Oral fat representation in human cerebral cortex

S. F. Eldeghaidy[1], L. Marciani[2], T. Hollowood[3], K. E. Head[1], J. Hort[3], J. Stokes[4], F. McGlone[5], J. Busch[6], A. Taylor[3], R. C. Spiller[2], P. A. Gowland[1], and S. T. Francis[1]

[1]Sir Peter Mansfield Magnetic Resonance Centre, School of Physics and Astronomy, University of Nottingham, Nottingham, United Kingdom, [2]Wolfson Digestive Diseases Centre, University of Nottingham, Nottingham, United Kingdom, [3]Division of Food Sciences, University of Nottingham, Leicestershire, United Kingdom, [4]Unilever Coporate R&D, Colworth, United Kingdom, [5]Perception & Behaviour Group, Unilever R&D, Wirral, Cheshire, United Kingdom, [6]Unilever Food & Health Research Institute, Unilever R&D, Vlaardingen, Netherlands

Introduction: Fat is added to foods to enhance appeal via changes in flavour and texture, but the frequent addition of fat to processed foods is thought to be one cause of the current epidemic of obesity in the developed world. A greater understanding of the neural systems involved in processing fat consumption, both at the sensory encoding level in the mouth and the perceptual encoding level in the brain, is an essential first step to improve understanding of how to mimic the effects of fat ingestion. So far only one fMRI study has assessed the cortical response to pure fat [1]. In this fMRI study we use more ecologically relevant, physically and sensorially complex fat emulsions to identify those brain areas which show a correlation with the fat concentration.

Materials and Methods: Subjects**:** 14 right-handed healthy subjects (10 male and 4 female) took part in the study. This study was approved by the local Research Ethics Committee and all subjects gave informed written consent before attending.

Paradigm: We used an automated stimulus delivery system [2], which allows delivery of a spray to the tongue and the oral cavity. In an fMRI cycle (**Fig. 1**) we delivered in random order 3ml of 5%, 10%, 20%, or 30% w/w oil fat emulsion over a 3sec period. The emulsions were iso-viscous and underwent full psychophysical characterisation (thickness, stickiness, mouth-coating, dispersion) in the sensory laboratory. After each stimulus we delivered 2 mouth rinses of 3 ml lime juice solution and then 3 ml water (each rinse over a 3 sec period) to clean the oral cavity. A small visual cue instructed the subjects to swallow immediately after each sample delivery. Electromyography (EMG) was recorded concurrently during fMRI acquisition to monitor and identifiy the exact timing of the swallow to accurately model the fMRI responses. A total of 36 cycles were acquired for each subject. After the scanning session subjects were asked to rank fat emulsion samples in order of preference.

fMRI Acquisition and Analysis: Data was acquired on a Philips Achieva 3T scanner using a SENSE head coil. 36 transverse double-gradient-echo (TEs of 30 ms and 49 ms), EPI (64x64 matrix, voxel size 4x4x4 mm^3) images were acquired every 2.6 sec (jittered) throughout the fMRI paradigm. Following the fMRI experiment a multi-gradient-echo EPI data set (TE's: 11, 30, 49, 68 and 87 msec) of the same slices was acquired to form a T_2* map. The fMRI data was analysed using SPM5. The data was corrected for slice timing, and then realigned. T_2* maps were calculated from the five-echo data set using a pixel-by-pixel, linear weighted least squares fit, and used to perform a weighted summation [3] of the two echoes of the fMRI data. The combined weighted fMRI data were then normalised to the standard EPI template and spatially smoothed with a 12 mm Gaussian kernel. Global scaling and temporal filtering with a 128 sec high pass filter cut-off were applied. A general linear model was then formed to identify firstly areas responding to 'all the attributes of the oral fat delivery' (viscosity, taste, swallow). The stimulus was modelled as a box function convolved with a canonical HRF. The length of the box function for delivery of the fat emulsion was set to the time between the beginning of the stimulus delivery and the actual time of each swallow as determined from the EMG traces, **Fig. 2**. The individual motion parameters and the two mouth rinse events were included as covariates of no interest. To identify cortical areas correlated solely with fat, a linear parametric modulation with fat concentration was included in the model. These results were masked by the map formed of 'all attributes of oral fat delivery'. A random effects group of the analysis was performed.

Results: The preference test showed that the 30 and 20 % emulsions were significantly preferred to 10 and 5 % emulsions ($P < 0.05$).The random group analysis of the linear parametric design revealed those areas positively correlated with increasing fat concentration. **Fig 3**. shows an example of those brain areas. Activated areas were found in: (a) taste areas including bilateral frontal opercular and R anterior insula, (b) areas associated with the intraoral somatosensory textural attributes of fat (postcentral gyrus, precentral gyrus, and superior parietal cortex), (c) areas that may represent the hedonic properties of the fat, (which were shown by the preference test to increase with fat concentration), including bilateral dorsolateral prefrontal cortex, R thalamus and R amygdala.

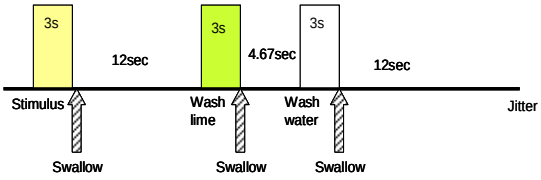

Fig. 1 One fMRI cycle

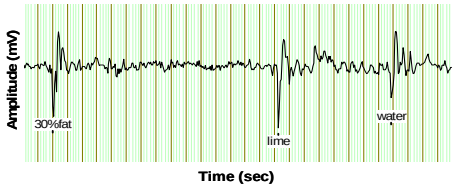

Fig. 2 Artefact corrected EMG traces to determine the timing of the swallow reflex.

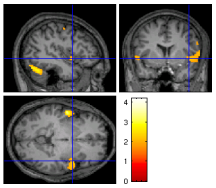

Fig. 3 RFX map of areas positively correlated with fat concentration (uncorrected $P<0.05$). Cross-hair shows activation in anterior insula (MNI: 44, 6, -4).

Discussion: We have mapped the cortical representation of oral fat in iso-viscous fat emulsions using a protocol closer to the normal experience of consuming liquid fatty foods than previous studies [1]. In addition, we have performed a parametric analysis against fat concentration to identify cortical areas purely responding to fat. This is in contrast to previous studies [1] that compared a pure fat stimulus with a control stimulus of carboxymethyl cellulose (CMC), which itself may not have neutral sensory attributes. Activation of the anterior insula in response to fat was found, confirming previous results [1]. In addition this study has found frontal opercular activation, which may reflect the fact that fat acts as a chemical stimulus in the oral cavity [4]. Moreover, this study also found additional activated areas in postcentral gyrus, precentral gyrus, superior parietal, dorsolateral prefrontal cortex, amygdala, and thalamus. This study (using parametric analysis) did not confirm activation previously observed for fat versus CMC control in the hypothalamus, OFC or cingulate [1], suggesting that this activation was actually related to the attributes of the CMC control rather than the fat. Improved knowledge of the cortical response to oral fat will improve our understanding of the oral effects that must be replicated to mimic fat ingestion, and thus assist in the development of food products that provide the same or similar reward states with low, or non-fat foods.

References: [1] de Araujo IE, et al (2004) J Neurosci 24:3086-93. [2] Marciani L et al (2006) J Neurosci Methods 158:186–194. [3] Posse S et al (1999) MRM 42:87-97 [4] Mattes R (2003) Food Australia 55:510-514. **Acknowledgements:** This work was funded by the BBSRC and Unilever.