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Taste-related activity in the human dorsolateral prefrontal cortex

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Taste remains one of the least-explored human senses. Cortical taste responses were investigated using neuroimaging in 40 subjects tasting a range of different taste stimuli compared to a neutral tasteless control. Activation was found in the anterior insula/frontal opercular taste cortex and caudal orbitofrontal cortex, both areas established as taste cortical areas by neuronal recordings in primates. A novel finding in this study was a highly significant response to taste in the dorsolateral prefrontal cortex. This may reflect an effect of taste on cognitive processing to help optimise or modify behavioural strategies involved in executive control; or it could reflect the engagement of this region in attentional processing by a taste input.

Keywords: Taste; Dorsolateral; Orbitofrontal; Insula; fMRI

Introduction

Taste is perhaps the most important primary reinforcer in all animals given that the necessary energy needed to sustain life comes from the nutrition obtained by eating different foods, yet relatively little is known about taste processing in the human brain. Evidence from nonhuman primates has indicated that the anterior insula and adjoining frontal opercular cortex is the primary taste cortex, and caudal parts of the orbitofrontal cortex are the secondary taste cortex (Baylis et al., 1994; Ogawa et al., 1989; Rolls, 1999; Scott et al., 1986). These two cortical areas have been shown to be activated by taste in human neuroimaging studies using positron emission tomography (PET) (Frey and Petrides, 1999; Kinomura et al., 1994; Small et al., 1997, 1999; Zald et al., 1998) and functional magnetic resonance imaging (fMRI) (Barry et al., 2001; De Araujo et al., 2003a,b,c; Faurion et al., 1999; Francis et al., 1999; Kringelbach et al., 2003; O'Doherty et al., 2001b, 2002). In addition, activations to taste have been found in the cingulate cortex (De Araujo et al., 2003a,b,c; Francis et al., 1999; Kringelbach et al., 2003; O'Doherty et al., 2001b, 2002; Small et al., 2003; Zald et al., 1998, 2002). Other studies have also found food-related activations in the dorsolateral prefrontal cortex (Small et al., 2001; Tataranni et al., 1999). However, it remains an open question if the dorsolateral prefrontal cortex and additional cortical areas are recruited by taste in humans irrespective of changes in internal state. Studies in nonhuman primates have found that neurons in the dorsolateral prefrontal cortex have responses related to food reward or expectancy (Tremblay and Schultz, 1999; Watanabe, 1996, 2002), but it is not known whether this reflects a taste input, and this has not been investigated in humans. We used event-related fMRI to investigate the different cortical areas activated by taste stimuli in humans, and describe here the new finding that the dorsolateral prefrontal cortex is activated by taste stimuli in humans irrespective of changes in internal states.

Experimental procedures

Subjects and tasks

Forty data sets were acquired using fMRI from 38 subjects (13 women and 25 men, of which two subjects participated in two experiments) in four separate taste experiments using very similar experimental protocols with event-related interleaved designs. Full details of the methods used in the four experiments are available in the published papers but here we briefly summarise the aims and methods.

A total of eight unimodal and six multimodal taste stimuli ranging from pleasant to unpleasant were used in the four experiments, which were designed to answer separate questions related to taste but shared identical taste delivery methods with minor variations in interstimulus intervals. Taste strictly refers to sweet, salt, bitter, sour and umami effects elicited through oral chemosensors. In this paper, we refer to these effects as unimodal taste. Flavour refers to effects elicited by oral stimuli that produce typically taste, olfactory and somatosensory stimulation. In this paper, we refer to these effects as multimodal taste, as taste is in common usage for these multimodal effects.

Ten subjects participated in one experiment using 0.5 M glucose (Sigma), 0.05 M salt (NaCl, Sigma) and mineral water (Evian, France) as unimodal taste stimuli (De Araujo et al., 2003b). The main aims of this experiment were to investigate cortical areas of the human brain activated by the delivery of small quantities of water to the mouth with an adequate control for nonspecific effects

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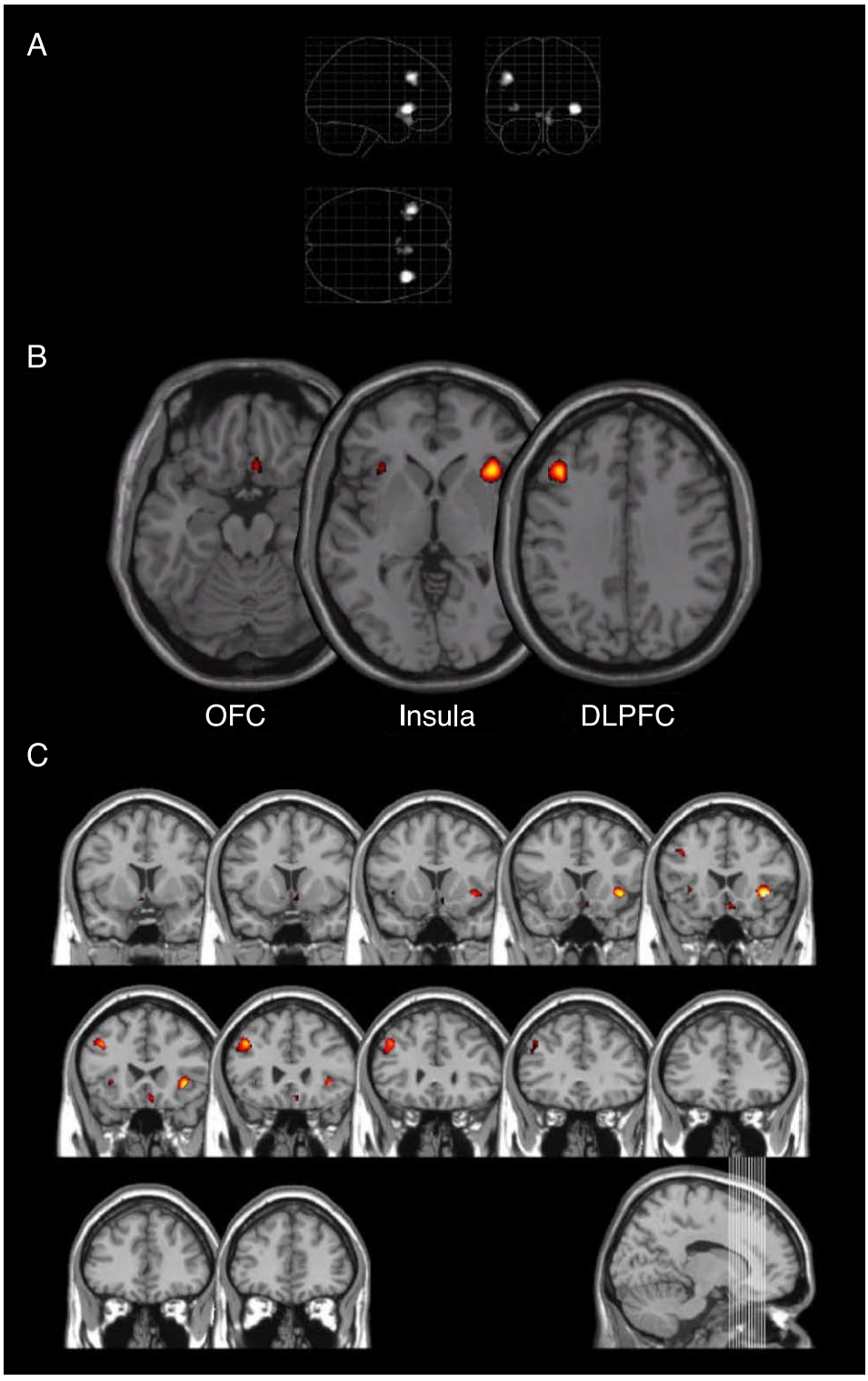

Fig. 1. Taste-related responses in the human brain. (A) All of the activations in a random-effects group analysis of 40 data sets using a wide variety of taste stimuli superimposed on a SPM99 glass brain ($P < 0.05$, corrected for multiple comparisons). (B) Group activations are superimposed on axial slices through the orbitofrontal cortex (OFC), insula/frontal operculum, and dorsolateral prefrontal cortex. (C) Group activations are superimposed on 12 coronal slices through frontal parts of the human brain, with the slicing indicated by the vertical white lines on the transverse slice at the bottom right of the figure.

of placing a fluid in the mouth provided by a tasteless solution with the main ionic components of saliva; to compare these areas with known taste cortical areas identified by prototypical taste stimuli such as sweet (glucose) and salt (NaCl) incorporated into the experimental design and to investigate the effects of thirst on water intake.

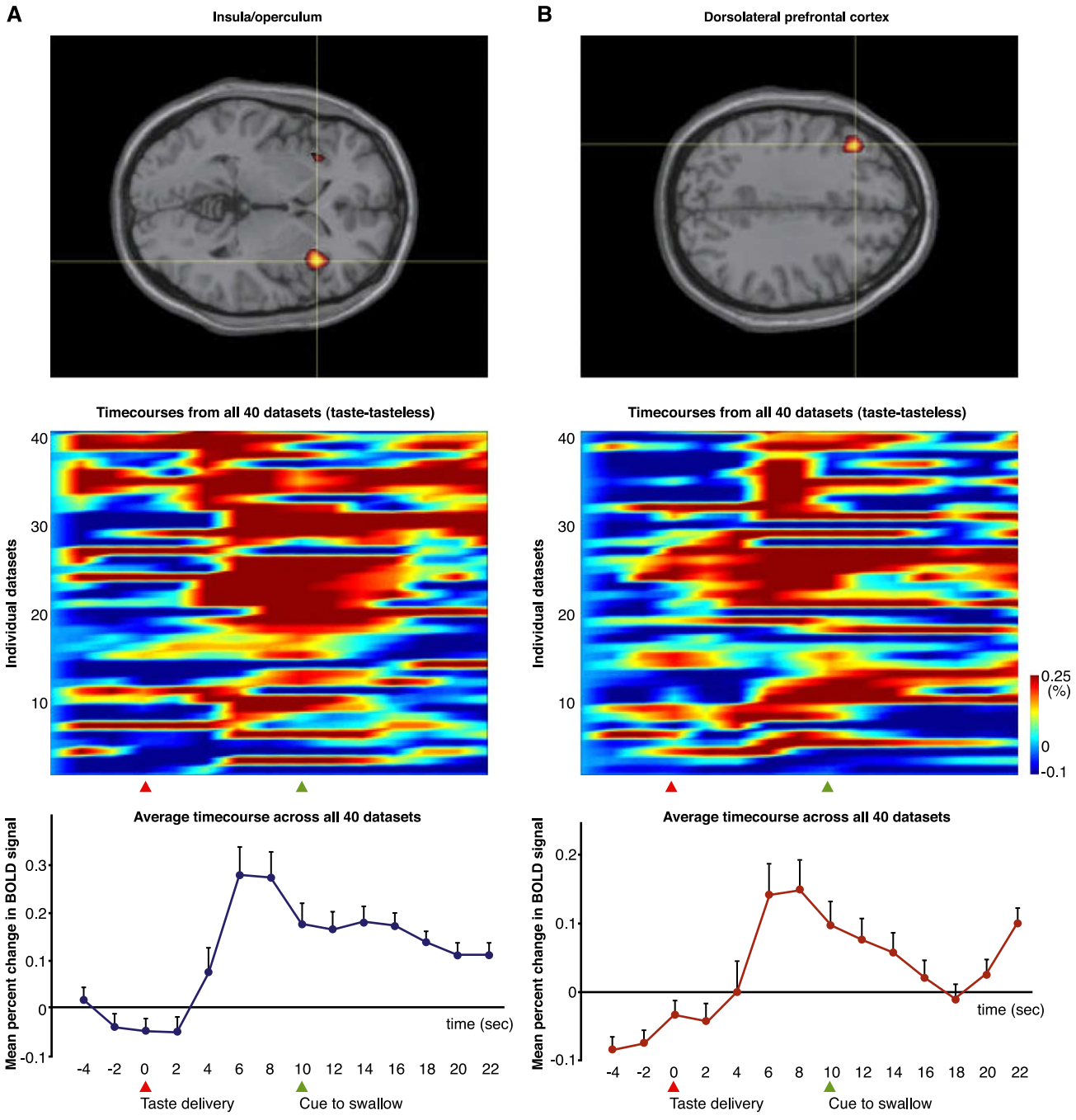

Fig. 2. Time course of changes in the BOLD signal for taste-related responses in the insula/operculum, and in the dorsolateral prefrontal cortex, for all of the 40 data sets, together with the average time course across these data sets. For the clusters in the insula/operculum (A, peak in MNI coordinates at *x*, *y*, *z*: 38, 20, − 4), and dorsolateral prefrontal cortex (B, peak at *x*, *y*, *z*: − 42,26,36) (top of the figure, yellow cross hairs), the time course of activation is shown separately for all 40 data sets (middle of figure), and the average time course across all data sets (bottom of figure). The ordinate shows each of the individual data sets, while the abscissa shows the time from the taste delivery (time '0' and indicated with an orange triangle) through when the subject is cued to swallow after 10 s (indicated with a green triangle). The magnitude of the activations is coded in a scale of percent change from red (activation) to blue (deactivation) relative to the mean (see scale on the far right). The data were averaged for each data set for all the tastants minus the tasteless solution. At the bottom of the figure, the average time course across the 40 data sets with the standard error is shown. The ordinate shows the percent change in BOLD signal, while the abscissa shows the same time as the time courses in the middle of the figure.

Nine subjects participated in a second experiment using tomato juice and chocolate milk as multimodal taste stimuli with taste, olfactory and texture components (Kringelbach et al., 2003). The aims of the experiment were to investigate which brain areas are activated by a whole food independently of satiation (and so might represent the whole range of sensory properties of the liquid food, including taste, olfactory and texture components) and in which brain areas the responses to a liquid food were modulated by

satiation (and so might reflect the affective properties of the whole food).

Eleven subjects participated in a third experiment using four multimodal taste stimuli consisting of combinations of 0.5 M sucrose (Sigma); 0.05 M MSG (the monosodium salt of L-glutamic acid, Sigma); 20 ppm strawberry odour (Firmenich) and 25 ppm of 1.9% Methional (chicken flavour, IFF), where the combinations used were sucrose + strawberry, MSG + methional, sucrose + methional, MSG + strawberry, plus unimodal sucrose (De Araujo et al., 2003c). The aim of the experiment is to investigate which brain areas respond unimodally to taste stimuli, to olfactory stimuli and to both taste and olfactory stimuli.

Ten subjects participated in a fourth experiment using 0.05 M MSG (the monosodium salt of L-glutamic acid, Sigma), or 0.005 M IMP (inosine 5′-monophosphate, which in this experiment was used in a form without sodium ions; Sigma), or a combination of the two (MSGIMP made to contain a concentration of 0.05 M MSG and 0.005 M IMP), or 1.0 M glucose (Sigma) as the unimodal taste stimuli (De Araujo et al., 2003a). The aim of the experiment was to investigate the cortical responses in humans to umami substances and their interactions.

In all four experiments, the taste stimulus was delivered in 0.75-ml aliquots to the subject's mouth through polythene tubes that were held between the lips. After 10 s (in all three experiments, except the first experiment where it was after 11 s), the swallowing was cued by a visual stimulus. (Instruction and training of the subjects preceded an experiment). It was an important feature of all four investigations that each of the taste stimuli was always followed by a tasteless solution (using the main ionic components of saliva: 25 mM KCl + 2.5 mM $NaHCO_3$) (O'Doherty et al., 2001b) that provided a rinse for the taste and was also used to control for nontaste (including somatosensory) effects of placing solutions in the mouth. After a delay of between 2 and 10 s, this tasteless solution was administered in exactly the same way as the taste stimuli and the subject was cued to swallow again after 10 s followed by another delay period of between 2 and 10 s. This cycle of taste delivery with swallowing followed by the delivery of the tasteless rinse with swallowing was then repeated according to a nonrepeating pseudorandom sequence over all the stimuli for between 9 and 16 cycles in each experiment such that order effects could be ruled out. There were minor variations in the length of the delay period and number of cycles with 3 s and 9 cycles in the first and third experiment, 6 s and 16 cycles in the second experiment and a random interval between 2 and 10 s and 12 cycles in the fourth experiment.

In all of the four experiments, the subject was prompted to rate at least the intensity and pleasantness of the food stimuli on a visual analog rating scale either after the taste delivery or after the delivery of the tasteless solution. In the first and the third experiments, the ratings took place after the taste delivery; in the second and fourth experiments, the ratings took place after delivery of the tasteless solution but only at cycles 4, 8 and 12.

Scanning procedures

Local brain shimming was performed using special weighting in the inferior frontal region before acquiring between 840 and 1800 volumes of typically 14 T2* weighted coronal EPI slices with TR = 2 s using a 960 Hz gradient switching frequency and a TE of 25 ms. Slice thickness was typically 7 mm and in-plane resolution was 3 ×3 mm. Coverage was typically obtained from − 38 (A/P) to + 60 (A/P). We used the techniques that we have developed over a number of years to carefully select the imaging parameters to minimise susceptibility and distortion artefact in the orbitofrontal cortex described in detail elsewhere (Wilson et al., 2002). The relevant factors include imaging in the coronal plane, minimising voxel size in the plane of the imaging, as high a gradient switching frequency as possible (960 Hz), a short echo time of 25 ms and local shimming for the inferior frontal area. Whole brain T2* weighted EPI volumes of the above in-plane dimensions and an anatomical T1 volume with slice thickness between 1.5 and 6 mm and in-plane resolution of typically 0.75 × 0.75 mm were also acquired.

Image analysis

Image preprocessing was performed with either SPM99 or FLIRT (FMRIB Linear Registration Tool, Jenkinson and Smith, 2001) for realignment, reslicing with sinc interpolation and normalisation to MNI coordinate system (Collins et al., 1994). SPM99 (Wellcome Department of Cognitive Neurology, London) was then used first in applying spatial smoothing with an 8-mm, full-width half-maximum isotropic Gaussian kernel and global scaling. The time series at each voxel were high-pass- and low-pass-filtered with a haemodynamic response kernel. A general linear model was then applied to the time course of activation of each voxel and linear contrasts were defined to test the specific effects of each condition. Specific effects were tested by performing analysis on individual linear contrasts corresponding to statistical parametric maps of the t statistic (then transformed into the unit normal distribution SPM Z). For each of the data set, we specified a contrast of the main effects of all the taste stimuli minus the tasteless control. Each individual statistical parametric map was then entered into a second-level, random-effects group analysis ($df = 39$). We also performed a second analysis where we specified a contrast using only unimodal taste stimuli minus tasteless control, which was then entered into a second-level, random-effects group analysis ($df = 30$). Reported P values based on this group analysis for a priori regions of interest (i.e. the insula and the orbitofrontal cortex) were corrected for the number of comparisons made within each region (Worsley et al., 1996). Checks were performed using the estimated motion as a covariate of no interest to rule out the possibility of the observed results being due to motion-related artefact.

Results

Forty data sets were acquired using fMRI from 38 subjects (13 women and 25 men, of which two subjects participated in two experiments) in four taste investigations that used identical delivery of the taste stimuli, the same control procedure in which a tasteless solution was delivered after every taste stimulus and event-related interleaved designs (see Experimental procedures). Taste strictly refers to sweet, salt, bitter, sour and umami effects elicited through oral chemosensors. In this paper, we refer to these effects as unimodal taste. Flavour refers to effects elicited by oral stimuli that produce typically taste, olfactory and somatosensory stimulation. In this paper, we refer to these effects as multimodal taste, as taste is in common usage for these multimodal effects. A total of eight unimodal and six multimodal taste stimuli ranging from pleasant to unpleasant were used in the four experiments. The

main analysis described includes both unimodal and multimodal taste stimuli, and a separate analysis, using only unimodal taste stimuli, confirms activations of the same areas.

A general linear model was applied to the time course of activation in each voxel for each of the 40 data sets. For each of the data sets, we specified a contrast of the main effects of taste stimuli minus the tasteless control. Each individual statistical parametric map was then entered into a second-level, random-effects group analysis ($df = 39$), which allowed us to reveal what is common to the taste responses across subjects. Given the stringency of the random-effects statistics using the large group of 40 data sets, the results can be generalised to very significant proportions of the general population.

The random-effects analysis of taste activation across the 40 data sets revealed four cortical activation foci to the main effects of taste in the human brain (see Fig. 1 and Table 1). Bilateral activation of the anterior insula–frontal opercular cortex (x, y, z: 38, 20, −4 and x, y, z: −32, 22, 0; $P < 0.05$, corrected for multiple comparisons) was found with a slightly stronger response on the right side. Activation of the medial caudal orbitofrontal cortex to taste stimuli was also found (6, 22, −16; $P < 0.05$, corrected for multiple comparisons). In addition, at a lower statistical threshold, we found taste-related activity in the anterior cingulate cortex (8, 18, 50; $P < 0.001$, uncorrected for multiple comparisons). Activations in these areas by taste stimuli have been described previously (De Araujo et al., 2003a,b,c; Kringelbach et al., 2003; O'Doherty et al., 2001b, 2002), but their consistency and location is confirmed by the large analysis described here.

In addition, the random-effects analysis revealed strong activation in the left dorsolateral prefrontal cortex (−42, 26, 36; $P < 0.05$, corrected for multiple comparisons) in the posterior part of the middle frontal gyrus (Brodmann Area 46; Rajkowska and Goldman-Rakic, 1995). To ascertain whether the activation in the dorsolateral prefrontal cortex was attributable to taste effects and was not due to the combined effects of taste and olfactory stimuli used in some experiments, we performed another random-effects analysis of the 31 data sets with only the unimodal taste events. Significant activations were found in the same region of the dorsolateral prefrontal cortex, as well as in the anterior insula–frontal operculum and the orbitofrontal cortex.

To further investigate this finding, we extracted the time courses of changes in the BOLD signal for the 40 individual data sets from the left dorsolateral prefrontal cortex and compared them with the BOLD signal from the right anterior insula–frontal opercular taste cortex (see Fig. 2), to compare the time courses of activation in these two brain areas. Fig. 2 shows that the time courses in these two areas are very similar, and that the activity in both brain regions is clearly locked to stimulus delivery.

To assess whether it is only taste or whether unimodal olfactory stimuli can also activate the dorsolateral prefrontal cortex, we also examined a data set in which three pleasant and three unpleasant odours were presented in an olfactometer (Rolls et al., 2003). Activation was found in the anterior middle frontal gyrus, centered on the right at (40, 46, 11), and ranging from $y = 40$ to $y = 50$. Although this activation is on the right, a region of less-intense activation was also found on the left at (−48, 23, 16), which is also in the middle frontal gyrus in an adjacent region to the activation in the left dorsolateral prefrontal cortex region activated by taste or by taste and odour combinations. The implication is that not just taste, but other stimuli with related properties, such as olfactory stimuli, may also activate the dorsolateral prefrontal cortex. We suggest that the sight of food is also likely to activate this region; as in some other brain regions where the taste and odour of food is represented, so is the sight of food (Rolls, 1999).

Table 1
Brain regions involved in taste

		MNI x	MNI y	MNI z	Z score
Taste (uni- and multimodal) [taste—tasteless]					
Anterior insula/ operculum	Right	38	20	−4	4.59
	Left	−32	22	0	3.56*
Orbitofrontal cortex	Right	6	22	−16	3.71*
Dorsolateral prefrontal cortex	Left	−42	26	36	4.21
Anterior cingulate/ paracingulate cortex	Right	8	18	50	3.10**

Activations are significant at $P < 0.05$, corrected for the entire brain volume, unless indicated with *, $P < 0.05$ using small volume correction **, $P < 0.001$ uncorrected with a priori prediction.

Discussion

To our knowledge, this is the first time that the dorsolateral prefrontal cortex has been implicated in responses to unimodal taste and multimodal flavour stimuli in the human brain. This unexpected and intriguing finding is not incompatible with the proposed roles of the dorsolateral prefrontal cortex in temporally organised behaviour (Fuster, 1997; Luria, 1966), working memory (Fuster and Alexander, 1971; Goldman-Rakic, 1995), attention to different kinds of information (Petrides, 1994), integration of diverse cognitive demands (Duncan and Owen, 2000) and response selection (Passingham, 1993; Rowe et al., 2000). The taste-related activation we describe could be important in the optimising or modifying behavioural strategies involved in executive control using the types of functionality proposed by these investigators, or the activations could reflect the recruitment of prefrontal processing in more general attentional processing by taste inputs, for which the results described here then provide the first evidence. We discuss next these possible functions of the taste-related activations of the dorsolateral prefrontal cortex.

Evidence that the activation we describe may not be related to working memory is that the activation by taste in the dorsolateral prefrontal cortex only lasts while the taste is in the mouth (allowing for the haemodynamic delay), and does not continue (see Fig. 2) as it does in relation to working memory (e.g. Dehaene-Lambertz et al., 2002; Rowe et al., 2000). Further evidence that the activation is not related to working memory perhaps required to make ratings of pleasantness and intensity in some of the studies is that activations were found only when these ratings were being made for the taste stimuli salt and glucose taste conditions and not when the ratings were being made for the tasteless solution (De Araujo et al., 2003b). (In that study, included in the metanalysis described here, the contrast of the taste with the tasteless control both with ratings showed significant activity in a region of left dorsolateral prefrontal cortex at x, y, z: −40, 20, 20, which is close to the peak found in the large random effects model described. Furthermore, subjects were not told in advance that one of the four stimuli that they were going to rate was a tasteless solution. Importantly, the memory load

was therefore equal across the stimuli as evidenced by the fact that the variances of the individual ratings were not significantly different ($P > 0.05$) between the taste stimuli and tasteless across all 10 subjects. Additional evidence that the dorsolateral prefrontal cortex activation by taste stimuli described here was not related to working memory functions involved in making the intensity and pleasantness ratings is that in two of the studies (De Araujo et al., 2003a; Kringelbach et al., 2003), most trials had no ratings, and yet activations were found. (These two studies provided data sets 1–19 in Fig. 2.)

We were also able to investigate whether the taste-related activity in the dorsolateral prefrontal cortex reflected the reward value of the taste, by performing additional analysis on another of the taste data sets included in our meta-analysis, which was designed to investigate change in reward value of a whole food stimulus (Kringelbach et al., 2003). The experiment was specifically designed to investigate the neural representation of the reward value of a whole food stimulus (such as chocolate or tomato) that occurs while that food is eaten to satiety. We looked for changes in reward value (using the same sensory-specific, satiety-related analysis described by Kringelbach et al., 2003) across the whole brain, and found significant effects in a region of the right dorsolateral prefrontal cortex [x, y, z: 56, 12, 42; $z = 4.76$, $P < 0.05$ corrected for multiple comparisons; consistent with the finding of a human PET study demonstrating activity in the right dorsolateral prefrontal cortex to monetary reward (Thut et al., 1997)], as well as in an anterior part of the left orbitofrontal cortex (x, y, z: −33, 44, −12). Thus, the left part of the dorsolateral prefrontal cortex with taste-related activation described in the present study does not appear to show reward-related activity, but there is a contralateral (i.e. right and rather more posterior) activation of the dorsolateral prefrontal cortex that does have activation related to food reward. Consistent with this, in the two studies (De Araujo et al., 2003b; Kringelbach et al., 2003) included in this meta-analysis that manipulated the reward value of tastes by investigation of the effects of satiety, no correlations with the pleasantness of the taste stimuli were found in the activations in the left dorsolateral prefrontal cortex.

PET studies have found changes in the dorsolateral prefrontal cortex related to reward value. In particular, increases in satiety was found to increase the blood flow in parts of left middle and inferior frontal gyri in a PET study of the effects of chocolate-induced satiety (Small et al., 2001). Other PET studies of hunger and satiation by Tataranni and colleagues have found that the dorsolateral prefrontal cortex appears to be important in terminating feeding behaviours and have noted differences in activity in this region between lean and obese subjects (Del Parigi et al., 2002; Tataranni et al., 1999). Judging from the published coordinates in these papers, these activations in dorsolateral prefrontal cortex are apparently not overlapping with the activation in left dorsolateral prefrontal cortex reported here but rather in adjacent regions similar to the reward-related activation reported above. [The distances from the peak in the left dorsolateral prefrontal cortex reported to the peaks of activation in these studies are larger than the spatial smoothing used (31.9 mm for the Small et al., 2001 study; and 16.8 and 33.0 mm for the Tataranni et al., 1999 study).]

Some supporting evidence for the finding of taste-related activation of the human dorsolateral prefrontal cortex described here is that in nonhuman primates, some dorsolateral prefrontal cortex neurons are activated by the foods being delivered in a delayed reaction task with an instruction cue to indicate the presence or absence of reward (Hikosaka and Watanabe, 2000; Watanabe, 1996; Watanabe et al., 2002), a memory-guided eye movement task with varying magnitudes of reward (Leon and Shadlen, 1999), and a memory-guided saccade task with an asymmetric reward schedule (Kobayashi et al., 2002b). A monkey PET study on olfactory and gustatory processing that found activation of the inferior frontal gyrus (Kobayashi et al., 2002a) is also consistent with our finding.

The bilateral activation of the anterior insula/frontal operculum is consistent with lesion studies in patients who may develop ageusia following damage to the operculum (Bornstein, 1940a,b), and with the gustatory auras in three patients with magnetic resonance imaging evidence of lesions to the insula (Cascino and Karnes, 1990). It is also compatible with findings in nonhuman primates where the primary taste cortex (defined by projections from the thalamic taste nucleus) has been found in the frontal operculum and the dorsal part of the anterior insula (Ogawa et al., 1989; Pritchard et al., 1986; Scott et al., 1986; Sudakov et al., 1971). Other sensory information related to oral stimulation by food, such as temperature and somatosensory input from the mouth, is processed by other neurons in the primary taste cortex (Norgren, 1990).

The fact that the strongest activation in our taste data set was found in the right anterior insula/frontal operculum corresponds well with the results of a meta-analysis of gustatory responses gathered from neuroimaging studies that suggested that the preponderance of peaks to gustation fall in the right hemisphere (Small et al., 1999). However, the present data clearly shows that taste is represented bilaterally in the normal human brain.

Intriguingly, other neuroimaging studies investigating negative feedback have found activations with similar coordinates in the insula region to those reported as primary gustatory cortex in this paper (e.g. Cools et al., 2002; Konishi et al., 2002; Monchi et al., 2001). These activations are usually labelled BA47/12 by the authors and not insula per se. None of these studies report activations in the orbitofrontal cortex, so a possible explanation for these findings could be that these peaks are really in adjacent parts of caudolateral orbitofrontal cortex but are not as seen as such because of the fMRI parameters used, which easily leads to dropout in the inferior frontal regions if special care is not taken (Wilson et al., 2002). This would be consistent with neurophysiological investigations in macaques (Thorpe et al., 1983) and with recent findings in our laboratory (Kringelbach and Rolls, 2003) where reversal following negative feedback from faces activated adjacent regions of bilateral caudolateral orbitofrontal cortex which were not overlapping with the taste peaks reported in this paper. Alternatively, it may be that the anterior insula is also involved in negative feedback, which is a possibility given that neurophysiological investigations in primates have found that only roughly 4% of neurons in the primary taste cortex showed broadly tuned responses to different tastes (Ogawa et al., 1989; Scott et al., 1986). However, direct neurophysiological or neuroimaging investigations are clearly needed to resolve this interesting question.

The activation by taste in the human orbitofrontal cortex described here is consistent with the responses of neurons in the primate caudolateral orbitofrontal cortex, which is the secondary taste cortex in that it does not receive projections directly from the thalamic taste nucleus but does receive projections from the primary taste cortex (Baylis et al., 1994). On the basis of the present finding of taste in the medial orbitofrontal cortex, it would be of considerable interest to record from single neurons in this

medial region in macaques, for the most medial part of the macaque orbitofrontal cortex has been relatively little explored with respect to taste and olfactory representations. Some neurons in this region have multimodal responses to both gustatory and olfactory (Rolls and Baylis, 1994), and it is in the orbitofrontal cortex that the flavour of food becomes represented (Rolls and Baylis, 1994). Moreover, orbitofrontal cortex neurons represent the reward value of food and other sensory stimuli, in that these neurons only respond to food when the monkey is hungry (Rolls et al., 1989). Furthermore, it is the relative reward value of stimuli that is represented in the orbitofrontal cortex, in that gradually, while one food becomes less rewarding as it is fed to satiety, orbitofrontal cortex neurons come to respond less and less to that food relative to other foods (Critchley and Rolls, 1996; Rolls et al., 1989). Neuroimaging studies in humans have also found that various taste stimuli can activate caudal parts of the orbitofrontal cortex (De Araujo et al., 2003a,b,c; Kringelbach et al., 2003; O'Doherty et al., 2001b, 2002; Small et al., 1999), which is consistent with the proposed role for the orbitofrontal cortex in general emotional processing and for example in reversal-learning of both social (Kringelbach and Rolls, 2003) and arbitrary reinforcers (O'Doherty et al., 2001a).

Taste is generally agreed upon as a primary or unlearned reinforcer (in that taste rather than the intragastric or intravenous delivery of food, is rewarding, and in that this occurs in very young animals, see Rolls, 1999), and as such elicits emotional states (Gray, 1975; Rolls, 1999; Weiskrantz, 1968) that are essential for guiding behavioural choice. While the orbitofrontal cortex is thought to be the most important area implicated in representing the reward value of primary and secondary reinforcers (Rolls, 1999), taste information has to be made available for further cognitive processing. The dorsolateral prefrontal cortex is an area where the consequences of actions, such as delivery of a particular taste of flavour may affect cognition, given that the dorsolateral prefrontal cortex is directly implicated in the preparation for and selection of responses (Passingham, 1993; Rowe et al., 2000). The present study has shown that not only are taste stimuli represented in the anterior insula/frontal opercular cortex and in the caudal orbitofrontal cortex, but that there is taste-related activity in the dorsolateral prefrontal cortex. This taste-related activity is very robust as demonstrated by the statistical significance in the stringent random-effects analysis employed in this study. This taste-related activity may be linked to functions including temporally organised behaviour (Fuster, 1997; Luria, 1966), working memory (Fuster and Alexander, 1971; Goldman-Rakic, 1995), attention to different kinds of information (Petrides, 1994), integration of diverse cognitive demands (Duncan and Owen, 2000) and response selection (Passingham, 1993; Rowe et al., 2000) that are important for optimising or modifying behavioural strategies involved in executive control.

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