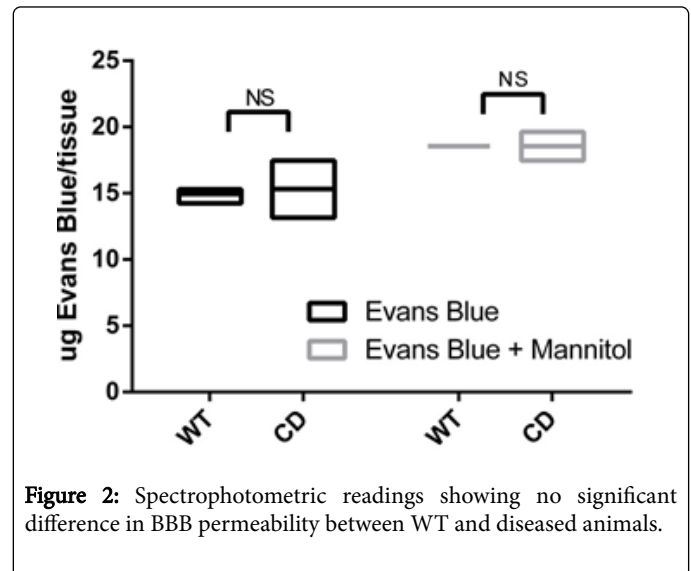


Figure 2: Spectrophotometric readings showing no significant difference in BBB permeability between WT and diseased animals.

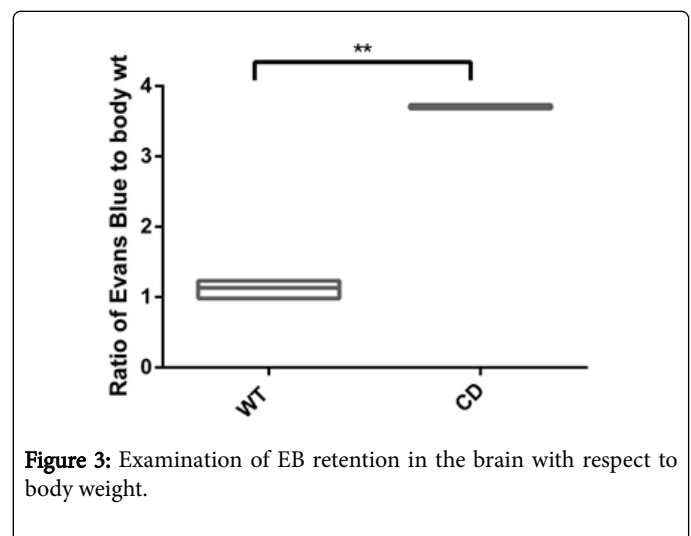


Figure 3: Examination of EB retention in the brain with respect to body weight.

References

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