Intra-uterine Exposure to Cannabinoid and its effects on the Ventilatory System of Newborn and Juvenile Rat's Life

[1]Luis Gustavo A. Patrone, [1]Kênia C. Bícego, [1]Luciane H. Gargaglioni

[1]Dept of Animal Morphology and Physiology, São Paulo State University, FCAVJ, Sao Paulo-Brazil.

Introduction: The prenatal period is highly sensitive to pharmacological interventions. The psychoactive compounds of *Cannabis* act directly on the endocannabinoid system, and the deleterious effects of external cannabinoids during gestation may be related to negative interference in the central nervous system (CNS) formation, structuring and functioning of the respiratory system. Nevertheless, the influence of external cannabinoids on the ventilatory network development as well as in the chemosensitivity and the future consequences during neonatal and juvenile period is still unclear.

Objective: To evaluate the effects of exposure to cannabinoid during the whole gestational period on the respiratory control system at P0, P6-7, P12-13 and P27-28 male and female rats.

Material and Methods: Osmotic pumps were implanted subcutaneously in pregnant rats at embryonic day 0 and delivered vehicle (VEH) or CB1 receptor agonist (WIN 55212-2, 0.5 mg/Kg/day) for 21 days. Ventilation (V_E) of animals was recorded by pressure-plethysmography (P0, P6-7 and P12-13) and whole body plethysmography (P27-28) during normoxia, hypercapnia (7% CO_2) and hypoxia (10% O_2), as well as the O_2 consumption (VO_2) was measured.

Results: At P0, WIN-treated male rats had a higher resting ventilation (~45%), hypercapnic (HCVR, ~41%) and hypoxic ventilatory response (HVR, ~35%) compared to vehicle group. At P6-7, WIN male group had a decreased HCVR (~19%) and also a lower HVR (~16%). For P12-13 animals, both male and female WIN-treated rats had an increase in the response to CO_2 (male - 33% and female - 18%). For P27-28 rats, the HCVR was significantly higher for male (~21%) as well as for female (~25%) WIN-treated groups, no difference was observed for HVR. All the respiratory changes observed were not caused by metabolic issues since no difference was observed in the VO_2.

Conclusions: A chronic and over activation of endocannabinoid system during gestation promotes alteration in the respiratory system development affecting the chemosensitivity to CO_2 and O_2 during neonatal and juvenile period. Financial support: FAPESP and CNPq.

Keywords: Cannabis, Cannabinoid system, ventilatory system, newborn, juvenile, rats