Prior feeding of fat modulates the cortical response to fat in the mouth in humans

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Target audience: Researchers in functional imaging, neuroscience, sensory and food sciences.

Introduction: The sensory properties of food, including taste, smell and texture, are rewarding when hungry, but reward value decreases after satiation. A few studies [1-3] have investigated how brain activity is modulated due to satiety, but none have directly assessed habituation and its relation to satiation. **Purpose**: To investigate the modulation of the cortical BOLD and CBF responses to a prior feeding a fat or water meal, and to assess habituation effects.

Methods: 16 right-handed healthy subjects (11 m/5 f) took part in the study which comprised two scan sessions at least 1 week apart. In each scan session, a fMRI training scan was performed, and a second fMRI scan at 45 minutes following consumption of 250 ml of either a "*water meal*" or flavoured fat emulsion "*fat meal*", **Fig.1A** (double-blinded, randomised cross-over). During the second fMRI scan, two emulsion samples were delivered in a random order: *i) a flavoured no fat "control" sample*: 10% sucrose and 6.25ml/kg volatile mix and *ii) a flavoured fat "fat" sample* designed to be iso-perceived to the control**:** 22% rapeseed oil, 9.07% sucrose, and 18.63ml/kg volatile mix. 3ml of either sample was delivered over a 3s period, followed by 2 mouth rinses (lime juice/water), **Fig. 1B**, repeated for 36 fMRI cycles. A visual cue instructed subjects to swallow immediately at the end of each sample delivery and electromyography (EMG) was recorded during fMRI acquisition to identify the time of each swallow. Arterial spin labeling (ASL) measures of cerebral blood flow (CBF) were collected at baseline, 40 and 65 minutes post meal. Subjective ratings of fullness, hunger, and appetite were assessed on a visual analogue scale (VAS). Venous blood samples collected to assess CCK plasma content (pmol/L) during the study.

Data Acquisition: fMRI data was acquired on a Philips 3T Achieva with 36 transverse double-gradient-echo EPI images (TE: 30/49 ms, 64x64 matrix, voxel size 4x4x4 mm^3, SENSE 2, TR = 2.6 s). A multi-gradient-echo EPI data set (TE's: 11, 30, 49, 68 and 87 ms) was also acquired to form a T_2* map. Cerebral blood flow (CBF) maps were acquired using QUIPSS II FAIR ASL with, a post-label delay (TI) of 1550 ms and TR_{ASL} of 6 s, with 11 slice transverse GE-EPI (TE 14 ms) coverage centred on the anterior insula to sample a subset of the fMRI slices.

Data Processing: fMRI data slice timing corrected and realigned (SPM5). A T_2* map was used for weighted summation [4] of the dual echo fMRI data, which was then normalised to MNI space, spatially smoothed (8 mm), globally scaled and temporally filtered (80 s cut-off). A GLM was formed for each subject to identify the cortical response to *"control"* and *'fat"* samples following the fat and the water meal (modelling each sample as a box function of duration determined from the EMG). Motion parameters and mouth rinse events were included as covariates of no interest. A random effects group (RFX) analysis was performed for *"control"* and *'fat"* samples, and a region of interest (ROI) analysis performed of the parameter estimates (β values) based on *a priori* areas including taste/aroma areas (anterior insula), oral somatosensory areas (mid and posterior insula), reward areas (amygdala, ACC), satiety areas (thalamus, hypothalamus, mid and lateral OFC). ASL datasets were transformed to MNI space, label and control images subtracted and averaged to form perfusion weighted (PW) images, which were quantified (ml/100g/min). Statistical Analysis*:* 1) To identify brain areas showing habituation to either samples, a parametric modulation in time was included in the GLM to the '*"control"* and *'fat"* samples, and the % BOLD signal change time course in *a priori* ROIs was assessed. 2) fMRI results were correlated with plasma CCK and VAS values in a one sample *t*-test. 3) Group CBF maps were formed at 0, 40, 65 minutes following the fat and water meal. CBF difference maps were formed between the 40 and 65 minute maps and the 0 minute maps ($P < 0.05$ few). Mean perfusion in *a priori* areas of interest was also assessed [5,6].

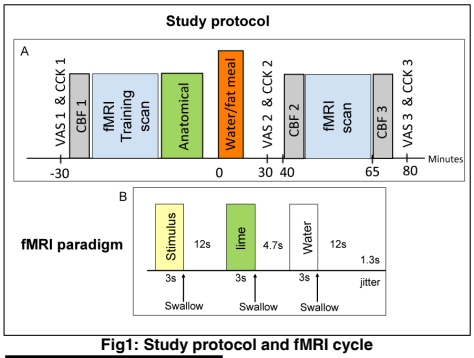

Fig1: Study protocol and fMRI cycle

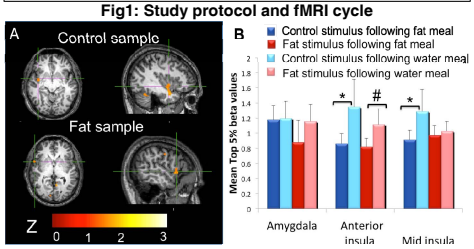

Fig2: Differential activation maps following fat meal compared to water meal for control and fat samples

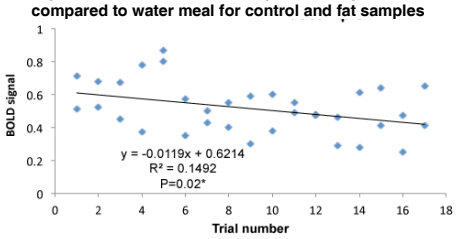

Fig3: Example trial-by-trial habituation in amygdala

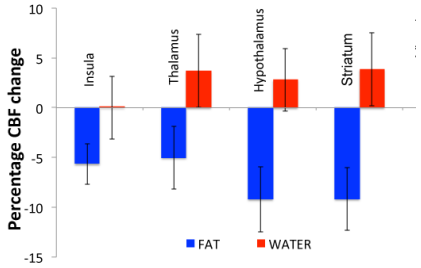

Fig.4: Percentage CBF change (± SEM) at 65 minutes following fat and water meal

Results: Statistical maps from *"control"* and *"fat"* samples resulted in a network of brain areas in anterior, mid and posterior insula (AI, MI and PI), somatosensory cortices (SI/SII), anterior cingulate (AC), thalamus, amygdala**.** Differential activation maps to the '*control'* and **'***fat' samples* following the fat meal compared to the water meal (**Fig. 2A**) showed significant suppression in bilateral AI and MI (**Fig. 2B**). Habituation maps and trial-by-trial analysis showed greater habituation following the consumption of the fat meal than water meal in reward areas (amygdala - **Fig. 3**), primary taste areas (AI), oral somatosensory areas (MI and PI) and thalamus. Across subjects, the CCK plasma values correlated negatively with the BOLD response following fat meal in SI and SII, MI, and amygdala**.** CBF data showed a significant reduction at 65 minutes after the fat meal in the hypothalamus, thalamus, striatum and insula, no such reduction was seen after the water meal, **Fig. 4**.

Discussion: The suppression in anterior insula activity in response to the *"control"* and *"fat"* samples following consumption of the fat meal reflects an increased rate of habituation [2,3], and habituation in the amygdala following the fat meal supports previous findings [1, 2]. CCK modulated the cortical response, supporting the role of the AI and MI in food intake. The reduction in baseline CBF following the fat meal in hypothalamus, thalamus, striatum, and insula may be responsible for the reduction in the acute BOLD responses following the fat meal, and the more rapid habituation.

Conclusion: These results indicate the importance of interpreting fMRI data related to taste perception and satiation in the context of physiological changes.

References: [1] Smeets et al (2006), Am. J. Clin. Nutr. 83, 1297–1305. [2] O'Doherty J. et al (1999), Chem. Senses 11:893-897. [3] Small et al (2001), Brain, 124:1720–33. [4] Posse et al (1999) MRM 42:87-97. [5] Frank et al (2012), Am J Clin Nutr 95:1342-1349. [6] Page et al (2013), JAMA 309:63-70.

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