Towards fMRI of physiological taste and aroma perception

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Background: The cortical representations of gustatory [1,2] and olfactory [3,4] stimuli have been studied previously. Typically these delivered the taste stimulus to the mouth in very small quantities (typically 50-75 microlitres), often to a specific part of the tongue, and subjects were asked to hold the sample in the mouth for several seconds before swallowing to avoid possible head motion. Olfaction was generally stimulated ortho-nasally (by sniffing), which is different from the retro-nasal stimulation that accompanies normal swallowing of liquids [5]. Some attempts have been made to deliver aroma retro-nasally [6] but without swallowing. To simulate the real-life consumption of liquid foods, prompt swallowing after sample delivery (to obtain odour transfer along the retro-nasal pathway [5]) and an increased volume of liquid stimulus (to stimulate the taste receptors more extensively) are necessary.
Aim: To assess the cortical representation of taste and retro-nasal aroma stimuli using fMRI with **(a)** a protocol closer to the normal consumption of liquid foods, including physiological swallowing; **(b)** larger liquid volumes; **(c)** a novel, automated and reproducible stimulus delivery system and **(d)** EPI techniques with wide brain coverage and improved sensitivity in the frontal lobes.
Materials and Methods: Subjects: This study was approved by the local Ethics Committee. 10 right-handed healthy subjects (7 male and 3 female, 25-36 yrs.) participated after giving written consent. **MRI:** A 3.0T purpose-built scanner was used with TEM head coil and inset head gradient coil. After acquisition of a 64 slice EPI set, the activation experiment was performed. 26 contiguous, multi-gradient-echo, EPI, coronal 5 mm thick slices were acquired from 64 to -66 MNI anterio-posterior co-ordinate units, with a volume repetition time of 2.6 s (jittered). Following each RF pulse, a double EPI acquisition was made with TEs of 22 ms and 39 ms (1.9 kHz gradient switching frequency, in-plane resolution 4 mm x 4 mm, 64 x 64 matrix). The blipped gradient was 'wound-back' in k-space between trajectories so that the 2 echoes had similar sensitivities to distortion. The high switching frequency, multi-echo acquistion and relatively thin coronal imaging minimised spatial distortion and improved sensitivity in frontal lobes. At the end of the activation experiment a T_2* map of the same 26 coronal slices was formed by acquiring 4 EPI images per pulse at TEs of 22, 39, 56 and 73 ms.
Paradigm: A novel, automated stimulus delivery system was designed. Electric pumps were placed outside the scanner room. Each had a liquid reservoir and a plastic tube connected to a small disposable spray nozzle (held between the lips of the supine subject) allowing delivery of a spray to the tongue and the oral cavity. In an fMRI cycle (**Fig. 1**) we delivered over a 3 sec period 3 ml of: (**a**) **stimulus:** [3% sucrose, 100ul/l isoamylacetate (which has a banana/pear aroma) and trace amounts of KCl and $NaHCO_3$]. (**b**) **control:** tasteless solution [only trace amounts of KCl and $NaHCO_3$]. Between each stimulus and control we delivered two mouth rinses of 5 ml tasteless solution (each rinse over a 5 sec period) (**mouth rinses**). A visual cue on a screen instructed the subjects to swallow immediately after each delivery. 15 cycles were acquired for each subject. **Analysis:** All data sets were processed using SPM2. T_2* maps were calculated using a pixel by pixel weighted least squares fit and used in a weighted summation [7] of the 2 echoes. The combined weighted data were then spatially normalised to the standard EPI template. 8 mm FWHM spatial smoothing and 128 s high pass filter cut-off were applied. The stimulus and control were modelled as a box function before the swallow (taste stimulus) and a box function after the swallow (aroma stimulus), each box function being convolved with a canonical HRF. The individual motion parameters and the two mouth rinse events were included as covariates of no interest. Comparisons between stimulus and control were made using a fixed effects group analysis. A conservative small volume correction [8] was applied using a mask of all regions showing a response to both the stimulus and the control at p<0.001. p values were corrected for false discovery rate [9].
Results: Some of the areas activated due to the difference between taste stimulus and control are summarised in the following **Table** and an example of such activation in the right anterior insula is shown in **Fig. 2** (overlaid on the SPM2 template with uncorrected p<0.01). A trend for right orbitofrontal cortex activation was also detected. **Fig. 3** shows that the average % signal change in a voxel which is active only in the contrast between the aroma stimulus and the control (MNI x, y, z = -46, 6, 14) effectively peaks later than a voxel which is active only in the contrast between the taste stimulus and the control (MNI x, y, z = 34, 14, 4).

TASTE GREATER THAN CONTROL							
Area	**Z-score**	**p**	**MNI coordinates x, y, z**	**Area**	**Z-score**	**p**	**MNI coordinates x, y, z**
Left anterior insula	3.97	0.002	-28, 18, 2	Left frontal operculum	4.34	0.001	-48, 10, -4
Right anterior insula	3.11	0.009	38, 24, 0	Right frontal operculum	3.46	0.004	56, 6, -6
Left mid-posterior insula	3.60	0.003	-38, -6, 8	Left parietal operculum	2.63	0.022	-62, -26, 30
Right mid-posterior insula	5.09	0.001	42, -4, 4	Right parietal operculum	4.68	0.001	64, -20, 24
Left amygdala	3.17	0.008	-20, -6, -12	Middle cingulate cortex	4.76	0.001	10, 18, 32
Right amygdala	3.71	0.003	18, -8, -14	Posterior cingulate cortex	4.01	0.001	-4, 4, 56
				Right thalamus	3.32	0.006	12, 4, -6

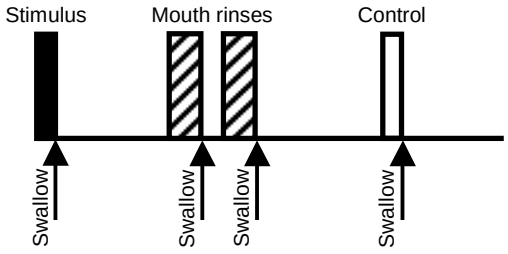

Figure 1

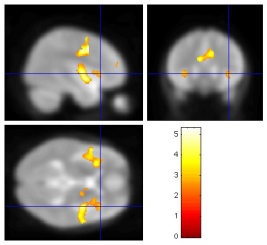

Figure 2

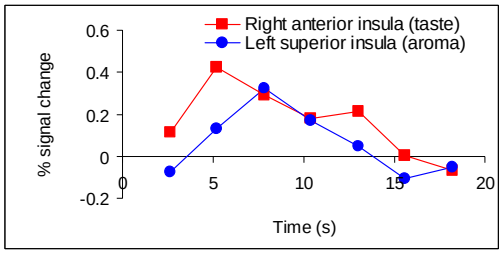

Figure 3

Discussion: We have mapped the cortical representation of taste and aroma in a protocol that is closer to the typical experience of consuming liquid foods. Figure 3 shows that the signal change in the aroma area occurs after the taste area and the timing suggests that it occurred after the swallow. Therefore it can be inferred that this shows for the first time the successful discrimination of activation due to oral taste and post-swallow retro-nasal aroma stimulation. The swallow of the 3 ml sample caused acceptable head motion in the fMRI experiment (less than 1 voxel). This protocol can be combined with subjects' sensory ratings to improve knowledge of the perception of taste, aroma and their interactions [10]. The novel delivery system is automated and reproducible and exposes a wider area of the mouth's receptors to the taste.
References: 1. Small DM et al (1999) Neuroreport 10:7-14. **2.** O'Doherty J et al (2001) J Neurophysiol 85:1315-1321. **3.** Cerf-Ducastel B et al (2001) Chem Senses 26:625-637. **4.** O'Doherty J et al (2000) Neuroreport 11:893-897. **5.** Buettner A et al (2001) Chem Senses 26:1211-1219. **6.** de Araujo IET et al (2003) Eur J Neurosci 18:2059-2068. **7.** Posse S et al (1999) MRM 42:87-97. **8.** Worsley KJ et al (1996) Hum Brain Mapp 4:58-73. **9.** Genovese CR et al (2002) Neuroimage 15:870-878. **10.** Cerf-Ducastel B et al (2004) Physiol Behav 81:389-396.