LONG EXPOSURE TO HIGH PALATABLE FOOD ON PAIN SENSITIVITY: ROLE OF CANNABINERGIC SYSTEM

Carmen Avagliano[1], Maria Vittoria Micioni Di Bonaventura[2], Maria Elena Giusepponi[2], Carmen De Caro[1], Claudia Cristiano[1], Giovanna La Rana[1], Adele Romano[3], Antonio Calignano[1], Silvana Gaetani[3], Roberto Russo[1], Carlo Cifani[2]

[1]Department of Pharmacy, "Federico II" University of Naples, Naples - Italy, [2]School of Pharmacy, Pharmacology Unit, University of Camerino, Camerino - Italy, [3]Department of Physiology and Pharmacology "V. Erspamer", Sapienza University of Rome, Rome - Italy

Introduction: Cafeteria (CAF) diet is based on human foods with high sugar, salt and spice contents that making it a palatable diet used in many animal obesity models. It has been demonstrated that there is a strong relationship between abstinence from palatable foods and pain, and that cannabinoid and opioid systems might play an important role in this correlation.

Materials and methods: Male Sprague-Dawley rats were divided in: (1) animals fed with standard chow only (CO) and (2) animals fed with both standard chow and extended-access to CAFdiet (EA) for 40 days. From day 41, a period of abstinence from CAF diet started for EA rats, which received only chow until day 68.During the same time window, CO rats were maintained on the chow only diet regimen as in the previous 40 days. Pain behavioral tests were performed on day 40, 54and 68and Western blot analysis was performed on day 40 and 68. In a second experiment, CO and EA groups were treated every other daywiththe selective Fatty Acid Amide Hydrolase (FAAH) inhibitor, PF-3845(10 mg/kg, subcutaneously),from day 41to day 54(abstinence period). On day 54hot plate testwasperformed andbrain collected for Western blot analysis.In a third experiment, CO and EA rats were treated with PF-3845and received on day 54an acute intraperitoneally administration of either cannabinoid receptor 1(CB1) or MU opioid receptor antagonists, SR141716A (SR) or Naloxone (Nal), 1h before performing the hot plate test.

Results: At the end of CAF diet (day 40) results clearly indicate that EA rats showed a significant increase in pain threshold compared to CO rats due to an up-regulation of MU and CB1receptors. Surprisingly, for the first time, we have shown that palatable food increasedCB1receptors expression in brain.On day 54, we observed a weak increase of pain sensitivity, which was significant only in hot plate test. Then, PF-3845was used to evaluate CB1receptor contribution in pain perception during abstinence period from CAF diet. Our results clearly showed that repeated PF-3845treatment decreased pain sensitivity in CO and EA rats if compared to the vehicle group and, surprisingly, a significant effect between in abstinence (EA+PF-3845) and normal (CO+PF3845) rats was observed. This activity was mainly MU receptors-mediated: Western blot analysis showed a significant MU up-regulation following PF treatment. Finally, results showed that pre-treatment with cannabinoid and opioid antagonists reduced PF-increased pain sensitivity.

Discussion and conclusions: Here we investigated whether a long-term exposure to CAF diet could modify pain sensitivity and which is the role of cannabinergic system. Our findings point out that a long exposure to palatable food induces significant changes in pain perception and reinforce the knowledge about the correlation between obesity and painand underline the role of CB1receptors in abstinence from palatable foods and pain, using an indirect agonist, such as PF-3845.Our data clearly indicate that endocannabinoid tone is necessary not only for its own activity in the resolution of "compulsive" state, but also for its abilities in preserving and/or modifying other systems compromised by this condition.