Palmitic acid could modify cognitive and behavioral functions through sex specific activation of hippocampal astrocytes

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The authors have nothing to disclose

BACKGROUND

Prolonged poor dietary habits can result in hypothalamic inflammation and gliosis with more recent studies suggesting that other brain areas may also be affected. Western or high fat diet intake has been associated with increased cognitive impairment and aberrant feeding behavior, with males and females being differentially affected. The hippocampus participates in both of these functions. Saturated free fatty acids can induce astrocyte inflammation and this could potentially result in adverse neurologic processes. Undoubtedly, a delicate balance between pro- and anti-inflammatory signals will determine long-term cellular homeostasis.

OBJECTIVE

Our aim was to determine the effects of palmitic acid on hippocampal astrogliosis and whether these effects are sex-specific.

METHODS

Primary hippocampal astrocyte cultures were established from male and female rats (P2) using standard procedures. After 10 days, cell cultures were shaken overnight to eliminate microglia and oligodendrocytes. Cells were plated at a density of 15,000 cells/cm^2. Twenty-four hours later, cells were treated in serum free media with palmitic acid (10, 25 or 50 µM, 24 h). Levels of glial fibrillary acidic protein (GFAP), vimentin and pro- or anti-inflammatory factors were measured by western blotting.

RESULTS

1. Effects of palmitic acid on specific intermediate filaments of astrocytes

Palmitic acid increased GFAP levels in males, but induced a decrease in females. On the contrary, palmitic acid at a low dose reduced vimentin levels in males and increased them in females.

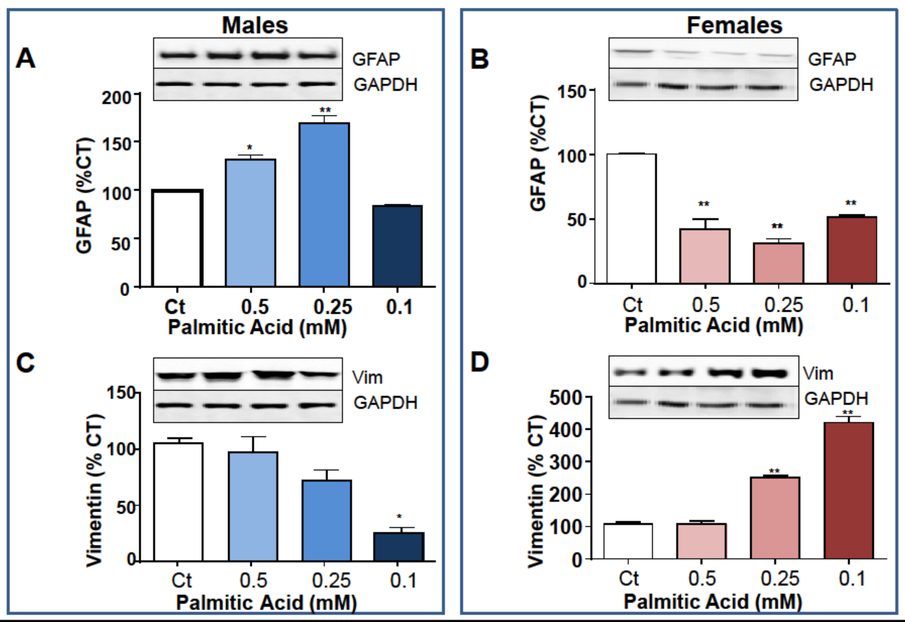

Figure 1: Immunoblots probed with antibodies towards GFAP (A, B) and vimentin (C, D) in primary astrocytes of males (A, C) and females (B, D). *p<0.05 *vs* CT; **p<0.01 *vs* CT. Mean of at least 3 experiments performed in duplicate.

2. Effects of palmitic acid on inflammatory cytokines

Levels of IL-6 increased in males and decreased in females. Levels of the pro-inflammatory intracellular signal p-IκB did not change in males or females (data not shown).

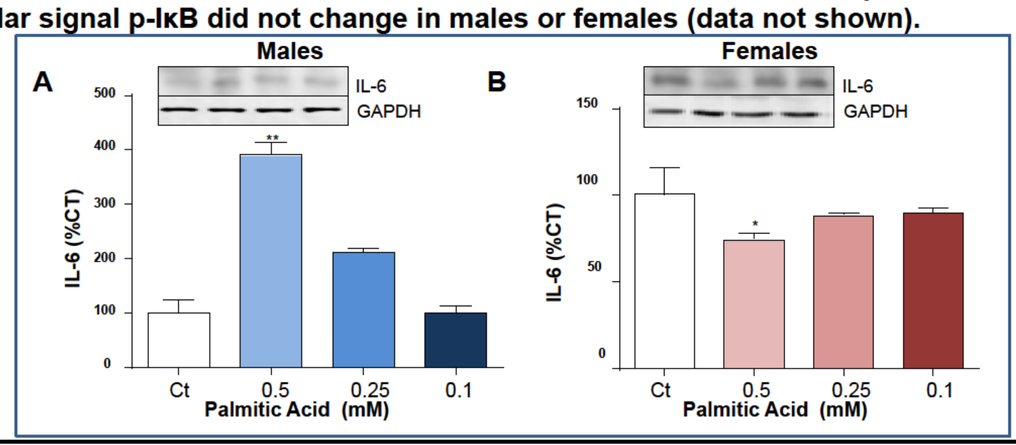

Figure 2: Immunoblots probed with antibodies towards IL-6 in primary astrocytes of males (A) and females (B). *p<0.05 *vs* CT; **p<0.01 *vs* CT. Mean of at least 3 experiments performed in duplicate.

RESULTS

3. Effects of palmitic acid on proliferation

Palmitic acid showed no effect on proliferating cellular nuclear antigen (PCNA) in males or females.

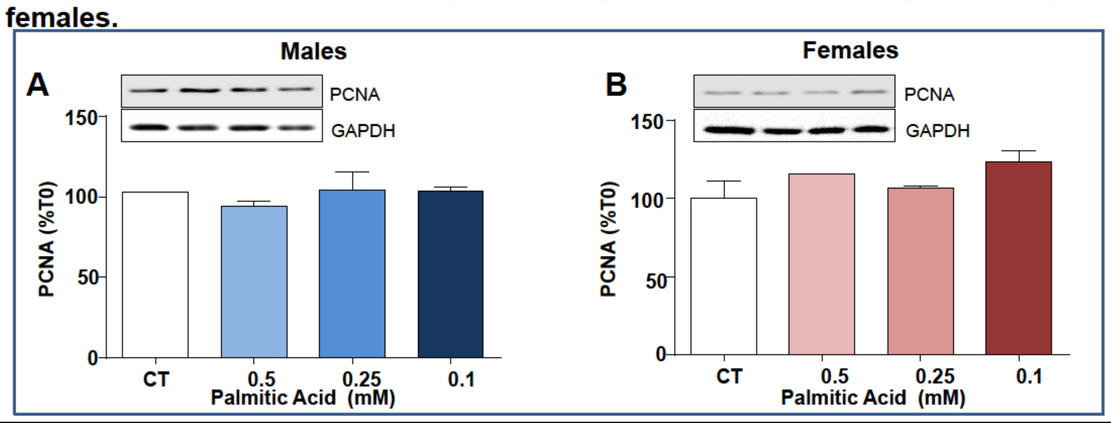

Figure 3: Immunoblots probed with antibodies towards PCNA in primary astrocytes of male (A) and female (B). Mean of at least 3 experiments performed in duplicate.

4. Intracellular signalling activated by palmitic acid

Palmitic acid decrease mitogenic ERK activation in males and females at 15 min. Palmitic acid increased activation of inflammation-related kinases p38 and JNK in males at 15 min; however, in females levels of p38 did not change, while JNK decreased at 15 min and 2 h. Finally, levels of Akt, a survival related kinase, decreased in males at 15 min and did not change in females.

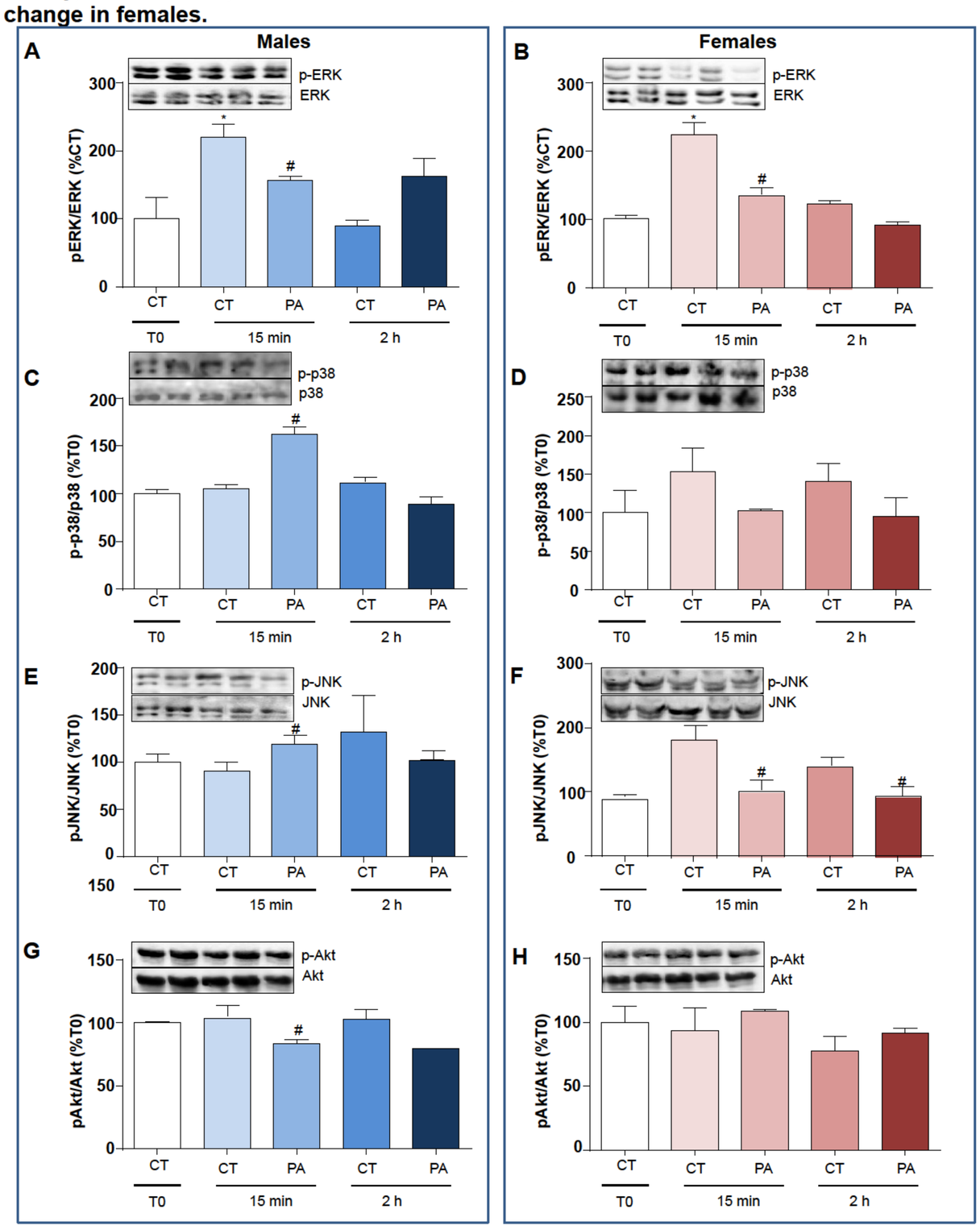

Figure 4. Immunoblots probed with antibodies towards pERK, ERK (A, B); p-p38 and p38(C, D); pJNK and JNK (E F); pAkt and Akt (G, H) in primary astrocytes of males (A, C, E, G) and females (B, D, F, H). Mean of at least 3 experiments performed in duplicate. *p<0.05 *vs* CT; # p<0.05 *vs* CT at corresponding time.

CONCLUSION

Glial cells of the hippocampus respond to palmitic acid in a sexually dimorphic manner. As these cells were derived from neonatal animals, the differential response could be an inherent difference between the sexes and could partially underlie the sex differences in propensity to develop some cognitive or behavioral dysfunctions.

Acknowledgements:

This study has been funded by BFU-27492, BFU2014-51836-C2-2-R (MICINN), and PI13/02195 (Fondo de investigación sanitaria), and CIBEROBN

ESPE 2015 341--P2

Fat Metabolism, Obesity

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DOI: 10.3252/pso.eu.54espe.2015

Poster presented at: 54th Annual Meeting 1-3 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology

PosterSessionOnline.com