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NEONATAL MORPHINE ADMINISTRATION LEADS TO CHANGES IN HIPPOCAMPAL BDNF LEVELS AND ANTIOXIDANT ENZYME ACTIVITY IN THE ADULT LIFE OF RATS

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Objectives: It is known that repeated exposure to opiates impairs spatial learning and memory and that the hippocampus has important neuromodulatory effects after drug exposure and withdrawal symptoms. Thus, the aim of this investigation was to assess hippocampal levels of BDNF, oxidative stress markers associated with cell viability, and TNF-alpha in the short, medium and long term after repeated morphine treatment in early life. **Methods:** Newborn male Wistar rats received morphine (morphine group) or saline (control group), 5 ug in the mid-scapular area (s.c.), starting on postnatal day 8 (P8), once daily for 7 days, and neurochemical parameters were assessed in the hippocampus on postnatal days 16 (P16), 30 (P30), and 60 (P60). BDNF and TNF-alpha levels were analyzed through ELISA. Cell viability and cell damage were analyzed in dissected hippocampus with or without H₂O₂ damage. Superoxide dismutase (SOD) activity was determined using RANSOD kit; Glutathione peroxidase (GPx) activity was determined as described by Wendel (1981), with some modifications; reactive species production by chemical oxidation of Dichlorodihydrofluorescein (DCFH) was evaluated in according method described by Sriram et al (1987); total Thiol level was evaluated in according method described by Aksenov and Markesbery (2001). The data analysis and interactions were evaluated using two-way ANOVA (morphine, age, morphine*age) followed by the Student-Newman-Keuls (SNK) method when indicated. The between group differences were considered significant at P<0.05. The number of animals was 4-7/group/age for each assay. **Results:** The two way ANOVA showed no effect of age (P = 0.327), but there is effect of morphine (P = 0.042), and interaction between age and morphine treatment (P = 0.049) in BDNF levels. In the TNF-alpha levels, showed effects of age (P = 0.036), of morphine treatment (P = 0.011), and no interaction between age and morphine treatment (P = 0.275). There is effect of morphine treatment (P = 0.01), no effect of age (P = 0.127) and no interaction between age and morphine treatment in the superoxide dismutase activity (P = 0.144); effect of age (P<0.001), no effects of morphine treatment (P = 0.624) and no interactions between age and morphine treatment in the glutathione peroxidase activity (P = 0.164); in the thiol levels was also observed effect of age (P = 0.041), no effects of morphine treatment (P = 0.178) and no interactions between age and morphine treatment (P = 0.254); there is effect of age (P<0.001), no effects of treatment (P = 0.541) and no interactions between age and morphine treatment in the analysis of reactive species production (P = 0.715). In the MTT assay, there are no interactions between age and morphine treatment and H₂O₂-induced cellular damage (P = 0.887), between morphine and age (P = 0.880) and between morphine and H₂O₂-induced cellular damage (P = 0.200). However, there is effect of H₂O₂-induced cellular damage (P<0.001), and interaction between age and H₂O₂-induced cellular damage (P = 0.034), and no effect of morphine treatment (P = 0.526). There is significant difference between P16 and P60 (P = 0.009). In the LDH assay, there are no interactions between age and morphine treatment and H₂O₂-induced cellular damage (P = 0.303), between age and H₂O₂-induced cellular damage (P = 0.502), and morphine treatment and H₂O₂-induced cellular damage (P = 0.664). **Conclusion:** These findings show that repeated morphine treatment in the neonatal period can lead to long-lasting neurochemical changes in the hippocampus of male rats, and indicate the importance of cellular and intracellular adaptations in the hippocampus after early-life opioid exposure to tolerance, withdrawal and addiction. **Financial Support:** FIPE-HCPA (08345), CAPES, CNPq, FAPERGS.