

CANNABIDIOL ADMINISTRATION DURING PREGNANCY AND LACTATION MODULATES THE SUPPRESSIVE EFFECT OF MATERNAL ALCOHOL EXPOSURE ON CELL PROLIFERATION AND SURVIVAL IN THE HIPPOCAMPUS OF OFFSPRING

M. Rodríguez-Pozo^{1,2}, P. Rubio-Rodríguez^{1,2}, F. Rodríguez de Fonseca^{1,3}, J. Suárez^{1,2}, P. Rivera^{1,4}

¹*Instituto de Investigación Biomédica de Málaga (IBIMA)-Plataforma BIONAND), Málaga, Spain.*

²*Department of Human Anatomy, and Forensic and Legal Medicine, University of Málaga, Málaga, Spain.* ³*Servicio de Neurología, Hospital Regional Universitario de Málaga,* ⁴*UGC Mental Health, Hospital Regional Universitario de Málaga, Málaga, Spain.*

Excessive alcohol consumption during pregnancy causes neurodevelopmental disorders due to vulnerability and neuroadaptation of the immature brain with serious consequences on cognition. Since the endocannabinoid system plays a role in neurogenesis and the phytocannabinoid cannabidiol (CBD) exerts a neuroprotective effect including anti-inflammatory, antioxidant, immunomodulatory and anxiolytic capacity, the role of CBD in neurogenesis in a context of alcohol exposure is still largely unknown. The present study examines the effect of maternal exposure of 20% ethanol (*ad libitum* orally during 2 and 4 hours/day, 4 days/week) on neurogenesis, locomotor activity, anxiety-like behaviour and memory in offspring, and their response to a prior subcutaneous injection of CBD (20 mg/kg) for 6 weeks during pregnancy and lactation. Cell proliferation in the subgranular zone (SGZ) of the dentate gyrus (DG) and cell survival in the hippocampal CA1, CA3 and DG were evaluated in mouse offspring of both sexes at PND21, and Open Field (OF), Elevated Plus Maze (EPM) and Novel/familiar Object Recognition (NOR) tests were performed in mouse offspring of both sexes at PND60.

CBD increased body weight in offspring of both sexes after maternal water exposure, and decreased it after maternal alcohol exposure. CBD increased exploration time in the OF central area in offspring of both sexes after maternal water exposure, and no CBD effect was found after maternal alcohol exposure. No CBD effect on anxiety-like behaviour was observed; only reduced exploration time in the EPM open arm was specifically found in female offspring after maternal alcohol exposure. CBD decreased NOR preference ratio in male offspring after maternal water exposure. Drinking effects on cell proliferation and survival resulted from lower number of BrdU+ cells in the SGZ and higher number of BrdU+ cells in the hippocampus, respectively, after maternal alcohol exposure. In addition, CBD decreased SGZ cell proliferation after maternal water exposure. Interestingly, CBD increased CA3 cell survival, but lowered cell survival in the CA1 stratum pyramidale after maternal alcohol exposure. In summary, our study suggests that CBD plays a specific role in modulating cell survival in the hippocampal CA1 and CA3 of offspring after maternal alcohol exposure, an effect that was not accompanied by significant behavioural improvement, in contrast to the CBD effects in control offspring.

Acknowledgements: We thank Phytoplant Research SLU for the supply of CBD. Consejería de Universidad, Investigación e Innovación (PI21/00291). P. Rivera is supported for the “Miguel Servet” (CP19/00068) research contract from the National System of Health, ERDF-EU-ISCIII, cofunded by European Social Fund, “Investing in your future”, Gobierno de España.

Key words: Pregnancy, ethanol, cannabidiol, neurogenesis, memory

Intended for: Poster communication