Effect of cafeteria diet on pain behavioral in rats

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Obesity is one of the most important public health problems in modern societies, being overconsumption of readily available high-palatable caloric-dense food the primary cause for its development. Epidemiological evidence suggest that obesity might be linked to increased incidence of depressive and anxiety disorders and to increased pain levels (1–3), although the link to these comorbidities was much less investigated with respect to other pathologies. The observation of addiction-like deficits in the brain reward system in obese patients (4–6), suggests that the increased risk for such disturbances might derive from neuroadaptive changes. The wearing off of the hedonical rewarding properties of food may gradually lead to a shift away from positive reinforcement and towards negative reinforcement so that consumption becomes necessary to prevent or relieve negative states (anxiety, depression, irritability and possibly somatic symptoms) that would result from abstinence (7). In support to this hypothesis, reward hypofunctionality, compulsive-like eating, anxiety and reduced pain threshold were observed in rats and mice that volitionally overate a palatable cafeteria diet consisting of palatable energy-dense food available for human consumption (8). Endocannabinoids play an important role in modulating all the neurobehavioral components of this scenario. Most of the evidence focused on anandamide (AEA), through the activation of type 1 cannabinoid receptor (CB1). These receptors are densely expressed by neurons of the reward system, where their activation, by plant-derived, synthetic or endogenous agonists, stimulates dopaminergic neurotransmission, produces rewarding effects and increases rewarding effects of abused drugs and food. Adult male Wistar rats (300-350g) were randomly divided into 3 groups with ad libitum access to standard chow and water but differential access to the cafeteria for 40 consecutive days. The first group was labeled as 'chow only' (CO) and was no access the cafeteria diet; the second group was labeled as 'restricted access' (RA) and was access for 1 h per day to the cafeteria diet; the third group was labeled as 'extended access' (EA) and was ad libitum access (24 h/day) to the cafeteria diet. At the end of the 40 days with differential access to the cafeteria diet all rats were undergo an 'abstinence' period of 28 days, with no access to the cafeteria diet. Animals were subjected to hot plate and tail flick tests at the end of the cafeteria exposure (day 40), and after 5 (day 45), 13 (day 53), and 28 (day 68) day. Result showed that, on day 40, RA and EA rats showed a significant increase of threshold pain in both models respect CO rats. Interesting, during abstinence period, at day 45, 53 and 68, RA and EA rats showed a lower threshold pain vs control group. Finally, we verify if endocannabinoid system are involved in these variation of pain sensitivity. At day 40,and 53, and 68 rats were euthanatized and the brain was removed for *ex-vivo* analysis. Result indicated that at day 40, RA and EA rats showed an increase of CB1 expression, while on day 53, and 68 the same receptor was decrease. In this study, we show that access to the cafeteria diet for 40 consecutive days produce an increase of threshold of pain, probably, due to up regulation of CB1 receptor. Moreover, during abstinence period characterize by negative sate, this receptor was reduced and rats showed a significant sensitivity to pain.

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