Dietary macronutrient composition and central leptin pathways

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A high dietary fat (HF) content is thought to be a major factor promoting obesity. Carbohydrates (C) seem to amplify HF diet induced obesity whereas it has been observed that a HF diet with a high protein (HP such as the "Atkins diet") content induces less weight gain. To explain this phenomenon, one hypothesis proposes that differential effects of macronutrient content on regulation of energy homeostasis require changes in the efficacy of CNS leptin signaling by hypothalamic neuronal networks, such as those containing melanocortins (MCs) and glucagon-like peptide-1 amide (GLP-1). To further investigate the underlying mechanisms, anorexigenic efficacies of icv-infused leptin (3, 6 and 10 µg), MT II (agonist of MC receptors, 10 and 50 ng) and GLP-1 (3 µg) were studied in rats fed a HF, HF/HP or HC diet for several weeks. No "diet composition" effect was observed on the anorexigenic efficacies of icv leptin and GLP-1 infusion, as well as for the low dose of MTII. However, when a high dose of MT II (50 ng) was infused, rats on the HF/HP diet had a significantly more pronounced decrease in FI when compared to the rats fed the other diets (18h-cumulative FI, expressed as a percentage of the control condition: HF/HP = 30 ± 5 %, HF = 35 ± 5 % and HC = 48 ± 3%, diet effect P=0.021). We conclude that neither leptin nor GLP-1 receptors are involved in the anorexigenic effects of the HF/HP diet. Since increased anorexigenic efficacy of MTII in HF/HP fed rats was observed with the high dose only, we speculate that the interaction between the HF/HP diet and the MC receptors resides somewhere outside the hypothalamus. One potential region where dietary macronutrients and the MC system may interact is the hindbrain. This new hypothesis is currently under investigation.

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