

# Functional Magnetic Resonance Imaging of BOLD Changes Accompanying Feeding in Rats

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## Introduction

Understanding the CNS control of satiety is an important step in developing strategies to reduce obesity. The hypothalamus is considered to be a major center for regulation of food intake and thus increased neural activity in this region would be expected to accompany the transition from hunger to satiety. Less is known of the involvement of other brain regions, although a recent study that measured cerebral blood flow (CBF) in humans has suggested that additional brain regions such as the frontal or insular cortex could have altered activity between hunger and satiated states (1). Functional magnetic resonance imaging (fMRI) can also measure with high spatial resolution changes in cerebral haemodynamics obtained using blood oxygen level dependent (BOLD) changes in MR signal related to alterations in paramagnetic deoxyhaemoglobin (2). The present study used fMRI in an animal model to investigate the cerebral response to satiety compared to hunger state.

## Materials and Methods

Stomach tubes were surgically implanted in Sprague-Dawley rats (n=4) that were on a reverse light-dark schedule. They recovered and received liquid Ensure-plus diet (10AM daily), and were food-deprived for 12 hours prior to imaging of feeding. During fMRI, rats were anesthetized with alpha-chloralose, and ventilated. Blood gases and other respiratory and cardiovascular parameters were monitored and recorded. Brain images were acquired using a 9.4T/21cm magnet (Magnex, UK) equipped with Avance MR console (Bruker, Germany) and a surface RF coil. Sets of fast spin echo images (effective TE=57.2ms, TR=9.7s) comprising up to 10 transverse slices of 1.5 mm thick through the brain were acquired for different sets of fMRI experiments: 1. an electrical forepaw stimulation experiment to demonstrate activation prior to feeding (6/7/6/5/8 images with stimulation off/on/off/on/off) 2. a baseline experiment (50 images, no intervention), 3. the feeding experiment (20 baseline images, 8 images during feeding and 22 images post feeding), and 4. an electrical stimulation experiment post feeding. During the feeding scan rats were infused with 8mL of liquid Ensure-plus at a rate of 2 mL/min via the stomach tube. A cluster analysis program (EvIdent, Winnipeg, Canada) was used to identify time courses of interest, which were selected according to mean centroid intensity changes of greater than 4% after the 20<sup>th</sup> image. A correlation of voxels within the brain to these selected time courses (p<0.0005) were considered 'activation' responses. Data are presented as mean±SD.

## Results

The investigation of the clusters of similar intensity changes resulted in 2 types of response consistent with a change in intensity (either increases or decreases) corresponding to an onset at the time of food delivery. In all animals there was an intense widespread reduction in MR intensity following feeding with 49±14% of the voxels in the brain correlating to a decrease in signal intensity (Fig 1). Voxels with an increased signal intensity after feeding were located near edges and border regions of anatomical features and a similar local response to trend increases could be observed on the baseline scan. Between the start and end of the feeding, blood glucose increased approx. 10 mmol/L, and arterial blood pCO<sub>2</sub> decreased (31.0±3.2 vs. 26.3±2.5). Stimulation of the forepaw during fMRI was accompanied by an activation response in the sensory motor cortex (correlation to the on/off paradigm) that increased from 74.8±22.5 voxels prior to feeding to 264.5±87.1 voxels post feeding (p<0.001) (Fig 2).

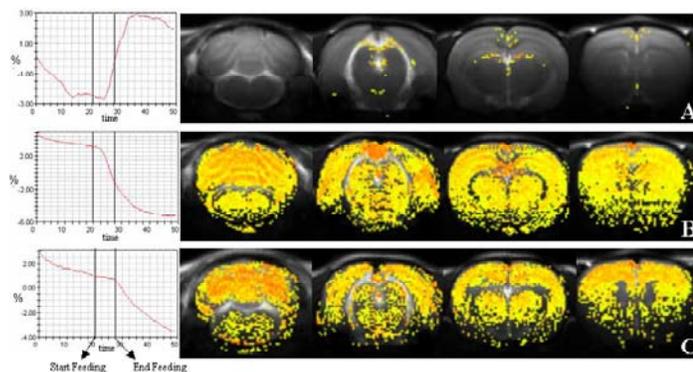


Figure 1: Average paradigm with corresponding voxels on a transverse brain slices correlating to an increase (A) or two animals (B,C) with a decrease in signal intensity after feeding (p<0.0005).

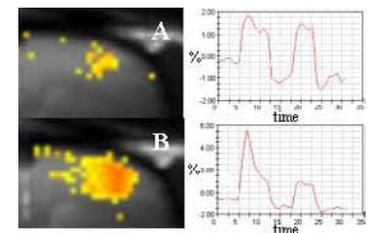


Figure 2: Voxels, shown with average time courses, correlating to on/off stimulation paradigm at p<0.001 A) before and B) after feeding

## Discussion and Conclusions

These results indicate that there is a widespread decrease in BOLD signal intensity between hunger and satiety states in the anesthetized rat. Although the reason for this is not clear, it indicates that feeding is associated with regionally homogenous increases in deoxyhaemoglobin (1). One possibility is that this is related to a decrease in CBF corresponding to the more localized decreases in perfusion observed between hunger and satiety in humans (2) or to altered blood gases. However the reduction in arterial PCO<sub>2</sub> was modest and unlikely to account for the relatively large (6-8%) decrease in BOLD signal intensity. Instead it is possible that over the course of feeding there is a resetting of the CBF-cerebral glucose/oxygen utilization coupling to lower levels. This could also explain the greater responsiveness of the cerebrovasculature to electrical forepaw stimulation observed after feeding. Thus, hunger and/or hypoglycemia may be another physiological parameter of interest to monitor or control in fMRI studies.

## References

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