TIME-DEPENDENT ALTERATIONS OF THE ENDOCANNABINOID SYSTEM AND SYNAPTIC MARKERS FOLLOWING ADOLESCENT Δ9-TETRAHYDROCANNABINOL (THC) ADMINISTRATION IN FEMALE RATS

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BACKGROUND

ADULT female rats chronically exposed to THC during adolescence show:

- A COMPLEX DEPRESSIVE-LIKE PHENOTYPE characterized by both emotional and cognitive impairments (Rubino et al., 2008, 2009; Realini et al., 2010);
- A MAJOR VULNERABILITY TO phencyclidine-induced PSYCHOTIC-LIKE SYMPTOMS (Rubino et al., ICRS 2010).

AIM

To clarify the POSSIBLE NEUROBIOLOGICAL CHANGES leading to the behavioral alterations observed in adult THC pre-treated rats, we analysed:

- CB1 RECEPTOR DENSITY AND G-PROTEIN COUPLING;
- ENDOCANNABINOID CONTENTS;
- PSD95 AND SYNAPTOPHYSIN LEVELS, two markers of synaptic plasticity;

...in the prefrontal cortex (Pf Ctx), nucleus accumbens (NAc), hippocampus (Hippo) and amygdala (Amy) of THC-treated and control rats.

...and performed all the biochemical tests at DIFFERENT TIME-POINTS AFTER DISCONTINUING THC EXPOSURE.

MATERIALS AND METHODS

At each time-point, brains were removed and the following assays were performed.

CB1 RECEPTOR FUNCTIONALITY:
- [3H]CP-55,940 autoradiographic binding;

ENDOCANNABINOID LEVELS

SYNAPTIC MARKERS

SYNAPTOPHYSIN

PSD95

CONCLUSIONS

Adolescent THC treatment induces:

- SIGNIFICANT CHANGES IN THE MATURATION OF THE ENDOCANNABINOID SYSTEM coupled with
- ALTERATIONS IN MARKERS OF SYNAPTIC PLASTICITY...

...THAT ARE PARTICULARLY EVIDENT IN THE PF Ctx AND NAC.

...brain areas characterized by a strong neuronal remodeling during adolescence since they are involved in processes of decision making and reward.

However, AN ENDURING FORM OF NEURAL ADAPTATION IN THESE BRAIN AREAS FOLLOWING ADOLESCENT CANNABINOID EXPOSURE might disrupt normal neuronal development, possibly leading to the development of the behavioural phenotype observed in THC-treated rats at adulthood.

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