HYPOTHALAMIC MELANIN-COMCENTRATING HORMONE INFLUENCES LIVER AND ADIPOSE METABOLISM

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INTRODUCTION

Melanin-concentrating hormone (MCH) is an orexigenic neuropeptide which is located in the lateral hypothalamus and regulate the energy balance. **MCH increases food intake and adiposity, so we sought to investigate the role of the MCH on adipocyte and hepatic metabolism.**

Methods: MCH were chronically administered into the lateral ventricles of rats brain, using osmotic pumps that released the MCH for a week. To study whether the sympathetic nervous system mediates the actions of MCH on white adipose tissue, deficient mice for the three beta-adrenergic receptors were used (triple knockout mice). To determine whether the central effect of MCH on the liver was mediated through the parasympathetic nervous system (PSNS), the vagus nerve was dissected. Adenoviral particles overexpressing MCH receptors (MCH-R) were estereotaxically administered into arcuate and lateral hypothalmus (LHA, ARC). Tissues were analyzed to determine the expression of genes and proteins involved in lipid metabolism of liver and fat.

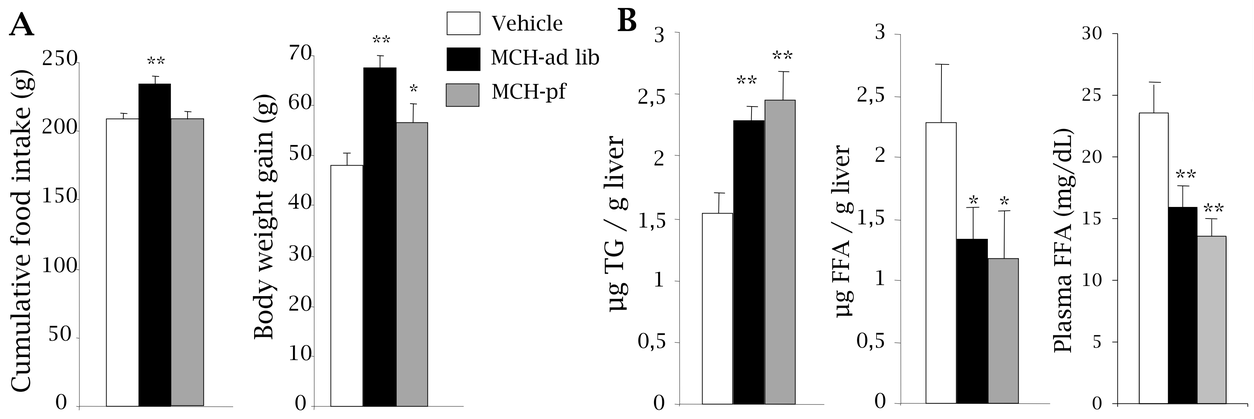


FIGURE 1. Periferal effect of a 7-day ICV MCH (10ug/day) infusion on cumulative food intake, body weight (A), trigliceride hepatic content and fatty free acids in liver and serum (B). Central MCH-infusion increase TG hepatic content and decreas FFA levels, indicatig a higher lipid storage and lower lipid oxidation.

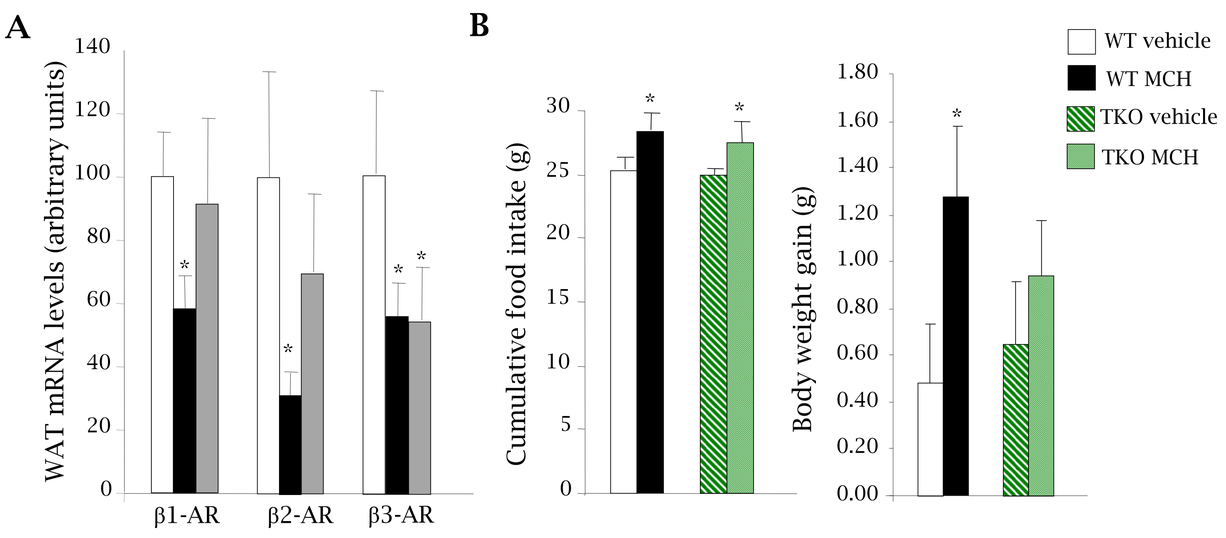


FIGURE 2. Effect of a 7-day ICV MCH infusion (2.5ug/day) on epididimal WAT mRNA expresion of β1, β2 and β3 adrenoreceptor (AR) (A) and on cumulative food intake/body weight in wild type (WT) and triple beta-adrenoreceptor knockout (TKO) mice. Central MCH infusion diminished the expresion of the three rceptors(A). The ICV MCH infusion in TKO mice showed an increase in food intake as in WT but body weight gain did not increase significantly (B). Those indicate the important role for SNS in mediating the control of lipid metabolism by the CNS-MCH.

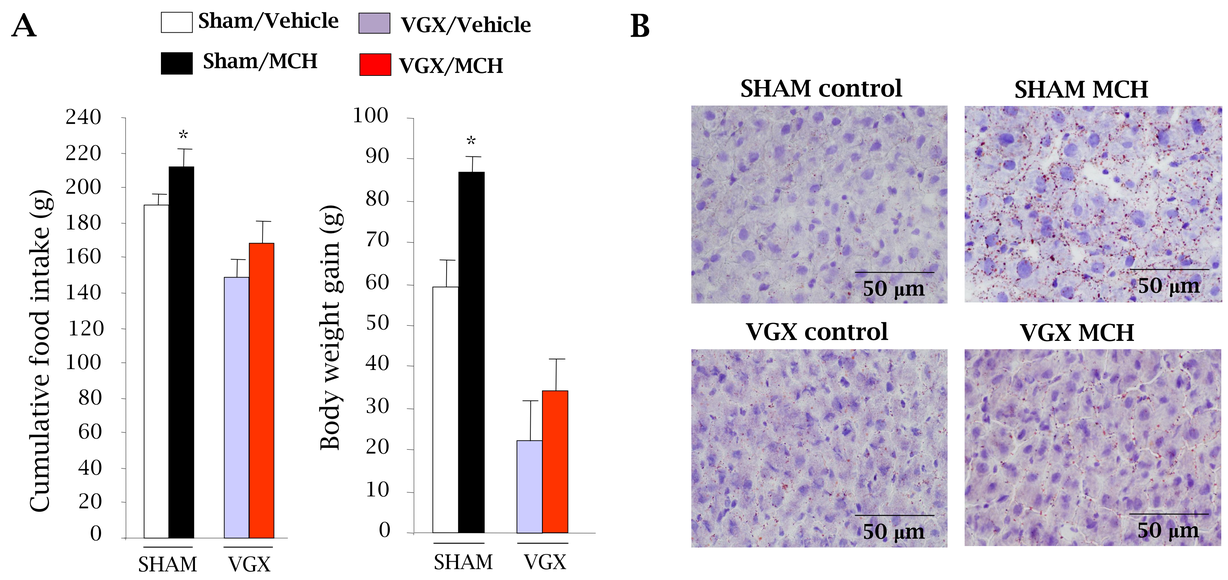


FIGURE 4. Effect of a 7-day ICV MCH (10ug/day) infusion in sham-operated rats and vagotomized (VGX) rats (A) and oil red staining showing lipid droplets in sham and VGX rats (B). Central MCH infusion didn´t increase cumulative food intake and body weight in VGX rats (A). Staining of lipid droplets was increased in sham MCH-trated rats, but not in VGX MCH treated animals. These findings indicate that the vagus nerve mediates the effects of central MCH on liver metabolism.

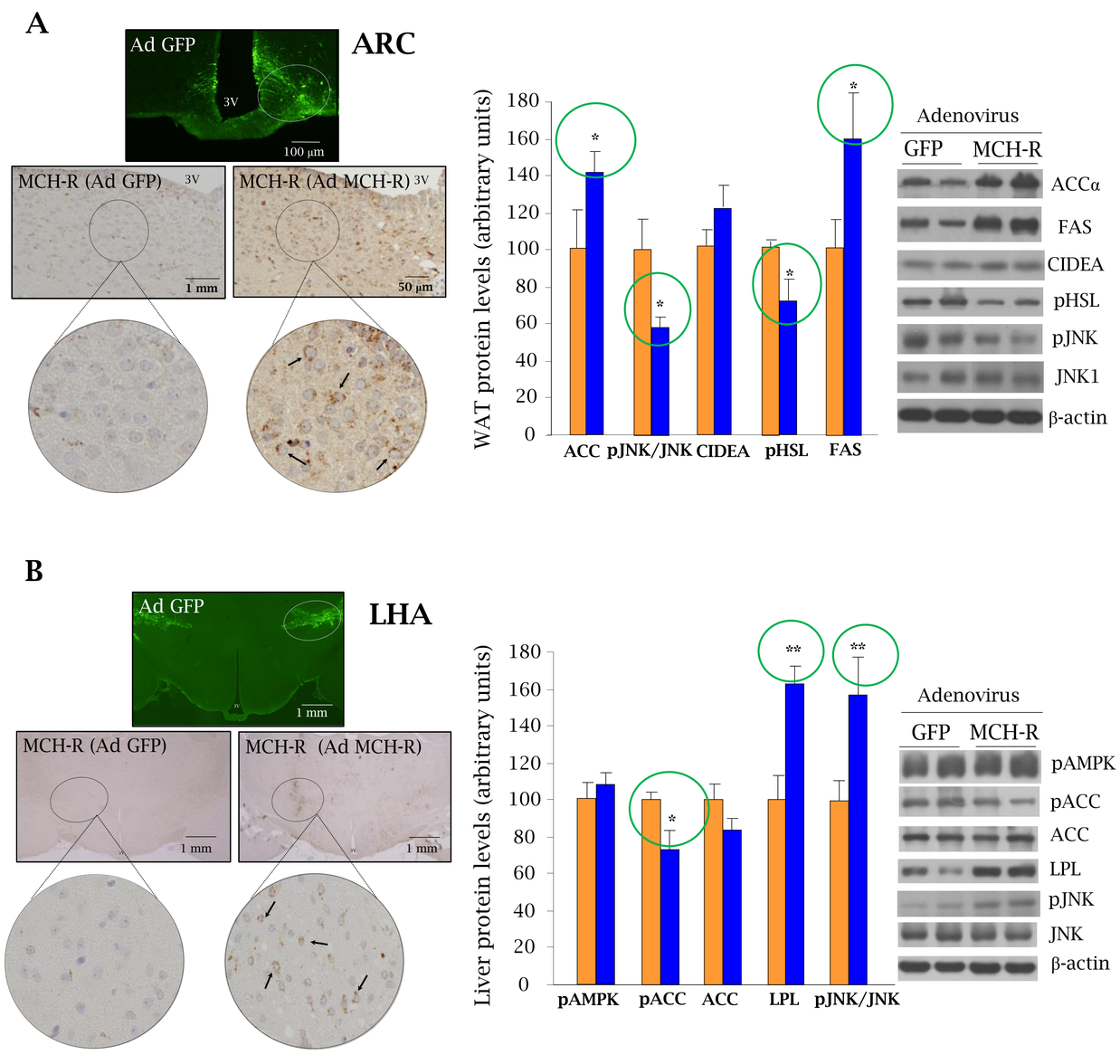
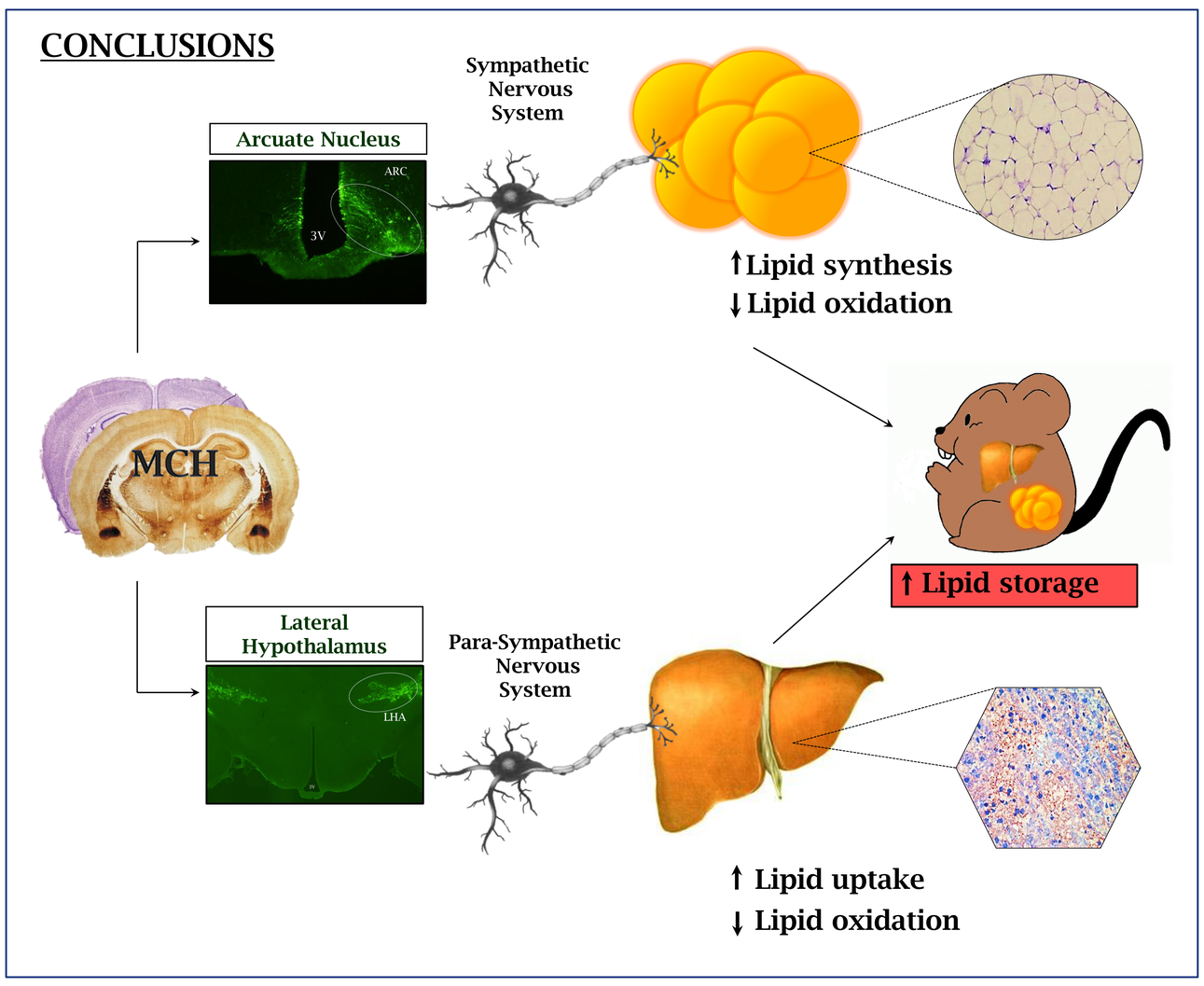


FIGURE 5. Protein level profiles in WAT and liver of rats stereotaxically treated with a GFP-expressing adenovirus or MCH-R dominant positive in the ARC (A) and in the LHA (B) hypothalamic nuclei. Corresponding images of GFP and MCH-R expression in respective brain sections are shown. The specific activation of MCH-R in the ARC and LHA increaeses body weight gain and food intake (data not show), but the the diference in protein levels are in WAT on ARC and in liver on the LHA. ARC-MCH-R are involved in the control of adipocyte lipid metabolism while this process in the liver is controlled by MCH-R located in the LHA.

CONCLUSIONS



Reference: Imbernón M. & Beiroa D. et al. Gastroenterology. 2013 Mar;144(3):636-649.e6. doi: 10.1053/j.gastro.2012.10.051.

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