IMPACT OF ENDOCANNABINOD SYSTEM MODULATION ON ADOLESCENT BRAIN MATURATION

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Cannabis is the illicit drug most commonly used by adolescents. Data suggest a relationship between adolescent Cannabis abuse and the risk for developing psychiatric diseases later in life. Thus, adolescence represents a vulnerable period for the psychiatric consequences of Cannabis exposure. During this sensitive period brain undergoes changes in morphology as a loss of gray matter (it contains the cell bodies, dendrites and axon terminals of neurons) and a rise of white matter (it is made of myelinated axons). Many works suggest that the Endocannabinoid System (ECS) is an important neuromodulatory system involved in perinatal neurodevelopment, but the involvement of the ECS in adolescent brain refinement remains to be elucidated.

On these bases, our aim was to elucidate the role played by the specific components of the ECS (CB1receptor, AEA and 2-AG) during adolescent brain maturation in the prefrontal cortex of female rats. In particular, we studied the effect of ECS modulation on markers of plasticity and myelination. To better analyze each step of the brain maturation, experiments were performed every 5day starting from 28to 37PND. Specifically we administered AM251(a selective antagonist of CB1receptor), URB597(an inhibitor of the enzyme fatty acid amide hydrolase), JZL184(a selective inhibitor of monoacylglycerol lipase) and THC (the main psychoactive component of cannabis).

We performed western blot assays to evaluate different proteins related to plasticity processes (e.g. PSD95, VGAT, CB1, Synaptophysin) and myelination (MOG and MBP).

Interestingly, data obtained indicate that the blockade of CB1receptor trough the administration of AM251completely prevented the physiological reduction of PSD95from 28to 37PND whereas the administration of THC and URB597similarly affected PSD95levels but only when administered from 28to 32PND. Regarding myelination events, the administration of AM251significantly decreased MOG levels.

Our results clearly suggest an involvement of CB1receptor in pruning events and myelination processes in the prefrontal cortex of adolescent female rats.