NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 34 (2007) 1744–1753

Empathy for positive and negative emotions in the gustatory cortex

Mbemba Jabbi,[a,b] Marte Swart,[a,c] and Christian Keysers[a,*]

[a]BCN NeuroImaging Center, University Medical Center Groningen, Antonius Deusinglaan 2, 9713 AW Groningen, The Netherlands
[b]Department of Psychiatry, University Medical Center Groningen, Hanze plein 1, 9700 RB Groningen, The Netherlands
[c]Department of Experimental and Work Psychology, University of Groningen, Grote Kruisstraat 2-1, 9712 TS Groningen, The Netherlands

Received 17 August 2006; revised 25 October 2006; accepted 27 October 2006
Available online 15 December 2006

Anterior insula and adjacent frontal operculum (hereafter referred to as IFO) are active during exposure to tastants/odorants (particularly disgusting ones), and during the viewing of disgusted facial expressions. Together with lesion data, the IFO has thus been proposed to be crucial in processing disgust-related stimuli. Here, we examined IFO involvement in the processing of other people's gustatory emotions more generally by exposing participants to food-related disgusted, pleased and neutral facial expressions during functional magnetic resonance imaging (fMRI). We then exposed participants to pleasant, unpleasant and neutral tastants for the purpose of mapping their gustatory IFO. Finally, we associated participants' self reported empathy (measured using the Interpersonal Reactivity Index, IRI) with their IFO activation during the witnessing of others' gustatory emotions. We show that participants' empathy scores were predictive of their gustatory IFO activation while witnessing both the pleased and disgusted facial expression of others. While the IFO has been implicated in the processing of negative emotions of others and empathy for negative experiences like pain, our finding extends this concept to empathy for intense positive feelings, and provides empirical support for the view that the IFO contributes to empathy by mapping the bodily feelings of others onto the internal bodily states of the observer, in agreement with the putative interoceptive function of the IFO.

Keywords: Gustatory; Emotion; Empathy; Insula; Frontal operculum

Introduction

When we see the facial expressions of other individuals, we can often intuitively feel what they are feeling. The neural basis of this process has received intense interest. Based on the observations that the sight of other individuals' actions activate similar action programs in the observer and that the observation of other individuals' emotion of disgust activates regions of the brain involved in experiencing disgust, it has been proposed (Keysers et al., 2004; Gallese et al., 2004; Goldman and Sripada, 2005; Keysers and Gazzola, 2006) that feeling the emotions of other individuals involves the following: (a) observing the states of others activates representations of similar states in the observer; (b) these activations, which represent a form of simulation of the observed states, are sensed by a network of brain areas that represent bodily states; and (c) the sensed states are interpreted and attributed to the other individual, distinguishing them from the observer's own emotions.

The distinction between these subprocesses relates to one made in psychology. Young babies, while witnessing the distress of other individuals, often cry as if they were unable to distinguish their own distress from that of others (for a review see Singer et al., 2006). This phenomenon has been termed 'emotional contagion'. In contrast, while more mature individuals are not immune to emotional contagion, they are increasingly able to attribute the shared distress to the other individual, leading to an empathic *understanding* of the state of others (for reviews see Preston and de Waal, 2002; Gallese, 2003; Gallese et al., 2004; Decety and Jackson, 2004). Emotional understanding here refers to the conscious knowledge that someone else is currently experiencing a certain emotional state, as measured for instance by asking the observer to rate the emotional state of another individual (e.g. "how angry is that person from 0 to 6", as used in Adolphs et al., 2003), or a forced choice labelling task, as used in Calder et al. (2000). The processes of simulating and sensing the simulated state of others, hypothesised earlier (Gallese et al., 2004, Keysers and Gazzola, 2006), would be common to emotional contagion and empathic understanding (for reviews see Critchley, 2005; Adolphs, 2006). Thus only the third process of attribution, that enables an observer to associate his/her own simulated emotional state to that of the observed, differentiates early emotional contagion from more mature empathic understanding (for reviews see Frith and Frith, 1999, 2003; Singer, 2006). According to that view (Gallese et al., 2004, Keysers and Gazzola, 2006), mirroring/resonance and/or contagion are important prerequisites for empathic understanding.

At present, the quest to provide empirical evidence for the simulation theory has focused on providing evidence for the fact that the brain creates a simulation of the states of other individuals,

* Corresponding author. Fax: +31 503638875.
E-mail address: c.keysers@med.umcg.nl (C. Keysers).

1053-8119/$ - see front matter © 2006 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2006.10.032

with current evidence suggesting that the observation of the *negative* states of others triggers neural activations that resemble those associated with experiencing similar negative states. Both the observation of disgusted facial expressions and the experience of disgust activate the anterior insula and the adjacent frontal operculum, which will jointly be referred to as IFO (Phillips et al., 1997; Zald et al., 2002; Small et al., 2003; Wicker et al., 2003; Dapretto et al., 2006). The IFO is also activated when participants observe facial expressions of pain, know a loved one is in pain or experience pain themselves (Singer et al., 2004, 2006; Decety and Jackson, 2004; Botvinick et al., 2005; Jackson et al., 2006; Lamm et al., in press; Saarela et al., in press), with the participants that report having more empathic concern activating their IFO more strongly while aware of others' pain (Singer et al., 2004, 2006). In addition, lesions in the IFO impair both the experience of disgust (Adolphs et al., 2003) and the understanding of other people's disgust (i.e. impaired labelling of facial and vocal expressions of disgust) (Calder et al., 2000; Adolphs et al., 2003). Together these experiments converge to ascribe a pivotal role for the IFO in the network of brain areas that underpin the process of simulating observed states of others making the insula a likely neural structure important both for emotional contagion and empathic understanding.

The IFO has also been identified as essential for sensing one's own visceral bodily state (Craig et al., 2000; Critchley et al., 2001, 2002, 2003, 2004, 2005; for reviews see Damasio, 1996, Craig, 2002, 2003; Critchley, 2005), with people more able to sense their own heart beat showing stronger IFO responses (for a review see Critchley, 2005). Altogether, the IFO might therefore be engaged in two aspects that are key to simulation: the activation of simulated states, and the sensing of one's own state, be it simulated or experienced (Keysers and Gazzola, 2006). In addition, the IFO has been shown to have the pattern of efferent and afferent connections necessary for performing both tasks (Mesulam and Mufson, 1982a,b; Mufson and Mesulam, 1982).

Is the IFO confined to the processing of negative states, such as pain and disgust, or does it also process positive states, as long as the latter are associated with the visceral sensations that the IFO is thought to represent? The ingestion of pleasant foods and liquids, associated with such positive bodily states, provide a way to test this prediction that has, to our knowledge, so far not been explored. We therefore scanned participants while they viewed short movie clips of actors sipping from a cup and displaying either an intensely pleased, intensely disgusted or a neutral facial expression. Subsequently, we then scanned the same participants while ingesting pleasant (sucrose), unpleasant (quinine) and neutral (artificial saliva) solutions to map their gustatory IFO.

Individuals differ in their sensitivity to the feeling states of others, and these differences can be measured using self-report questionnaires, such as the Interpersonal Reactivity Index (IRI, Davis, 1980). Here, we measured participants' IRI scores and then searched for regions that respond more strongly to the gustatory experiences of others in participants with higher IRI scores. We restricted such a search to participants' functionally defined gustatory IFO. As argued previously (Singer et al., 2004, 2006; Gazzola et al., 2006) this approach searches for areas underpinning our inter-individual variation in transforming the states of other people into our own, a process thought to be essential for emotional contagion and empathic sharing.

Materials and methods

Participants and procedures

The institutional review board of the University Medical Center Groningen approved the study. Thirty-three healthy volunteers free from any known gustatory, olfactory, visual, neurological or psychiatric disorders gave written informed consent and participated in a screening and training sessions. Participants were screened for their taste sensitivity using labeled magnitude scaling (LMS) (Green et al., 1996), for the goal of excluding super/non tasters during the initial rating of the quinine and sucrose solutions as reported earlier (Small et al., 2003). We used quinine and sucrose for the taste screening with the participants reporting their perceived taste intensity on the LMS scale, ranging from 0 (barely detectable) to 100 (strongest imaginable). As we examine the influence of empathy on interindividual differences in brain activity, it is important to keep other sources of variance in check. In accordance with other studies (Small et al., 2003), we therefore restricted our experiments to participants in the normal range of tasting. Normal tasters were defined as those whose score for sucrose fell within the range of 15–75; while the normal tasting for quinine was define by scores ranging from 30 to 75. Normal tasting scores were obtained for all but 10 participants (9 non tasters and 1 super taster) who were excluded from fMRI. Of the remaining 23 participants that were scanned, two were excluded because of excessive movement, two for not being able to follow the taste and swallow instructions and one because of a vomiting spell. The final sample included in the analysis consisted of 18 right-handed healthy individuals (10 females; mean age 24, SD 2.64) as classified by the Edinburgh scale (Oldfield, 1971). Participants were questioned to ensure they were ignorant about the aim of the study before the event-related fMRI sessions (see Figs. 1 and 2).

Visual runs

Visual runs consisted of the observation of disgusted, pleased and neutral facial expressions (see Fig. 1). Actors were recruited from the Noord Nederlands toneel and the Jeugd theatre school, Groningen. They were asked to taste the content of a cup and express their resulting emotion in a naturally vivid manner (see Fig. 1). A separate group of 16 individuals rated the facial expressions of all the edited movies in terms of the intensity, naturalness and vividness of pleased, disgust, and the neutral expressions they recognized for each movie on a 7-point Likert scale. The 10 best clips for each emotional category in terms of the intensity, naturalness and vividness of expression of the emotions (as rated by the 16 individuals) for the three emotional conditions were selected for the final experiment. Each visual run contained all of the final selected 30 movie clips (3 s each, 10 movies per condition × 3 conditions) presented in a randomized event-related fashion with a red fixation cross between two movie clips.

Gustatory runs

Participants sampled and rated the intensity and pleasantness/unpleasantness of quinine (unpleasant taste) with a concentration of 1.0×10^{-3} M and sucrose (pleasant taste) with a concentration of 1.8×10^{-2} M as used previously (Small et al., 2003). The neutral taste consisted of artificial saliva (Saliva Orthana; Farmachemie BV Haarlem, the Netherlands; art no. 39.701.130) diluted with

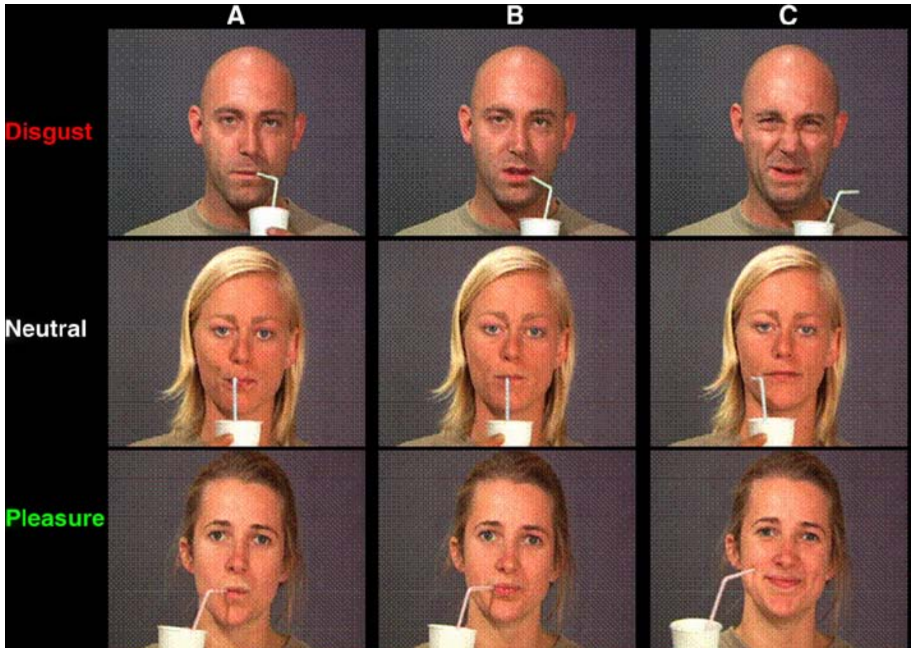

Fig. 1. Gustatory visual stimuli. Above are picture frames of three sample movies portraying actors while tasting concentrated citric acid (shown in the first row) leading to the experience (expression) of disgust, water (middle row) portraying an neutral gustatory experience and orange juice (last row) leading to the experience (facial expressions) of pleasure. Each movie shows an actor holding a cup and eventually sipping the content by means of a plastic straw (~ 1 s) as can be seen in column (A). This was followed by the actor releasing the straw and simultaneously swallowing the liquid (column B), and finally, the actor then expresses a neutral, pleased, or disgusted facial expression (~ 2 s) shown in column C. During the visual experiment, 10 movie clips for each emotional category was presented with a red fixation cross between each movie lasting for a variable duration of 8–12 s in a fully randomized event-related fashion. Two repetitions of the original run were present in a fully randomized event-related design.

distilled water to a subject-specific neutral taste (participants chose the most neutrally tasting solution from concentrations of 5%, 10% and 20% artificial saliva in water). In the fMRI experiment, taste solutions were delivered as a 0.5 cm^3 bolus over a 5-s period (Small et al., 2003). The solutions were delivered by an experimenter standing beside the MRI scanner using a tubing system that consisted of a syringe (for each taste condition) connected to a 45-cm infusion tube that was inserted into a pacifier through a perforation at the top with the tip of the tube protruding slightly through the sucking tip of the pacifier (see Fig. 2). Taste instructions were given before scanning using water. Regardless of the strong unpleasant sensations as a result of the quinine delivery, the data obtained from the realignment procedure confirmed that all but two participants (excluded from the study for this reason) did not move their heads in reaction to the taste solutions for more than 1 mm.

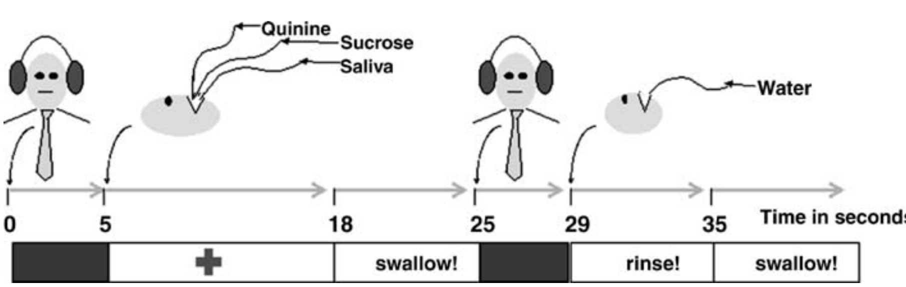

Fig. 2. Gustatory procedures. Procedures involving presentation of auditory instructions to the experimenter (shown with a tie). Visual instructions were presented to the subject (shown supine). At the start of the experiment, participants saw a black screen (lowest row), the experimenter simultaneously hears a voice instructing him to deliver either quinine, sucrose or artificial saliva (depending on the trial at hand) by means of the 5-ml syringe connected to the tubing (upper row). Timing of delivery of the taste and rinsing solutions was controlled with a voice counting from three to start as in Keysers et al. (2004) (middle row). For each individual taste stimulus, delivery of the solutions coincides with the presentation of a cross that follows the black screen, instructing subjects to keep the liquid in their mouth and taste it. This is followed by the text "swallow!" appearing on the screen, instructing participants to swallow the liquid. The experimenter then receives another auditory instruction to deliver the rinsing water, the delivery of which coincides with a visual instruction to the subject to rinse their mouth, followed by an instruction to swallow the rinsing solution. For each run, a total of three deliveries for each taste condition were carried out, and a total of four taste runs were presented in a fully randomized slow event-related fashion with a black screen being presented between two consecutive stimuli with variable durations of 4–6 s. A total of 12 conditions (3 × 4) were modeled for final analysis (i.e., 3 tasting conditions for quinine, sucrose and saliva; 3 swallowing of these tasting conditions; 3 rinsing of these tasting conditions and 3 swallowing of the rinsing solutions).

Self-report measures

We rated participants' subjective reaction to the sight of others' gustatory emotions by asking how willing they are to drink some of the beverage the individuals in the movies just tried (from −6 'absolutely not' to 6 'very much') see Fig. 3b. Furthermore, we asked participants to rate the quinine, sucrose and neutral solution that they had to ingest during the experiment on a scale ranging from −6 'extremely disgusting' to 6 'extremely delicious'. Both scales measure participants' evaluation of the beverages involved in the third person (He tastes) and first person perspective (I taste) of the experiment, and thus allow a direct comparison of these two perspectives. Additionally, the IRI (Davis, 1980) was administered to assess participant's interpersonal reactivity index.

fMRI acquisition

Images were acquired using a Philips 3T whole-body scanner (Best, The Netherlands) equipped with a circular sense head coil. For functional imaging, we used a T2*-weighted echo-planar sequence with 39 interleaved 3.5 mm thick axial slices with 0 mm gap (TR = 2000, TE = 30 ms, flip angle = 80°, FOV = 224 mm, 64 × 64 matrix of 3.5 × 3.5 × 3.5 mm voxels). At the end of the functional scans, a T1-weighted anatomical image (1 × 1 × 1 mm) parallel to the bicommissural plane, covering the whole brain was acquired.

General fMRI data analysis

Data were preprocessed and analyzed using Statistical Parametric Mapping (SPM2; Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk). All functional volumes were realigned to the first acquired volume. Images were coregistered to the participant's anatomical space and spatial normalization was then carried out on all images (Friston et al., 1995) to obtain images with a voxel size of 2 × 2 × 2 mm). All volumes were then smoothed with an 8 mm full-width half-maximum isotropic Gaussian kernel. For time series analysis on all

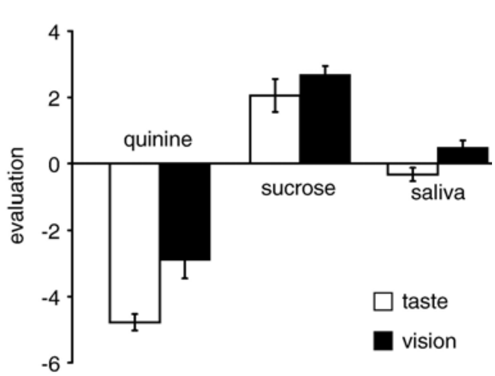

Fig. 3. Mean subjective ratings ± SEM of how disgusting/delicious the liquids were perceived by participants during tasting of quinine, sucrose and artificial saliva (taste ratings blank bars) and ratings of ones' willingness to drink the liquids they saw the actor drinking (visual ratings black bars). Participants were asked to rate the taste experience of others in their own person-relevant perspective (i.e., how willing they were to taste the drink they saw the actors just took), this way, we could judge the affective states the facial expressions induced in them by means of their willingness/unwillingness ratings as a result of the perceived pleasure/disgust.

participants, high-pass filters with cut-off points at 106 s and 310 s for the visual and gustatory conditions, respectively, were included in the filtering matrix in order to remove low-frequency noise and slow drifts in the signal, which could bias the estimates of the error. Condition-specific effects at each voxel were estimated using the general linear model. Single participant's t contrast maps and random effects analyses were carried out (Wicker et al., 2003). Furthermore, a simple regression analysis (using the individual scores of each IRI subscale and individual disgust sensitivity scores as a predictor) of the activations of the whole brain was carried out at the second level using the basic models function in SPM2 and a statistical threshold of $p < 0.005$ (uncorrected) (see Table S2).

Functional definition of the gustatory IFO

We defined the gustatory IFO functionally using the data from the taste experiment. We calculated at the second level, the contrasts quinine–saliva and sucrose–saliva, thresholded both contrasts individually at $p < 0.005$ (uncorrected) and applied a logical OR. The resulting map thus included all voxels involved in tasting (be they positive of negative) relative to saliva. Since this map included more than the IFO, we additionally required that voxels had MNI coordinates in the following range: X = (22 to 70 or −70 to −22), Y = (−4 to 40) and Z = (−20 to 18). The resulting map is shown as Fig. S1, and was used as an inclusive mask for the correlation analyses between participant's IFO activation during the viewing of facial expressions of other's gustatory experiences and their own tendency to empathise with others as measured by the IRI scale.

Correlation analysis

To identify correlations between empathy and visual activations in the IFO, for each subject, we calculated the parameter estimates for viewing disgusted, pleased and neutral facial expressions separately. Using a separate simple regression model at the second level, we then searched for voxels in which a correlation between the individuals' IRI score and parameter estimate for each of the facial expressions existed. These maps where inclusively masked with the gustatory IFO mask. This analysis was performed for the total IRI score (composite IRI), and separately for each of the four subscales (i.e., empathic concern 'EC', Fantasy 'FS', perspective taking 'PT' and personal distress 'PD').

Additional analyses within identified clusters of correlation were performed using Marsbar (http://marsbar.scourceforge.net; M. Brett, J.-L. Anton, R. Valabregue, and J.-B. Poline, 2002, Region of Interest analysis using an SPM toolbox, Abstract).

Results

Ratings

In order to determine how much the emotional facial expressions in the movies affect the participants, we rated their subjective reaction to the gustatory emotions depicted in the films by asking how willing they would be to drink some of the beverage the individuals in the movies just tried (from −6 'absolutely not willing' to 6 'very much willing'); see Fig. 3. Furthermore, we asked them to rate the quinine, sucrose and neutral solutions that they had to ingest during the experiment on a scale ranging from

−6 'extremely disgusting' to 6 'extremely delicious'. Both the willingness and the direct taste rating scales measure participants' evaluation of the beverages (albeit from different perspectives), and were therefore directly compared using a repeated measurement ANOVA with 2 perspectives (tasting vs. viewing) × 3 beverages (unpleasant, pleasant and neutral).

This analysis revealed a main effect of perspective ($F(1,17)=9.9$, $p<0.006$), with tasting leading to more negative ratings than observing and a main effect of beverage ($F(2,34)=184$, $p<10^{-18}$) were observed. Importantly, there was no interaction of perspective and beverage ($p<0.386$), suggesting that the difference between the beverages was similar for the two perspectives. During tasting however, quinine was rated as more disgusting than sucrose as pleasant ($p<0.001$, after comparing absolute values by changing the negative scores for quinine into positive scores). This phenomenon has been reported earlier (Wicker et al., 2003; Nitschke et al., 2006), and explained as related to differences in perceived intensity as well as valence (Small et al., 2003; Liberzon et al., 2003). Finally, post-hoc examination (Newman–Keuls) shows that negative and positive stimuli were rated as more negative and more positive respectively than neutral stimuli (all $p<0.001$).

Neuroimaging results

To identify the relationship between individual's gustatory IFO responses to the gustatory experience of others during the witnessesing of these experiences, we correlated individuals' IRI scores with their brain activations during the viewing of other's gustatory emotions. The IRI is a 28-item with a 5-point Likert-type scale (0 = does not describe me well to 4 = describes me very well) that assesses four dimensions of empathy: FS, PD, PT and EC (Davis, 1980, 1994). To restrict our analysis to the gustatory IFO we masked these correlation maps with the functionally defined gustatory IFO (see Materials and methods and Fig. S1).

As a first step, we analysed correlations with the composite IRI obtained from summing the scores obtained on the four distinct subscales. Fig. 4 shows that positive correlation exist between this composite IRI and the parameter estimates obtained during the vision of disgusted facial expressions, in both the right and left gustatory IFO. In the left IFO, similar correlations were observed between the vision of pleased facial expressions and the composite IRI. Correlations with neutral facial expressions were smaller, and restricted to the right hemisphere.

The composite IRI pools data from four different subscales measuring different aspects of empathy, and it has been advocated that a better approach stems from examining the individual contribution of each subscale (D'Orazio, 2004). We therefore examined the pattern of correlation observed for each individual subscale.

Both the PD and FS scales correlated significantly with visual activations during the observation of *both* the disgusted and pleased facial expressions of others in bilateral gustatory IFO (Fig. 5A–B). The center column of Fig. 5A–B shows this spatial pattern of correlation. Voxels shown in red correlated with the empathy scores while viewing disgusted faces, but not while viewing neutral or pleased faces; voxels shown in white correlated with the empathy scores during both the vision of pleased and disgusted facial expressions, but not during the vision of neutral facial expressions. No other combination of correlations was observed within the IFO for the PD and FS scales. To examine the nature of the correlational relationship further, we extracted the mean BOLD signal from the compound clusters of correlations (combining the white and red voxels circled in the figure), and calculated parameter estimates for all visual and gustatory conditions (see graphs in the right and left column of Fig. 5). For both scales, and both hemispheres, parameter estimates for the vision of pleased and disgusted facial expressions correlated significantly with the empathy measures at $p<0.005$ if the entire cluster was considered (Fig. 5A and B, left column). The right column illustrates the overall trend in these clusters if the low and highly empathic participants are combined, and shows that over all, their mean activations to pleased and disgusted facial expressions were extremely similar.

For PT and EC scores, the link to the visual brain activations was less clear. None of the voxels in the gustatory IFO had visual activations that correlated with the EC scale during the vision of any facial expressions. For PT, only one cluster (relatively smaller than the ones predictive for PD and FS) in the right gustatory IFO correlated significantly with the parameter estimate for viewing disgust and neutral, but not pleased, facial expressions (shown in red in Fig. 5C). Results of whole brain–IRI correlations are reported in the Supplementary data (Table S1).

To test if our correlations of empathy with IFO activation during the viewing of others gustatory experience is specific for the

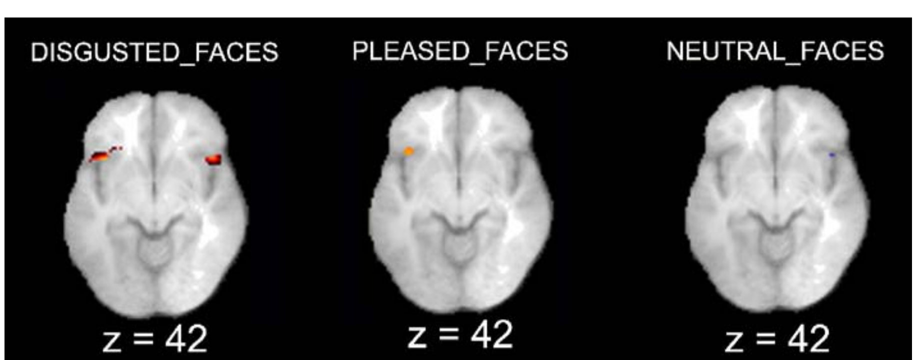

Fig. 4. Composite IRI scores (i.e., total scores on the whole IRI questionnaire) predicted IFO activations during the observation of different facial expressions. Results show voxels where the correlation between the parameter estimate obtained during the vision of the facial expression and the composite IRI was significant at $p<0.005$, uncorrected, and the cluster contained at least 5 contiguous voxels. Results were masked with the gustatory IFO. Results are overlaid on the mean T1 image of the 18 participants.

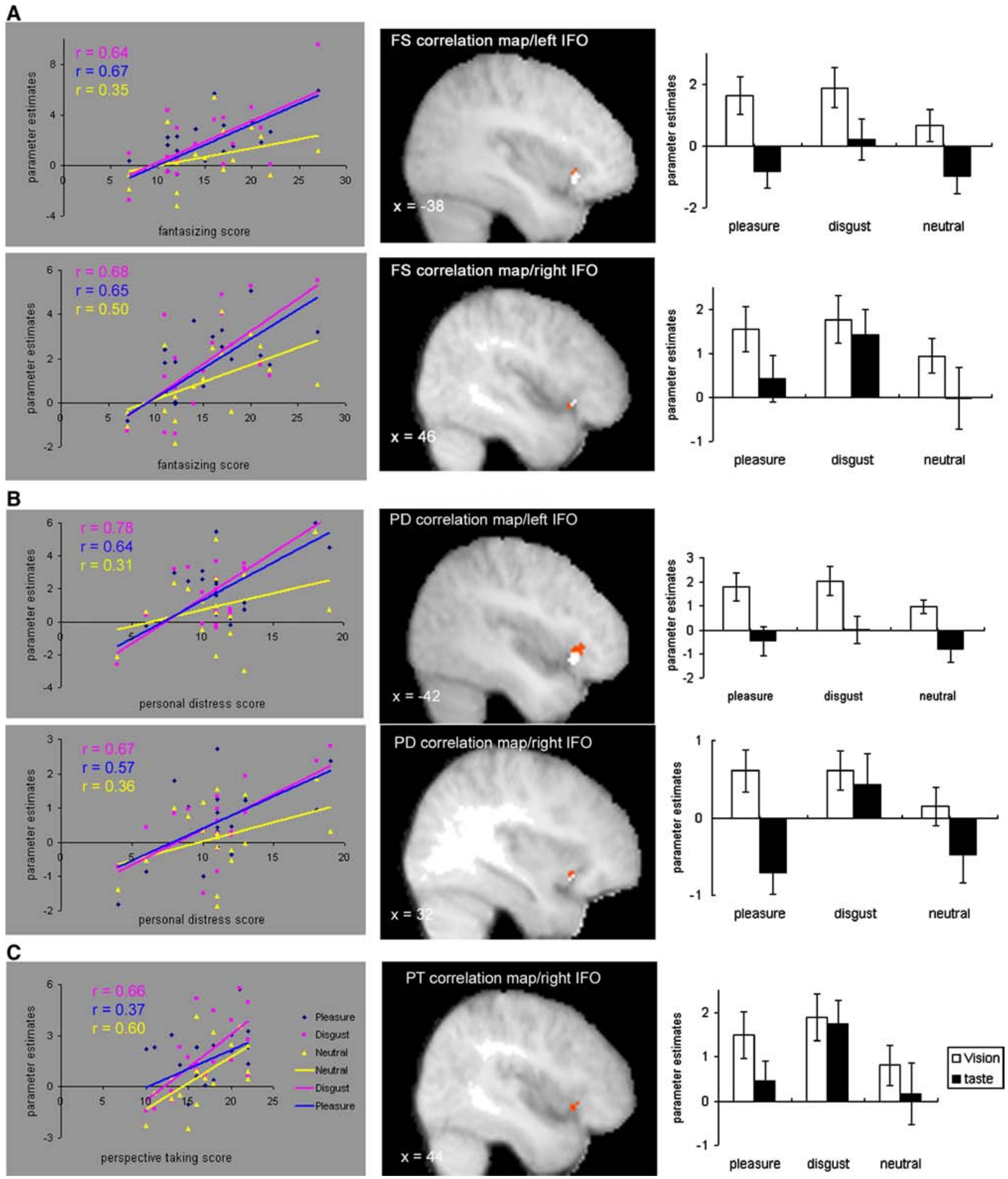

Fig. 5. Empathy and the IFO. Center column: voxels showing significant correlations between individuals' IRI subscales and parameter estimates derived during the observation of disgusted, pleased or neutral facial expressions (see text for colour coding). Results were thresholded at $p<0.005$ uncorrected at the voxel level, and masked with the gustatory IFO. The mean signal in the compound cluster of correlation was then extracted, and further analysed in the left and right column, showing the relationship between participants' IRI score (x-axis) and visual parameter estimates (y-axis) together with regression line and correlation value on the left, and mean parameter estimated during vision and taste (±SEM) on the right. The color-coding for the right and left columns defined in panel C applies to all panels. Our results of FS- and PD-predicted activations in IFO during the viewing of disgusted faces, and PD-predicted cluster during the viewing of pleasure survived FDR correction at $p<0.05$. The FS-predicted activations during the viewing of pleased faces also survived FDR correction at $p<0.075$ while the PT-predicted IFO activation during the viewing of disgusted and neutral faces did not survive FDR corrections.

viewing condition, we performed a similar correlational analysis between participants' individual IRI sub-scale scores and their IFO activation during the experience of disgusting and pleasant taste. We found no significant correlations in the IFO between individuals' IRI scores and their IFO activations during tasting making our empathy-related IFO findings specific for the observation of social gustatory experiences of others.

Within all five empathy-correlating clusters outlined in Fig. 5, during vision, pleasant and disgusted facial expressions seemed to cause similar average activations, both of which exceeded that observed during the viewing of neutral faces. We performed a 5 cluster × 3 faces ANOVA to examine this effect. The analysis revealed no significant interaction between cluster and faces indicating that the effect of stimulus was similar in all clusters. A planned comparison between pleased and disgusted faces showed no significant difference ($F(1,17)<0.33$, $p>0.57$), while both emotional faces caused stronger activations than the neutral faces ($F(1,17)>6.56$, $p<0.02$). During tasting, the same analysis revealed a different pattern of activation: quinine exceeded both saliva and sucrose in activation (both $p<0.02$), and sucrose did not differ from saliva ($p>0.6$).

Discussion

Here, we examined whether the gustatory IFO activations during the vision of pleased and disgusted facial expressions correlated with how participants scored on a self report measure of their sensitivity to other people's feeling states (IRI). We found that for both pleased and disgusted facial expressions, participants that obtained higher scores in the PD and FS subscales of the IRI activated their functionally defined gustatory IFO more strongly than participants obtaining lower scores. This relationship was less prominent in the case of PT and EC scores.

These results demonstrate for the first time, that during the vision of facial expressions of other people's gustatory emotions, the amplitude of activations in the gustatory IFO go hand-in-hand with differences in self reported interpersonal reactivity. This finding extends our previous demonstration, that the IFO contains voxels involved in the experience and the observation of negative states such as disgust (Wicker et al., 2003), and provides further support for the hypothesis that the IFO activation during emotion observation may represent a transformation of observed states into experienced emotional states (Wild et al., 2001; Hess and Blairy, 2001; Lawrence et al., 2005; Saarela et al., in press; for reviews see Damasio, 1996; Craig, 2002; Gallese et al., 2004; Critchley, 2005; Singer, 2006). In addition, by using a correlation approach, we provide the first demonstration that the IFO is involved in the processing of positive states of other individuals.

A number of studies have suggested that the insula is particularly involved in the processing of negative states, including disgust and pain (Phillips et al., 1997; Calder et al., 2000; Adolphs et al., 2003, Wicker et al., 2003; Singer et al., 2004, 2006; Jackson et al., 2005; Botvinick et al., 2005; Lamm et al., in press, for reviews see Calder et al., 2001; Adolphs, 2003). In contrast, others have shown that the insula is also important for the experience of positive visceral states such as positive tastes and flavours (Zald et al., 2002, Small et al., 2003; O'Doherty et al., 2006; Nitschke et al., 2006; for a review see Phan et al., 2002) and a PET study has shown preliminary evidence for the fact that the vision of bodily pleasure in others causes activations of the Insula (movies of pleasant heterosexual coitus, Stoleru et al., 1999). Our current study extends these findings to positive food-related pleasure and suggests a link between these activations and interpersonal reactivity. It thereby confirms the involvement of the IFO in the processing of both the positive and the negative states of others.

The pain, disgust and bodily pleasure that have been found to activate the insula so far all involve sensations triggered by strongly somatic stimuli such as food, electroshocks or sexual stimulation. Further research will be needed to test whether states such as primary disgust/distaste-, pain-, food- and sex-related pleasure do rely on the IFO because they are associated with a somatic *trigger*.

Our finding that different subscales of the IRI differ in their correlation with visual activations requires some consideration. According to Gallese et al. (2004) and Keysers and Gazzola (2006) the sight of the states of others: (a) triggers similar states in the observer, which are then (b) sensed, and eventually (c) attributed to the other individuals. The IFO is thought to contribute mainly to the first two stages of this process. If this is true, IFO activity should correlate primarily with subscales of the IRI that tap into the sharing of feeling states (i.e. emotional contagion). The FS subscale taps directly into respondents' ability to transpose themselves into the feelings and behaviors of actors in movies (Davis, 1980, 1994). The PD subscale measures people's emotional arousability-related to both *negative* and *positive* emotions (Eisenberg et al., 1991; Davis, 1994). Both scales thus measure interindividual differences in emotional contagion and the fact that these scales were found to correlate with the activations in the IFO thus supports the view that the IFO may be part of a network that maps the states of others onto similar states in the observer (Critchley et al., 2002, 2003, 2004: for reviews see Gallese et al., 2004; Keysers and Gazzola, 2006; Critchley, 2005). Based on our results, it is impossible to conclude whether the role of the IFO is primarily to activate a state resembling that of the observed subject or to sense and feel that simulated state. It remains for future research to test the hypothesis that the involuntary sharing of observed states is common to emotional contagion and empathic understanding.

The EC and PT scales on the other hand tap into aspects that go beyond the sharing of feeling states of others. The EC subscale focuses on sympathy for 'victims' (people less fortunate, people that are taken advantage of, people treated unfairly). Participants scoring high on EC thus do not primarily respond to the sight of the misfortunes of others with states directly resembling those observed (which would be rage, pain or fear), but with sympathy. This involves a process that according to simulation theories would occur after a simulated state has been sensed and attributed to another individual. While negative findings should always be interpreted with caution, the stronger correlation between PD and IFO activation compared to EC might relate to two aspects. First, EC might be more related to the function of other structures. Second, our actors were not prototypical victims: they voluntarily tried a variety of drinks, making most of the questions in the EC subscale irrelevant to our movies. In support of this latter interpretation, Singer et al. (2004) showed that when the stimuli relate to the pain inflicted by someone else to a loved victim (i.e., an electroshock), EC scores do predict activations in a region that overlaps with our IFO findings. Finally, the PT subscale mainly measures interpersonal reactivity from a more cognitive, emotionally neutral perspective that taps into people's voluntary attempts to understand the goals and motivations of other people (Davis, 1980, 1994). Here we focused on the gustatory IFO to examine the function of this structure. The stronger correlation with PD and FS and the weaker correlation with PT and EC suggest that this structure is primarily involved in the involuntary sharing of observed states common to emotional contagion and empathic sharing (as measured by PD and FS). The IFO thus appears less involved in the more deliberate concern or cognitive perspective taking that requires an explicit and mature concept of self and other. Other areas of the insula, the anterior cingulate and other limbic structures appear more involved in these latter processes (see Table S2).

The present report focused on the role of the IFO in social cognition. However, our findings of positive correlations between individual's IRI scores and activations of other brain areas outside of the functionally defined IFO, such as the medial prefrontal and posterior cingulate cortices, thought to mediate social cognitive processes such as theory of mind (e.g. Saxe and Powell, 2006; for reviews see Frith and Frith, 1999; Saxe, 2006; Amodio and Frith, 2006) are of importance. The medial prefrontal cortex in particular is believed to be important in mentalizing, i.e. thinking about the mental states of others. It is activated both when participants reflect about their own emotions (Gusnard et al., 2001) and when they reflect about the mental states of others (see Frith and Frith, 2003 for a review). The fact that our empathy correlations involve both the IFO and structures such as the medial prefrontal cortex suggest that the mapping of observed bodily states onto similar states of the self (in the IFO) might go hand in hand with mentalizing about ones own states and those of others (in the medial prefrontal cortex). The interaction of these brain areas may be critical in transforming sheer emotional contagion into a conscious understanding of other individuals' mental states (see Keysers and Gazzola, 2006). Further research will be required to examine the connectivity between these areas and disentangle the intricate relationship between emotional contagion, simulation and mentalizing.

By capitalizing on inter-individual differences in empathy, we show that the regions of the IFO involved in the processing of our own sensation of drinking are activated both when participants witness other individuals drinking pleasant and disgusting beverages. These findings suggest that the role of the IFO in the representation of bodily states of others is broader than previously thought (Craig et al., 2000; Critchley et al., 2001, 2002, 2003, 2004, 2005; Krolak-Salmon et al., 2003; for reviews see Damasio, 1996, 1999; Craig, 2002; Churchland, 2002; Preston and de Waal, 2002; Gallese et al., 2004; Critchley, 2005; Adolphs, 2006; Keysers and Gazzola, 2006) and not limited to negative emotions. The fact that our activations depended on differences in interpersonal reactivity expands the original observation of a link between IFO activity and empathy for pain (Singer et al., 2004, 2006) to gustatory pleasure and disgust/distaste and strengthens the link between activations in these areas and our ability to share other people's emotions. The human bilateral IFO may constitute a critical component of the neural mechanism that allows the mapping of the bodily states of others onto our own inner states and thereby facilitate our understanding of the social environment and ultimately survival. How strongly individuals mirror socially relevant bodily experiences may depends on the reactivity of their inner milieu (as measured by disgust sensitivity scales etc.) or their capacity to sense their inner milieu (as measure for instance by alexithymia scales). Future experiments will need to disentangle these processes and to determine the neural basis of the interaction between emotional contagion and empathic understanding.

Acknowledgments

The authors thank the participants for their time, Anita Kuiper and Remco Renken for help in the acquisition of data, Dana Small for information on the chemosensory stimuli, Marina Maura and Johan van der Heiden for the preparation of the chemosensory stimuli, and Christian van der Gaag for the acquisition of the visual stimuli. We thank Tania Singer, Vittorio Gallese and John O'Doherty for their valuable comments. The research was supported by a Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO) VIDI grant to CK and a Marie Curie Excellence Grant to CK, as well as an NWO grant no. 904-53-092 to Johan A den Boer and Johan Ormel. MJ conceived and designed the study, acquired and analysed the data and wrote the paper. CK contribute equally to conceiving the study, performing data analysis and writing the paper. MS contributed equally to acquiring the data. We thank all members of the social brain lab for valuable comments on earlier versions of the manuscript.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2006.10.032.

References

Adolphs, R., 2003. Cognitive neuroscience of human social behaviour. Nat. Rev., Neurosci. 4, 165–178.

Adolphs, R., 2006. How do we know the minds of others? Domain-specificity, simulation, and inactive social cognition. Brain Res. 1079, 25–35.

Adolphs, R., Tranel, D., Damasio, A.R., 2003. Dissociable neural systems for recognizing emotions. Brain Cogn. 52, 61–69.

Amodio, D.M., Frith, C.D., 2006. Meeting of minds: the medial frontal cortex and social cognition. Nat. Rev., Neurosci. 7, 268–277.

Botvinick, M., Jha, A.P., Bylsma, L.M., Fabian, S.A., Solomon, P.E., Prkachin, K.M., 2005. Viewing facial expressions of pain engages cortical areas involved in the direct experience of pain. NeuroImage 25, 312–319.

Calder, A.J., Keane, J., Manes, F., Antoun, N., Young, A.W., 2000. Impaired recognition and experience of disgust following brain injury. Nat. Neurosci. 3, 1077–1088.

Calder, A.J., Lawrence, A.D., Young, A.W., 2001. Neuropsychology of fear and loathing. Nat. Rev., Neurosci. 2, 352–363.

Churchland, P.S., 2002. Self-representation in nervous systems. Science 296, 308–310.

Craig, AD., 2002. How do you feel? Interoception: the sense of the physiological condition of the body. Nat. Rev., Neurosci. 3, 655–666.

Craig, AD., 2003. Interoception: the sense of the physiological condition of the body. Curr. Opin. Neurobiol. 4, 500–505.

Craig, A.D., Chen, K., Bandy, D., Reiman, E.M., 2000. Thermosensory activation of insular cortex. Nat. Neurosci. 3, 184–190.

Critchley, H.D., 2005. Neural mechanisms of autonomic, affective, and cognitive integration. J. Comp. Neurol. 493, 154–166.

Critchley, H.D., Mathias, C.J., Dolan, R.J., 2001. Neuroanatomical basis for first- and second-order representations of bodily states. Nat. Neurosci. 4, 207–212.

Critchley, H.D., Melmed, R.N., Featherstone, E., Mathias, C.J., Dolan, R.J., 2002. Volitional control of autonomic arousal: a functional magnetic resonance study. NeuroImage 16, 909–919.

Critchley, H.D., Good, C.D., Ashburner, J., Frackowiak, R.S., Mathias, C.J., Dolan, R.J., 2003. Changes in cerebral morphology consequent to peripheral autonomic denervation. NeuroImage 18, 908–916.
Critchley, H.D., Wiens, S., Rotshtein, P., Ohman, A., Dolan, R.J., 2004. Neural systems supporting interoceptive awareness. Nat. Neurosci. 7, 189–195.
Critchley, H.D., Rotshtein, P., Nagai, Y., O'Doherty, J., Mathias, C.J., Dolan, R.J., 2005. Activity in the human brain predicting differential heart rate responses to emotional facial expressions. NeuroImage 24, 751–762.
Damasio, A.R., 1996. The somatic marker hypothesis and the possible functions of the prefrontal cortex. Philos. Trans. R. Soc. Lond., B Biol. Sci. 351, 1413–1420.
Damasio, A.R., 1999. The Feeling of What Happens: Body and Emotion in the Making of Consciousness. Harcourt Brace, New York.
Dapretto, M., Davies, M.S., Pfeifer, J.H., Scott, A.A., Sigman, M., Bookheimer, S.Y., Iacoboni, M., 2006. Understanding emotions in others: mirror neuron dysfunction in children with autism spectrum disorders. Nat. Neurosci. 9, 28–30.
Davis, M.H., 1980. A multidimensional approach to individual differences in empathy. Catal. Sel. Doc. Psychol. 10, 85 (MS. 2124).
Davis, M.H., 1994. Empathy: A Social Psychological Approach. Westview Press, Colorado, p. 671.
Decety, J., Jackson, P.L., 2004. The functional architecture of human empathy. Behav. Cogn. Neurosci. Rev. 3, 71–100.
D'Orazio, D., 2004. A comparative analysis of empathy in sexually offending and non-offending juvenile and adult males. Sex. Abus. 16, 173–174.
Eisenberg, N., Fabes, R.A., Schaller, M., Miller, P., Carlo, G., Poulin, R., Shea, C., Shell, R., 1991. Personality and socialization correlates of vicarious emotional responding. J. Pers. Soc. Psychol. 61, 459–470.
Friston, K.J., Holmes, A.P., Worsley, K.J., Poline, J.B., Frith, C.D., Frackowiak, R.J.S., 1995. Statistical parametric maps in functional imaging: a general linear approach. Hum. Brain Mapp. 3, 189–210 b.
Frith, C.D., Frith, U., 1999. Interacting minds—A biological basis. Science 286, 1692–1695.
Frith, U., Frith, C.D., 2003. Development and neurophysiology of mentalizing. Philos. Trans. R. Soc. Lond., B Biol. Sci. 358, 459–473.
Gallese, V., 2003. The roots of empathy: the shared manifold hypothesis and the neural basis of intersubjectivity. Psychopathology 36, 171–180.
Gallese, V., Keysers, C., Rizzolatti, G., 2004. A unifying view of the basis of social cognition. Trends Cogn. Sci. 8, 396–403.
Gazzola, V., Aziz-Zadeh, L., Keysers, C., 2006. Empathy and the somatotopic auditory mirror system in humans. Curr. Biol. 16, 1824–1829.
Goldman, A.I., Sripada, C.S., 2005. Simulationist models of face-based emotion recognition. Cognition 94, 193–213.
Green, B.G., Dalton, P., Cowart, B., Shaffer, G., Rankin, K., Higgins, J., 1996. Evaluating the 'Labeled Magnitude Scale' for measuring sensations of taste and smell. Chem. Senses 21, 323–334.
Gusnard, D.A., Akbudak, E., Shulman, G.L., Raichle, M.E., 2001. Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. Proc. Natl. Acad. Sci. U. S. A. 98, 4259–4264.
Hess, U., Blairy, S., 2001. Facial mimicry and emotional contagion to dynamic emotional facial expressions and their influence on decoding accuracy. Int. J. Psychophysiol. 40, 129–141.
Jackson, P.L., Meltzoff, A.N., Decety, J., 2005. How do we perceive the pain of others? A window into the neural processes involved in empathy. NeuroImage 24, 771–779.
Jackson, P.L., Brunet, E., Meltzoff, A.N., Decety, J., 2006. Empathy examined through the neural mechanisms involved in imagining how I feel versus how you feel pain. Neuropsychologia 44, 752–761.
Keysers, C., Gazzola, V., 2006. Towards a unifying neural theory of social cognition. Prog. Brain Res. 156, 383–406.
Keysers, C., Wicker, B., Gazzola, V., Anton, J.L., Fogassi, L., Gallese, V., 2004. A touching sight: SII/PV activation during the observation and experience of touch. Neuron 42, 335–346.
Krolak-Salmon, P., Henaff, M.A., Isnard, J., Tallon-Baudry, C., Guenot, M., Vighetto, A., Bertrand, O., Mauguiere, F., 2003. An attention modulated response to disgust in human ventral anterior insula. Ann. Neurol. 53, 446–453.
Lamm, C., Batson, D.C., Decety, J., in press. The neural substrate of human empathy: effects of perspective-taking and emotion regulation. Journal of Cognitive Neuroscience.
Liberzon, I., Phan, K.L., Decker, L.R., Taylor, S.F., 2003. Extended amygdala and emotional salience: a PET activation study of positive and negative effect. Neuropsychopharmacology 28, 726–733.
Lawrence, E.J., Shaw, P., Giampietro, V.P., Surguladze, S., Brammer, M.J., David, A.S., 2005. The role of 'shared representations' in social perception and empathy: an fMRI study. Neuroimage 29, 1173–1184.
Mesulam, M.M., Mufson, E.J., 1982a. Insula of the old world monkey: I. Architectonics in the insulo-orbito-temporal component of the paralimbic brain. J. Comp. Neurol. 212, 1–22.
Mesulam, M.M., Mufson, E.J., 1982b. Insula of the old world monkey: III. Efferent cortical output and comments on function. J. Comp. Neurol. 212, 38–52.
Mufson, E.J., Mesulam, M.M., 1982. Insula of the old world monkey: II. Afferent cortical input and comments on the claustrum. J. Comp. Neurol. 212, 23–37.
Nitschke, J.B., Dixon, G.E., Sarinopoulos, I., Short, S.J., Cohen, J.D., Smith, E.E., Kosslyn, S.M., Rose, R.M., Davidson, R.J., 2006. Altering expectancy dampens neural response to aversive taste in primary taste cortex. Nat. Neurosci. 9, 435–442.
O'Doherty, J.P., Buchanan, T.W., Seymour, B., Dolan, R.J., 2006. Predictive neural coding of reward preference involves dissociable responses in human ventral midbrain and ventral striatum. Neuron 49, 157–166.
Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97–113.
Phan, K.L., Wager, T., Taylor, S.F., Liberzon, I., 2002. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. NeuroImage 16, 331–348.
Phillips, M.L., Young, A.W., Senior, C., Brammer, M., Andrew, C., Calder, A.J., Bullmore, E.T., Perrett, D.I., Rowland, D., Williams, S.C., et al., 1997. A specific neural substrate for perceiving facial expressions of disgust. Nature 389, 495–498.
Preston, S.D., de Waal, F.B., 2002. Empathy: its ultimate and proximate bases. Behav. Brain Sci. 25, 1–20.
Saarela, M.V., Hlushchuk, Y., Williams, A.C., Schurmann, M., Kalso, E., Hari, R., in press. The compassionate brain: humans detect intensity of pain from another's face. Cereb. Cortex.
Saxe, R., 2006. Uniquely human social cognition. Curr. Opin. Neurobiol. 16, 235–239.
Saxe, R., Powell, L.J., 2006. It's the thought that counts: specific brain regions for one component of theory of mind. Psychol. Sci. 17, 692–699.
Singer, T., 2006. The neuronal basis and ontogeny of empathy and mind reading: review of literature and implications for future research. Neurosci. Biobehav. Rev. 30, 855–863.
Singer, T., Seymour, B., O'Doherty, J., Kaube, H., Dolan, R.J., Frith, C.D., 2004. Empathy for pain involves the affective but not sensory components of pain. Science 303, 1157–1162.
Singer, T., Seymour, B., O'doherty, J.P., Stephan, K.E., Dolan, R.J., Frith, C.D., 2006. Empathic neural responses are modulated by the perceived fairness of others. Nature 439, 466–469.
Small, D.M., Gregory, M.D., Mak, Y.E., Gitelman, D., Mesulam, M.M., Parrish, T., 2003. Dissociation of neural representation of intensity and affective valuation in human gustation. Neuron 39, 701–711.
Stoleru, S., Gregoire, M.C., Gerard, D., Decety, J., Lafarge, E., Cinotti, L., Lavenne, F., Le Bars, D., Vernet-Maury, E., Rada, H., Collet, C.,

Mazoyer, B., Forest, M.G., Magnin, F., Spira, A., Comar, D., 1999. Neuroanatomical correlates of visually evoked sexual arousal in human males. Arch. Sex. Behav. 28, 1–21.

Wicker, B., Keysers, C., Plailly, J., Royet, J.P., Gallese, V., Rizzolatti, G., 2003. Both of us disgusted in my insula: the common neural basis of seeing and feeling disgust. Neuron 40, 655–664.

Wild, B., Erb, M., Bartels, M., 2001. Are emotions contagious? Evoked emotions while viewing emotionally expressive faces: quality, quantity, time course and gender differences. Psychiatry Res. 102, 109–124.

Zald, D.H., Hagen, M.C., Pardo, J.V., 2002. Neural correlates of tasting concentrated quinine and sugar solutions. J. Neurophysiol. 87, 1068–1075.