

Autophagic Molecular Alterations in the Mouse Cerebellum Experimental Autoimmune Encephalomyelitis Model Following Treatment with Cannabidiol and Fluoxetine

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Abstract :

The crosstalk between autophagy and apoptosis is one of the most important processes involved in the cell program death, and several mechanisms including oligodendrocyte apoptosis and autophagy play significant roles in activating macrophages, microglial cells, and finally demyelination in neurodegenerative disease. The antidepressants and anti-apoptotic mechanisms of fluoxetine (FLX) and cannabidiol (CBD) commence an autophagic event that can effectively repair myelin. This study aimed to investigate the effect of those reagents on the rate of demyelination in the cerebellum, an important site for white matter in a mouse model of experimental autoimmune encephalomyelitis (EAE). EAE was induced in twenty four adult female C<sup>57</sup>Bl/6 mice were induced

the EAE model; FLX treatment which was performed (10 mg/kg/IP) and CBD; were treated (10 mg/kg/IP); and their cerebellum was used for Western blotting, real-time PCR to autophagic markers of LC3II, Beclin-1, and apoptotic markers Bax and Bcl2 evaluation and Luxol Fast Blue staining to the assessment of demyelination. The level of autophagic markers was expressively elevated ( $P < 0.01$ ) but the pro-apoptotic markers and Bax/Bcl2 ratio were reduced ( $P < 0.05$ ). Luxol Fast Blue staining confirmed the noteworthy diminution of demyelination in treatment groups ( $P < 0.001$ ). This finding clarified that FLX and CBD ameliorate the severity of the EAE model. Combinatory treatments of these two agents are suggested for future investigations.

## **BIOGRAPHY**

*My name is Mehdi Mehdizadeh and I am Full professor in Anatomical Sciences and head of Reproductive Sciences and Technologies Research Center. Iran University of Medical Sciences (IUMS), I graduated from Tehran University of Medical Sciences in 1990 with PhD, Fellowship in Transgenic Animals from German Research Center for Biotechnology (GBF) 2009.*