

Abstract

Comparison the effects of Fluoxetine and environmental enrichment on anxiety-like behavior, learning, memory and pain threshold in adult female rats following neonatal use of Tryptophan Hydroxylase inhibitor

Background: The infant stage is a neuro- developmental stage and is a critical time for the growth of neural networks, any disturbance in this period can cause disorders such as mental, anxiety-like behaviors, learning and memory problems, and pain threshold disorders in adulthood. Tryptophan hydroxylase is an enzyme that plays a role in the production of the neurotransmitter serotonin, and its inhibition by tryptophan hydroxylase inhibitors reduces serotonin levels. Serotonin is an important neurotransmitter in the brain during development and throughout a person's life. Its reduction in early life will lead to developmental disorders in adulthood. SSRI drugs (selective serotonin reuptake inhibitor) such as Fluoxetine are used for disorders that occur due to the reduction of serotonin levels. Enriched environment includes brain stimulation by social and physical life and persuasive factors. As this environment is more exciting for rats, the more it causes the expansion of hippocampal synapses. These stimulations ultimately lead to increased learning and improvement of cognitive disorders.

Aim: Investigation of the comparative effect of fluoxetine and enriched environment as a treatment for anxiety-like disorders, learning and memory, and pain threshold has not been done until now, and the positive effects of enriched environment on these disorders remain unknown, so the present study aims to investigate the effects of fluoxetine And the enriched environment for the mentioned disorders and their comparison.

Materials and Methods: After approving the title and receiving the code of ethics from Ardabil University of Medical Sciences, 56 female rats from pregnant Wistar rats were obtained from the Pasteur Institute of Iran and kept under light conditions of 12 hours of light and 12 hours of darkness and a temperature of 23 ± 1 degrees Celsius. Enough water and food were provided to them during the experiment.

The neonate rats were weaned on the 21st day after birth and kept separately in groups. In this study, female babies were divided into 7 groups of 8, which were evaluated for the effect of tryptophan hydroxylase inhibitor, fluoxetine and enriched environment.

Results: The obtained results showed that the administration of Para chloro phenylalanine (PCPA) drug in the neonatal period with a dose of 100 $\mu\text{g}/\text{kg}$ causes disturbances in behavioral tests and as a result decreases serotonin in the brain structure. Passive avoidance memory and new object recognition memory tests showed that inhibition of tryptophan hydroxylase enzyme by Para chloro phenylalanine with a dose of 100mg/kg causes memory impairment and loss.

Conclusion: The findings of the present study showed that the use of fluoxetine significantly improved memory, including passive avoidance memory, compared to the control groups. Also, exposure to EE compensates the cognitive impairment caused by the reduction of serotonin, and living in an enriched environment is a non-pharmacological intervention that, along with fluoxetine, doubles learning and memory in healthy rats.

Key words: Fluoxetine, Environmental enrichment, Learning, memory, Anxiety like behavior, Pain threshold, Tryptophan Hydroxylase inhibitor