

Valproic acid improves regeneration in kainic acid induced hippocampal degeneration

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Introduction: Some agents enhance Neural Stem Cells (NSCs) and Neural Progenitor Cells (NPCs) proliferation and differentiation. They can be used to enhance oligodendrogenesis and neurogenesis after neurodegenerative diseases or injuries in the Central Nervous System (CNS). Valproic acid (VPA) is a well-known anticonvulsant and mood stabilizer that has effects on epigenetic modifications. There are evidences that VPA has had beneficial effects in multiple animal models of neurodegenerative disorders such as Multiple Sclerosis, Alzheimers Diseases and Parkinsons disease. It also increases the efficiency of reprogramming of somatic cells to Stem Cells. In this study, we examined the effect of VPA in hippocampal oligodendrogenesis and neurogenesis, following kainic acid induced neurodegeneration.

Methods: To achieve hippocampal neuronal degeneration, Kainic Acid (KA) was administrated intranasally to female C57bl/6 mice. VPA (300 mg/kg/day) was gavaged twice a day for 7 days before KA administration. 5 days after KA administration, brain samples were taken. The histological assessment of neurodegeneration was done by cell counting of Nissl-Stained hippocampus sections. For immunohistochemical studies, we used antibody against PSA-NCAM as a marker of early oligodendrocyte progenitors, immature neuron and different interneuronal populations.

Results: Pre-treatment with VPA increased repair in CA3 region of C57bl/6 mice hippocampi. Statistical analysis of cell counting showed that the number of neurons is significantly increased in CA3 region of mice hippocampi. Immunohistochemical studies showed the presence of PSA-NCAM positive cells in the lesion sites of pre-treated animals.

Conclusion: VPA application can improve regeneration in KA induced model of neurodegeneration. Increased neurogenesis was observed in the CA3 region of both hippocampi. The presence of early oligodendrocyte progenitors shows the oligodendrogenesis in the lesion sites.

Keywords: Valproic acid, Regeneration, Oligodendrogenesis, Neurogenesis, Neurodegeneration, Kainic acid.