SEXUAL DIMORPHISM IN ASTROCYTES IN RESPONSE TO FATTY ACIDS

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The authors have nothing to declare

INTRODUCTION

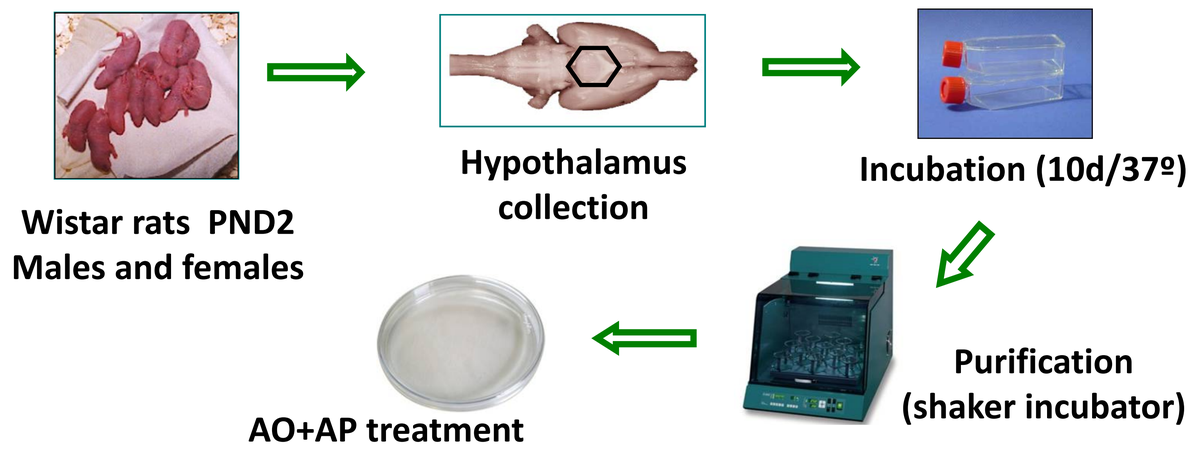
It is well accepted that obesity is associated with chronic systemic inflammation. Recently hypothalamic inflammation has been described in response to high fat diet (HFD)-induced obesity and proposed to participate in central insulin/leptin resistance and the perpetuation of weight gain and systemic affectation. The weight gain and central responses to HFD differ between males and females. As hypothalamic glial cells are implicated in the central inflammatory response it is possible that their response to free fatty acids (FFAs) differs between the sexes.

HYPOTHESIS

We hypothesized that astrocytes have an active response to free fatty acids (FFAs) and that this response is sexually dimorphic.

METHODOLOGY

Primary hypothalamic astrocyte cultures from postnatal day 2 (PND2) male and female Wistar rats were used. The cells were treated with vehicle or a mixture of palmitic (PA) and oleic acid (OA) at 0.5 mM or 1 mM for 24 hours. Nitrates and nitrites, as a marker of oxidative stress, released to media and mRNA levels of carnitine palmitoyltransferase (CPT)1a, glial fibrillary acidic protein (GFAP), glucose transporter (GLUT)2, IL6, IL1β, TNFα were quantified.



RESULTS

After 24 hours of OA plus PA (1:1) treatment: As expected, CPT1a increased according to the dose of FFAs. The amount of nitrites and nitrates released also increased in a dose responsive manner in both sexes (p<0.0001). Basal levels of IL1β, IL6 and TNFα were higher in male cultures compared to females (p<0.0001). In response to FFAs, IL6 increased in males and females (p<0.0001). However, IL1β only increased in male astrocytes (p<0.0001). GFAP mRNA levels were decreased in males at a concentration of 0.5mM, while in females a higher concentration was needed.

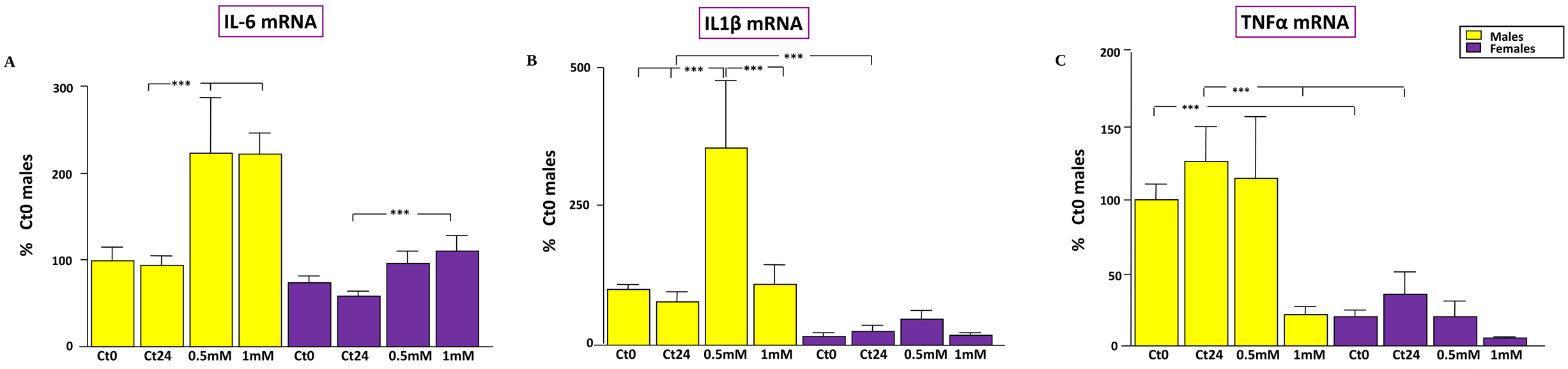
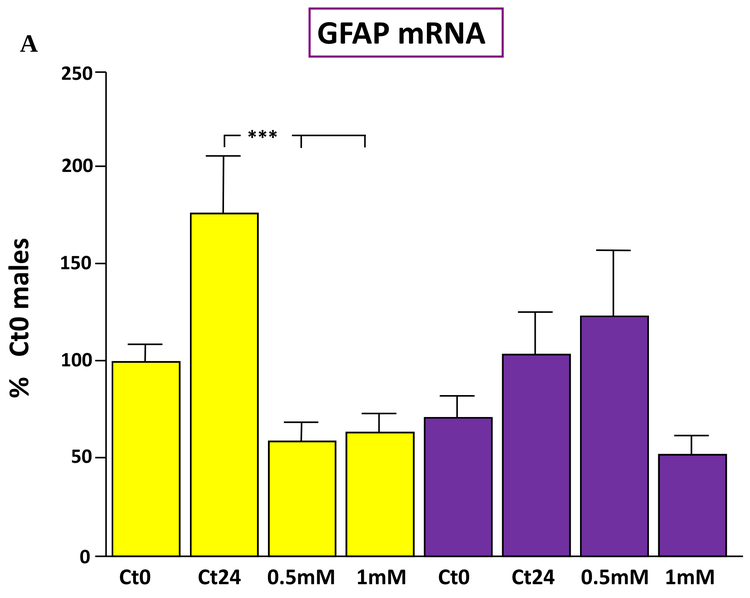


Figure 1. mRNA levels of IL6 (A), IL1β (B) and TNFα (C) in hypothalamic astrocytes from males and females in response to oleic and palmitic acid * * * p<0.0001.



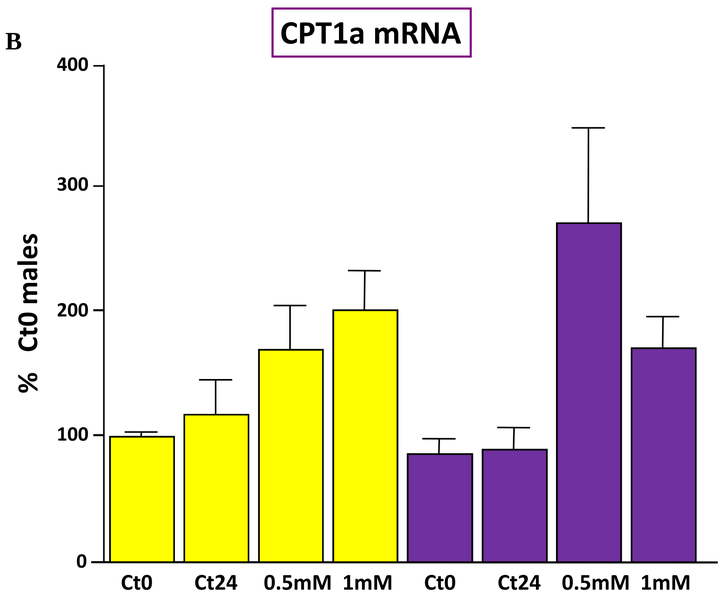


Figure 2. GFAP and CPT1a mRNA levels of hypothalamic astrocytes from males and females in response to OA+PA treatment. * * * p<0.0001

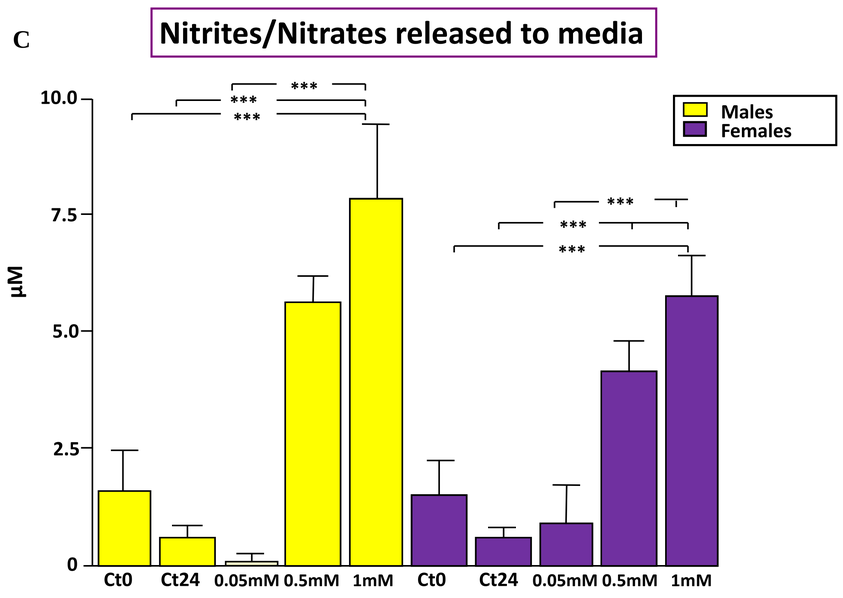


Figure 3. Nitrites and nitrates conentration realeased to the media * * * p<0.0001

CONCLUSION: FFAs have a direct effect on astrocytes, inducing cytokine production and oxidative stress, suggesting that these glial cells participate in the response to a HFD. Moreover, astrocytes from males are more sensitive to FFAs, indicating that this might be involved in their increased sensitivity to HFD.