Ingested lipid modulates hypothalamic and brainstem neuronal activity in man: A phMRI study

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Introduction

Ingested lipid releases cholecystokinin (CCK) from the upper gut which regulates food intake via CCK-1 receptors[1]. cFOS studies have shown that this signalling pathway activates brainstem and hypothalamic nuclei which are known to be key sites for processing feeding regulation signals[2]. Recent studies using a combination of pharmacological challenge and fMRI (pharmacoMRI; phMRI) have shown that it is feasible to measure neuronal activity in response to ingested glucose[3], however, the effect of ingested lipid on brainstem and hypothalamic neuronal activity in man is unknown. The purpose of this study was to explore the changes in brainstem and hypothalamic neuronal activity in response to ingestion of a CCK-releasing lipid in man.

Methods

8 non-obese, healthy volunteers were studied in the morning after a 12 hour overnight fast on two separate occasions, each receiving an intra-gastric infusion of either 250ml 0.05M C12 fatty acid solution or 0.9% saline in a randomised, double blind manner. Each subject underwent a 40 minute fMRI scan, 10 minutes into which they received the infusion. Subjects were also asked to rate their sensations of hunger, fullness and nausea every 5 minutes.

Images were acquired on a 3T Philips Achieva MR scanner with a multi-slice, single-shot EPI sequence to achieve whole brain coverage. An anatomical MRI scan was performed at the beginning and end of each study to measure the emptying of the gallbladder which is dependent on CCK release. Data were analysed using SPM2 (Friston, The Wellcome Department of Cognitive Neurology, London, UK). Data analysis identified voxels showing significant changes in successive 2 minute time-bins compared to the pre-infusion baseline and compared to saline infusion responses.

Results

The comparison of lipid infusion to saline highlighted a statistically significant increase in the BOLD response due to lipid ingestion in the hypothalamic region and brainstem (Figure 1). Gallbladder volume decreased significantly compared to baseline with intra-gastric lipid but not saline, indicating that CCK release only occurred with lipid. Intra-gastric infusion was associated with increased fullness and decreased hunger sensations but there was no difference in effect between lipid and saline. Neither infusion had an effect on nausea sensations.

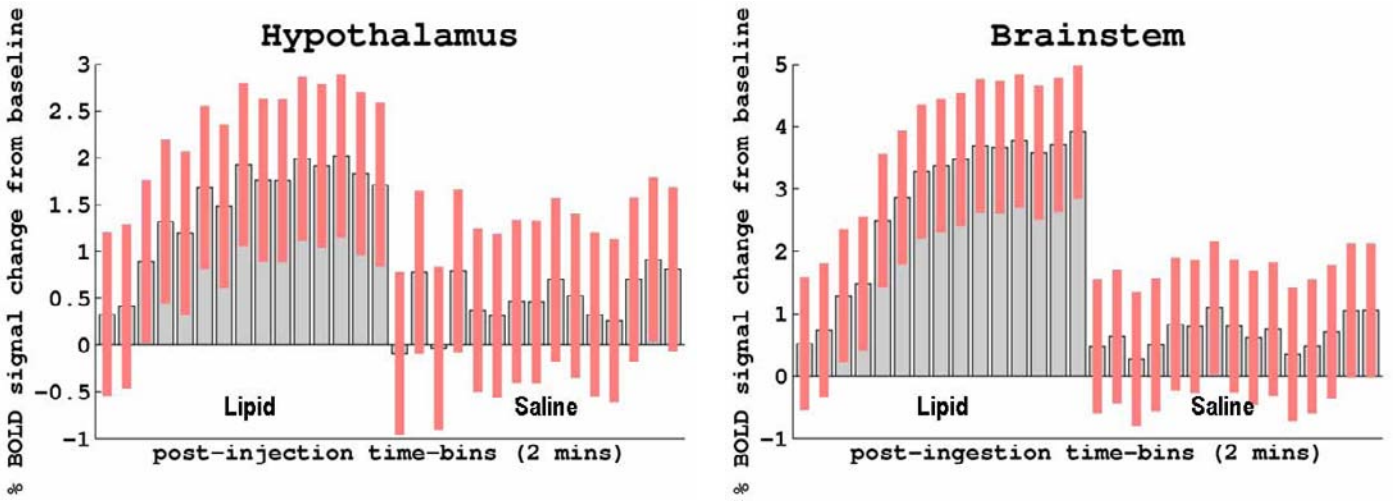

Figure 1: The percentage BOLD signal changes observed in the hypothalamus and brainstem with lipid and saline infusion.

Discussion

We have demonstrated that ingestion of a CCK-releasing lipid causes an early and prolonged increase in neuronal activity in both the brainstem and the hypothalamus. Given that the lipid-induced increases in BOLD signal were not associated with changes in conscious perception of hunger or fullness compared to saline, these changes are compatible with the role of the brainstem and hypothalamus in the subliminal control of food intake in man. We hypothesise that these changes are dependent on CCK-1 receptors and we will test this hypothesis by performing similar phMRI studies using the CCK-1 receptor antagonist, dexloxiglumide.

References

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