Abstract

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Project Title : Effect of Asiatic acid on a reduction of hippocampal cell proliferation and survival and cognitive deficits caused by 5 fluorouracil chemotherapy in rats

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Abstract:

Valproic acid (VPA) is commonly prescribed as an anticonvulsant and mood stabilizer used in the treatment of epilepsy and bipolar disorder. A recent study has demonstrated that VPA reduces histone deacetylase (HDAC) activity. This action is believed to contribute to the effects of VPA on neural stem cell proliferation and differentiation which may explain the cognitive impairments produced in rodents and patients. The hippocampus has a crucial role in cognition which is associated with cell proliferation in the SGZ of the hippocampal dentate gyrus. Asiatic acid is a triterpenoid derivative from medicinal plant, Centella asiatica. Asiatic acid has demonstrated biological effects such as antioxidant, anti-inflammatory and neuroprotective properties both in vitro and in vivo. Previous work in rodents has shown that asiatic acid stimulates learning and memory. An analytical study has shown that asiatic acid increases cell proliferation in the SGZ of the dentate gyrus (unpublished data). Furthermore, asiatic acid has been shown to improve memory and reduce cell death in primary cultured cortical neuronal cells. Asiatic acid has shown the ability to have neuroprotective effect and induce learning and memory. It also stimulates cell proliferation the SGZ of the hippocampal dentate gyrus which is associated to cognition. Therefore, the aim of this study is to explore the effect of asiatic acid on cognitive deficit and reduction of cell proliferation caused by VPA. Male Sprague Dawley rats were orally administered asiatic acid (30 mg/kg/day) for 28 days, while VPA-treated rats received VPA injections (300 mg/kg) twice a day from Day 15 to Day 28 for 14 days. Spatial working memory was determined using the novel object location (NOL) test. Hippocampal cell proliferation and survival were quantified by immunostaining for Ki-67 and Bromodeoxyuridine (BrdU), respectively. The results demonstrated that VPA-treated animals were unable to discriminate between objects in familiar and novel locations. Moreover, VPA significantly reduced numbers of Ki-67 and BrdU positive cells. These results indicate that VPA treatment caused

impairments of spatial working memory, cell proliferation and survival in the SGZ of the hippocampal DG. However, these abnormalities were restored to control levels by co-treatment with asiatic acid.

Keywords : 3-5 words

Asiatic acid, valproic acid, spatial memory, neurogenesis