In vivo 1H-MRS reveals neurometabolic effects of a high fat diet

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Introduction

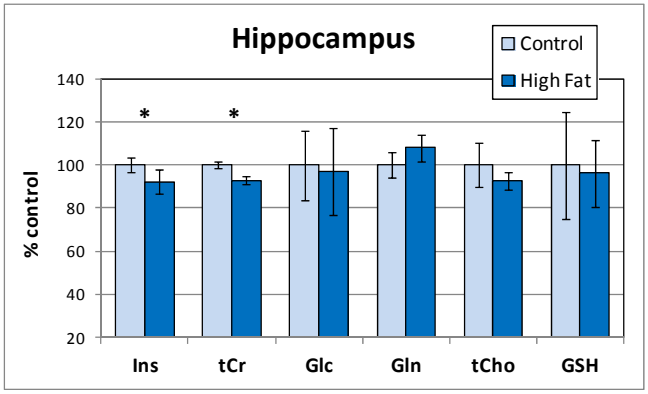
Although an increasing number of people in Western societies consume a diet that is high in fat, the potential effects of this diet on the central nervous system are not well understood. Epidemiological data and preclinical studies in rodents point to a link between a high fat (HF) diet and cognitive decline[1]. Previous studies using classical invasive methods have shown increased brain markers of inflammation and oxidative stress in rodents fed a HF diet [2, 3]. In order to better understand the relationship between excessive fat consumption and the metabolic status of the brain *in vivo*, we used proton magnetic resonance spectroscopy (^{1}H-MRS) to examine two brain regions in rats fed either a HF diet or standard low fat chow.

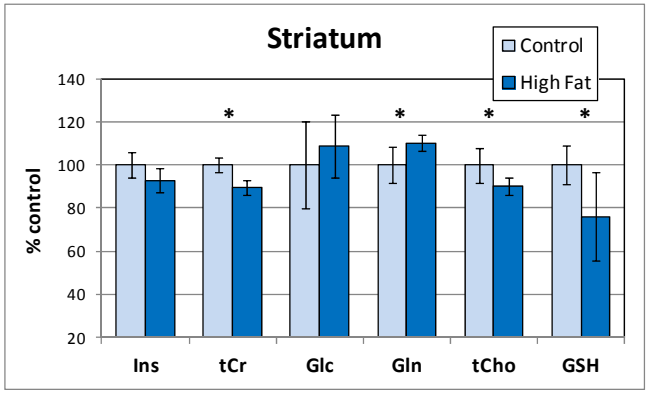
Methods

Two month old male F344 rats were given access *ad libitum* to a HF diet (60% calories from fat, Teklad; n=6) or standard rat chow (4% calories from fat, Teklad; n=6) for four months. This HF feeding protocol is an established model of insulin resistance characterized by increased adiposity and hyperglycemia. We collected water-suppressed STEAM spectra (Varian 9.4T spectrometer, TE=2ms, TR=4000ms; [4]) from two (3 x 2.5 x 3mm^3) volumes of interest over the hippocampus and striatum. First and second order shims were adjusted using FASTMAP [5] and spectra were analyzed with LCModel [6]. Metabolite concentrations with Cramer-Rao lower bounds ≤ 30% were accepted, and metabolite levels in the HF vs. control groups were compared using two-tailed Student's t-tests (*p<0.05).

Results

High quality spectra allowed quantification of 18 metabolites within the hippocampus and striatum. Animals on the HF diet had lower total creatine (tCr; creatine + phosphocreatine) in both brain regions. Other neurometabolic effects of the HF diet were region-specific: in hippocampus myo-inositol (Ins) levels were reduced, while in striatum total choline (tCho) and glutathione (GSH) were reduced and glutamine was elevated. Surprisingly, despite a characteristic hyperglycemia in the HF animals, we did not observe significant differences in brain glucose levels in response to HF feeding.





Discussion

Accumulating evidence from humans and animal models has linked HF diets with declining cognitive function. The neurometabolic changes we observed in the present study point to specific mechanisms that may underlie the negative effects of excess fat consumption on cognition. For example: lower tCr suggests global disturbances in brain energetics, decreased tCho indicates changes in membrane biodynamics, lower GSH suggests increased oxidative stress, and higher Gln points to altered glutamatergic activity and/or changes in the astroglial population. The fact that brain glucose remains unchanged in rats on the HF diet suggests that brain glucose is under tighter control than peripheral blood glucose in this hyperglycemic, but pre-diabetic animal model. The present study demonstrates that excess fat consumption significantly alters cerebral metabolic homeostasis. We conclude that ^{1}H-MRS biomarkers may provide valuable insight into the effects of a HF diet on brain cognitive function.

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