Both of Us Disgusted in *My* Insula: The Common Neural Basis of Seeing and Feeling Disgust

Bruno Wicker,[1] Christian Keysers,[2,3]
Jane Plailly,[4] Jean-Pierre Royet,[4]
Vittorio Gallese,[2] and Giacomo Rizzolatti[2,*]
[1]Institut de Neurosciences Physiologiques
   et Cognitives
CNRS
Chemin Joseph Aiguier
13402 Marseille cedex 20
France
[2]Physiology section
Department for Neuroscience
University of Parma
Via Volturno 39
43100 Parma
Italy
[3]BCN Neuroimaging Center
University Groningen
Antonius Deusinglaan 2
9713 AV Groningen
The Netherlands
[4]Laboratoire de Neurosciences et
   Systèmes Sensoriels
UMR CNRS 5020
Universite Claude-Bernard LYON 1 Gerland
50, Avenue Tony Garnier
69007 Lyon cedex 07
France

Summary

What neural mechanism underlies the capacity to understand the emotions of others? Does this mechanism involve brain areas normally involved in *experiencing* the same emotion? We performed an fMRI study in which participants inhaled odorants producing a strong feeling of disgust. The same participants observed video clips showing the emotional facial expression of disgust. Observing such faces and feeling disgust activated the same sites in the anterior insula and to a lesser extent in the anterior cingulate cortex. Thus, as observing hand actions activates the observer's motor representation of that action, observing an emotion activates the neural representation of that emotion. This finding provides a unifying mechanism for understanding the behaviors of others.

Introduction

In a natural environment, food poisoning is a substantial threat. When an individual sees a conspecific looking disgusted after tasting some food, he or she automatically infers that the food is bad and should not be eaten.

What happens in the observer's brain to keep him or her from eating the potentially damaging food? According to a cognitive account, the processing of the facial expression occurring in the visual cortical areas

*Correspondence: giacomo.rizzolatti@unipr.it

leads to a propositional representation of the inferred state of disgust. This representation then determines our decision not to eat the food. Another interpretation of the phenomenon may be based on a "sensory motor resonance" hypothesis. Observing the facial expression of another person evokes a similar facial motor representation in the observer (see Hess et al., 1999, for a review). This motor representation (Lipps, 1907) and its associated somatosensory consequences (Adolphs et al., 2000; Adolphs, 2001, 2002) might be sufficient to understand the meaning of the other's facial expression. Neither of these hypotheses predicts that the observer shares the emotion of disgust with the observed individual, in that they both—although in different ways—assign a causal role to mechanisms not directly involved in the *experience* of emotions. We will refer to them jointly as "cold hypotheses." A third possibility is that, in order to understand the facial expression of disgust displayed by others, a feeling of disgust must occur also in the observer. This hypothesis predicts that brain areas responsible for experiencing this emotion will become active during the observation of that emotion in others. We will refer to this hypothesis as the "hot hypothesis."

So far, there is only indirect evidence to support the latter hypothesis. A number of investigations show that, among other structures, the insula and the amygdala are activated when subjects are exposed to disgusting odors or tastes (Royet et al., 2003; Small et al., 2003; Zald and Pardo, 2000; Zald et al., 1998a). Independently, a number of functional imaging studies (Phillips et al., 1997, 1998; Sprengelmeyer et al., 1998; Schienle et al., 2002) and electrophysiological investigations (Krolak-Salmon et al., 2003) have suggested that the insula is activated during the observation of disgusted facial expressions. The aim of the present study will be to directly determine whether the same locations in the insula are activated during the experience of disgust and the observation of the facial expression of disgust in others.

To this purpose, we performed an fMRI study composed of four functional runs. In the first and second ("visual runs"), participants passively viewed movies of individuals smelling the contents of a glass (disgusting, pleasant, or neutral) and expressing the facial expressions of the respective emotions. In the third and fourth ("olfactory runs"), the same participants inhaled disgusting or pleasant odorants through a mask placed on their nose and mouth. Our core finding is that the anterior insula is activated both during the observation of disgusted facial expressions and during the emotion of disgust evoked by unpleasant odorants. This result indicates that, for disgust, there is a common substrate for feeling an emotion and perceiving the same emotion in others.

Results

The experiment was carried out on 14 healthy right-handed male subjects. As mentioned in the Introduction, all subjects took part in two visual and two olfactory

Figure 1. Frames from Movies Used in the Visual Runs

The demonstrators leaned forward to sniff at the content of a glass (top two rows) and then retracted the torso and expressed a facial expression of disgust (left) pleasure (center) or neutral (right column). Each movie lasted 3 s. Six different demonstrators (three are shown here) expressed the three types of facial expressions, leading to six variants of each expression. A vision-of-disgust block, for instance, was then composed of the six variants of the disgusted emotion separated by 1 s pauses.

functional acquisition sessions. Visual runs contained three experimental conditions: "observation of disgust," "observation of pleasure," and "neutral." Each condition was composed of blocks of six movies showing individuals leaning forward to smell the content of a glass. Depending on the condition, the glass contained an unpleasant, pleasant, or neutral odorant, and the individuals in the movie reacted accordingly with a disgusted, pleased, or neutral facial expression (see Figure 1). Movies were used instead of static facial expressions for three reasons. First, under ecological conditions, facial expressions are intrinsically dynamic stimuli. Second, emotions are recognized better from movies compared to static displays (Wehrle et al., 2000). Third, in a recent neuroimaging study, Kilts et al. (2003) compared the brain activity during the recognition of emotions from static and dynamic displays of facial expressions and concluded that the encoding of facial expressions of emotion by static or dynamic displays is associated with different neural correlates for their decoding.

Olfactory runs were composed of two experimental conditions separated by periods of rest. Conditions were composed of blocks of olfactory stimulation during which subjects were exposed to different disgusting or pleasant odorants ("disgusting odorant" and "pleasant odorant" conditions, respectively). Full details of the procedures are provided in the Experimental Procedures section. The data obtained during the olfactory and visual runs were analyzed separately using random-effect analyses (n = 14 subjects, p < 0.005 uncorrected, and k = 20).

Olfactory Stimulation

The results of the disgusting odorant – rest and pleasant odorant – rest contrasts are reported in Table 1. Among

the activated structures, two are of particular interest for the present study: the amygdala and the insula (Figure 2). Amygdala activations were present with both disgusting and pleasant odorants, with a clear overlap between the two types of activations (Figure 2A). The fact that the amygdala is activated by both pleasant and unpleasant odorants is in accord with previous findings (Gottfried et al., 2002; Hudry et al., 2001; Anderson et al., 2003; Zald, 2003). In contrast, disgusting and pleasant odorants produced clearly separated activation foci in the insula. Disgusting odorants activated the anterior sector of the insula bilaterally, whereas pleasant odorants activated a more posterior site of only the right insula (Figure 2B).

Visual Stimulation

The visual runs were analyzed using two contrasts: observation of disgust – neutral and observation of pleasure – neutral. Both contrasts revealed significant BOLD signal changes in various locations (see Table 2). The insula in particular was only activated in the observation of disgust – neutral contrast. Most importantly, clusters of overlap were found between the observation of disgust – neutral and the disgusting odorant – rest contrasts (Figure 3 and Table 3). These clusters were located in the left anterior insula and in the transition zone between the insula and inferior frontal gyrus. A smaller overlap was also observed in the anterior right cingulate cortex. The amygdalae were not activated by the observation of disgusted facial expressions. This lack of amygdalar activation is in agreement with previous studies suggesting a dissociation between the neural basis of the recognition of fear, in which the amygdala is strongly involved, and that of disgust, in which the amygdala does not appear to play a crucial role (Calder et al., 2001).

To test if the BOLD signal increases in these zones of overlap were selective for disgust, we performed direct comparisons between the disgusting odorants and pleasant odorants conditions and between the observation of disgust and the observation of pleasure conditions within these regions of interest (see Table 3, last two columns). In all cases, responses were stronger to the disgust compared to the pleasure stimuli, be they olfactory or visual (i.e., all t values were positive). For two of the insular clusters, both the visual and olfactory responses were significantly larger for the disgust stimuli (p < 0.05). The third cluster of the insula responded significantly more to the observation of disgust compared to the observation of pleasure but did not significantly discriminate between the two types of odorants. Finally, the cluster located in the anterior cingulate cortex showed significantly stronger activations for the observation of disgust versus observation of pleasure conditions but only showed a nonsignificant trend for disgusting odorants versus pleasant odorants.

To confirm the presence of the overlaps observed between the observation of disgust – neutral and the disgusting odorant – rest contrast t maps, we performed a modified conjunction analysis (p < 0.005, k = 20) between these two contrasts (see Experimental Procedures). The results confirmed the presence of overlaps between these two conditions, showing a cluster [33 voxels with a peak at x = −38, y = 26, z = −6, and a

Table 1. Olfactory Activations

Anatomical Description	Hem.	MNI			TAL			t Value	Size (Voxels)
		x	y	z	x	y	z		
A. Disgusting odorant − rest, random effect, p < 0.005, k = 20, n = 14 s									
Amygdala/uncus	L	−24	−2	−30	−24	−3	−25	6.57	64
Amygdala	R	20	−4	−16	20	−5	−13	5.82	200
Anterior insula/inferior frontal gyrus	R	36	28	−2	36	27	−3	4.89	155
Anterior insula	R	36	10	4	36	10	3	5.78	64
Middle frontal gyrus	L	−44	52	8	44	51	5	4.71	38
Anterior insula	L	−36	22	8	−36	22	6	6.28	149
Inferior frontal gyrus	R	50	26	14	50	26	12	4.82	32
Inferior frontal gyrus	R	46	16	18	46	16	16	6.63	66
Middle frontal gyrus	R	44	36	22	44	36	18	4.59	31
Anterior cingulate	R + L	4	26	26	4	26	23	5.14	69
Precentral sulcus	L	−34	0	36	−34	2	33	7.43	54
Superior parietal lobule	R	36	−70	56	36	−65	55	4.53	25
B. Pleasant odorant – rest, random effect, p < 0.005, k = 20, n = 14 s									
Cerebellum	L	−20	−54	−30	−20	−54	−23	5.23	20
Amygdala/uncus	L	−18	−2	−28	−18	−3	−23	6.51	40
Brain stem	R + L	2	−20	−24	2	−20	−19	5.35	43
Amygdala	R	26	0	−22	26	−1	−18	8.37	327
Inferior frontal gyrus pars orbitalis	R	34	34	−12	34	32	−12	4.84	114
Cerebellum (culmen)	L	−2	−42	−6	−2	−41	−3	5.36	64
Anterior insula	R	38	−2	2	38	−2	2	4.5	48
Anterior tip of caudate	R	26	28	10	26	28	8	9.31	34
Middle frontal gyrus	R	48	42	24	48	42	20	5	80
Middle frontal gyrus	L	−46	34	24	−46	34	20	6.52	183
Precentral sulcus	R	46	8	28	46	9	25	4.77	41
Middle frontal gyrus	R	40	30	30	40	30	26	5.13	43
Rostral inf. parietal lobule	R	44	−62	48	44	−58	47	4.48	58
Superior parietal lobule	R	34	−70	54	34	−65	53	4.83	23

Location in MNI and Talaraich (TAL) coordinates (x, y, z), anatomical description, maximum t value, and number of voxels for all clusters found to be significantly activated during the olfactory contrasts. Activations are shown in ventrodorsal order. The voxel size was $2 \times 2 \times 2$ mm^3.

t(13) = 5.41, p < 0.001] corresponding to the first cluster of Table 3. All the three remaining clusters of Table 3 are significant in this conjunction analysis if k is lowered to the cluster size of these remaining clusters.

Applying the same modified conjunction analysis to the observation of pleasure – neutral and pleasant odorant – rest conditions revealed no significant clusters of overlap. Nor did the conjunction analysis between the nonmatching contrasts, i.e., observation of pleasure – neutral with disgusting odorants – rest or observation of disgust – neutral with pleasant odorants – rest. The lack of overlap between the observation of pleased facial expressions and the olfaction of pleasant odorants is probably due to the fact that, in contrast to the emotion of disgust, which is tightly linked to bad odorants/tastes, the emotion of pleasure can be triggered by many stimuli, only few of which are olfactory or gustatory. There is therefore a strong link between bad tastes/smells, the emotion of disgust, and the facial expression of disgust, while there is a much weaker link between pleasant odors/smells, the emotion of pleasure, and pleased facial expressions.

Discussion

The main finding of the present study is that the observation of disgust automatically activates neural substrates that are selectively activated during the feeling of disgust. This suggests that the understanding of the facial expressions of disgust as displayed by others involves the activation of neural substrates normally activated during the experience of the same emotion. These shared neural substrates are the left anterior insula and the right anterior cingulate cortex.

The Insula

Cytoarchitectonically, the monkey's insula can be divided into three zones (agranular, dysgranular, and granular; Mesulam and Mufson, 1982a). Functionally, however, the insula is formed by two major functional sectors: an anterior sector comprising the agranular and the anterior dysgranular insula and a posterior sector comprising the posterior dysgranular and the granular insula (Mesulam and Mufson, 1982b; Mufson and Mesulam, 1982). The anterior sector is an olfactory and gustatory center that appears to control visceral sensations and the related autonomic responses. Additionally, it receives visual information from the anterior sectors of the ventral bank of the superior temporal cortex, where cells have been found in the monkey to respond to the sight of faces (Bruce et al., 1981; Perrett et al., 1982, 1984, 1985; Keysers et al., 2001). In contrast, the posterior sector of the insula is characterized by connections with auditory, somatosensory, and premotor areas and
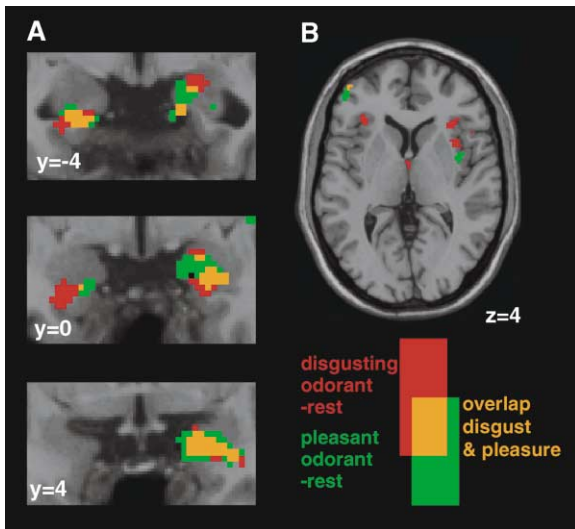
Figure 2. Results of the Olfactory Stimulation

Results of the olfactory stimulation superimposed on the anatomical image of a standard MNI brain using neurological conventions (right is right). (A) Coronal sections focusing on the amygdalae. Note the large degree of overlap (orange) between the activations determined by disgusting (red) and pleasant odorants (green) in the right amygdala and left parahippocampal cortex. (B) Axial slice showing the response to odorants in the insula. The activity is bilateral and anterior for the disgusting odorants and is confined to a more posterior location of the right insula for the pleasant odorants. There is no overlap in the insula between the activations determined by the two odorants. The color coding is indicated on the bottom right.

is not related to the olfactory or gustatory modalities. A direct comparison between the macaque monkey's insula and the human one showed that, although the human insula is substantially larger than the macaque's counterpart, the general architectonic organization is strikingly similar in the two species and shows the same subdivisions (Mesulam and Mufson, 1982a).

The activations observed during the disgusting odorant condition of our experiment fall within the anterior half of both insulae, most likely corresponding to the anterior sectors of Mesulam and Mufson (1982a, 1982b). No activations were found in the posterior sectors. An activation of the same anterior sector, but restricted to the left insula, was found during the observation of the disgusted facial expression, a finding in agreement with the higher-order visual information reaching the insula from the superior temporal sulcus. Most interestingly, there was a clear overlap between both activations. This is, to our knowledge, the first direct neuroimaging demonstration that the same sites in the insula mediate both the observation and the feeling of disgust.

The activation of the anterior insula during disgusting olfactory stimulation found in the present experiment is in accord with previous neuroimaging findings showing its activation during olfactory stimulation. These studies indicate that the transition zone between the anterior insula and the frontal operculum located in the left hemisphere was preferentially activated for unpleasant compared to pleasant odors (Zald and Pardo, 2000; Royet et al., 2003). Indeed, emotional responses to disgusting stimuli are generally reported to be stronger in the left

hemisphere (Zald and Pardo, 1997, 2000; Zald et al., 1998b; Royet et al., 2000, 2001, 2003; Gottfried et al., 2002; Anderson et al., 2003; Zald, 2003). Investigations using gustatory stimuli confirm this finding, showing that the left anterior insula/opercular region responded preferentially to unpleasant compared to pleasant tastes (Zald et al., 1998a; Small et al., 2003).

While unpleasant tastes and smells are often perceived as more intense than their pleasant counterparts, recently, Small et al. (2003) showed that the left anterior insula preference for unpleasant tastes is maintained even if these unpleasant tastes are perceived as less intense than the pleasant tastes they are compared against. The cluster showing this property included the coordinates at which we found the overlap between the observation of disgust and the disgusting odorants.

Finally, Yaxley et al. (1990) and Scott et al. (1991) report the existence of single neurones in the macaque anterior insula and opercular frontal cortex responding selectively to particular gustatory stimuli (see also Augustine, 1996, and Dolan, 2002, for reviews). None of these studies, however, addressed the issue of whether the same area was also activated during the observation of facial expressions of disgust. Taken together the anatomical and functional data indicate that the left anterior insula and neighboring opercular frontal cortex are structures strongly involved in the sensation of disgusting stimuli.

The insula, however, is not only a center for elaborating olfactory and gustatory stimuli. Electrical stimulation of the anterior sector of the insula conducted during neurosurgery (Penfield and Faulk, 1955) evoked nausea or the sensation of being sick ("Feeling as if she were going to be sick," Penfield and Faulk [1955], p. 451). It also evoked visceromotor activity ("My stomach went up and down like when you vomit," ibidem, p. 451). More recently, Krolak-Salmon and colleagues (2003) showed that electrically stimulating the anterior insula through implanted depth electrodes produced sensations in the throat and mouth that were "difficult to stand." Taken together, these findings demonstrate a role for the anterior insula in transforming unpleasant sensory input into visceromotor reactions and the accompanying feeling of disgust.

Here we show that the *same* visceromotor region, related to such an evolutionary ancient basic emotion as disgust, can be directly activated by the observation of the facial expression of disgust displayed by others. This finding is in agreement with previous experiments showing that the vision of disgusted static facial expressions leads to activations in the anterior insula (Phillips et al., 1997, 1998; Sprengelmeyer et al., 1998; Schienle et al., 2002; Krolak-Salmon et al., 2003). None of these studies, though, evoked the sensation of disgust in the participants to investigate if the activated locations are common to both the experience of disgust and the perception of the same emotion in others.

Carr et al. (2003) showed an activation of the anterior insula/inferior frontal gyrus during both the observation and imitation of facial expressions. In their block design, each block contained examples of all six basic emotions in random order: happy, sad, angry, surprised, afraid, and disgusted. It is important to stress that imitation usually does not require experiencing the imitated emo-

Table 2. Visual Activations

Anatomical Description	Hem.	MNI x	y	z	TAL x	y	z	t Value	Size (Voxels)
A. Observation of disgust – neutral, random effect, p < 0.005, k = 20, n = 14 s									
Fusiform gyrus/declive	L	−30	−74	−20	−30	−73	−13	5.37	82
Middle occipital	R	44	−70	−14	44	−68	−8	5.23	107
Brain stem	L	−4	−26	−10	−4	−26	−7	5.77	46
Inferior frontal gyrus	L	−38	26	−6	−38	25	−6	5.41	103
Pulvinar/lentiform nucleus	R	22	12	0	22	12	−1	5.2	39
Anterior insula/inferior frontal gyrus	L	−24	30	4	−24	29	2	4.03	67
Superior temporal sulcus	R	62	−44	8	61	−42	9	4.48	43
Anterior insula	L	−24	8	12	−24	8	11	4.59	30
Precentral gyrus	R	64	12	14	63	12	12	5.11	29
Dorsal bank of the silvian fisure	L	−50	−14	18	−50	−13	17	6.13	60
Middle frontal gyrus	L	−36	56	24	−36	55	19	5.33	23
Supramarginal gyrus	R	40	−50	28	40	−47	28	4.71	30
Cingulate gyrus	R	4	24	30	4	25	26	5.59	20
Middle frontal	R	54	8	40	53	10	36	5.07	51
Cingulate/medial frontal gyrus	L	−4	12	48	−4	14	44	4.22	36
Postcentral gyrus	L	−52	−20	52	−51	−17	49	6.63	33
Superior/medial frontal gyrus	R	8	12	52	8	14	47	6.12	101
B. Observation of pleasure – neutral, random effect, p < 0.005, k = 20, n = 14 s									
Cerebellum (declive)	L	−2	−64	−24	−2	−63	−17	5.90	26
Parahippocampal gyrus	L	−16	−10	−22	−16	−11	−18	4.10	38
Fusiform gyrus	R	40	−74	−20	40	−73	−13	3.73	34
Precentral gyrus	L	−50	−12	10	−50	−11	10	4.68	28
Inferior frontal gyrus	R	48	24	18	48	24	15	4.81	46
Precuneus	R	6	−70	44	6	−66	44	4.40	34

Location in MNI and Talaraich (TAL) coordinates (x, y, z), anatomical description, maximum t value, and number of voxels for all clusters found to be significantly activates during the visual contrasts. Activations are shown in ventrodorsal order. The voxel size was $2 \times 2 \times 2$ mm^3

tion. Their data, therefore, indicate that the insula is involved in imitation but *not* that it is directly involved in the experience of emotions. However, in the light of our findings, it is possible that, during imitation, some of their participants felt the imitated emotion—as actors do when using the "Stanislavsky" method of emotion induction (Stanislavsky, 1936). The relatively low statistical significance of the activation in the insula reported by Carr et al. (2003) during the observation of emotions (t = 3.02) is probably a consequence of their experimental design: they used blocks of mixed emotions, while we show the anterior insula to respond to disgusted but not to happy dynamic facial expressions.

The fact that the feeling of disgust and the perception of that emotion in others share a common neural substrate confirms previous neuropsychological studies (Calder et al., 2000, and Adolphs et al., 2003). After lesions affecting the insulae and neighboring structures, two patients were selectively impaired in recognizing the facial expression of disgust as compared to other facial expressions and reported having reduced sensations of disgust themselves. In those patients, the le-

Table 3. Overlap between Observing and Feeling Disgust

Anatomical Description	Hem	MNI x	y	z	TAL x	y	z	t Value Vis.	Olf.	Size (vox.)	Direct Comparisons Disg. – pleas. odorants	Observ. of disgust – pleasure
Anterior insula/inferior frontal gyrus	L	−38	26	−6	−38	25	−6	5.41	4.07	25	**t(13) = 2.44, p = 0.01**	**t(13) = 2, p = 0.03**
Anterior insula/inferior frontal gyrus	L	−34	28	6	−34	27	4	3.92	4.00	12	t(13) = 0.02, p = 0.49	t(13) = 1.64, p = 0.06
Anterior insula	L	−34	10	16	−34	10	14	3.55	4.22	2	**t(13) = 2, p = 0.03**	**t(13) = 2.52, p = 0.01**
Anterior cingulate cortex	R	4	24	30	4	25	26	5.59	4.43	6	t(13) = 1.29, p = 0.11	**t(13) = 3.63, p = 0.002**

Location in MNI and Talairach space and size of the clusters common to both the disgusting odorants – rest and the observation of disgust – neutral contrasts together with the anatomical description of their location. The maximal t score observed in the clusters of overlap is shown separately for the visual and olfactory contrasts. The last two columns show the result of a direct comparison between the BOLD signal evoked by disgusting versus pleasant odorants and between the observation of disgusted versus pleased faces. Results that are significant at p < 0.05 are shown in bold. The probability of finding five or more significant t tests with a p < 0.05 criterion is less than 2×10^{-5} according to a binomial distribution.
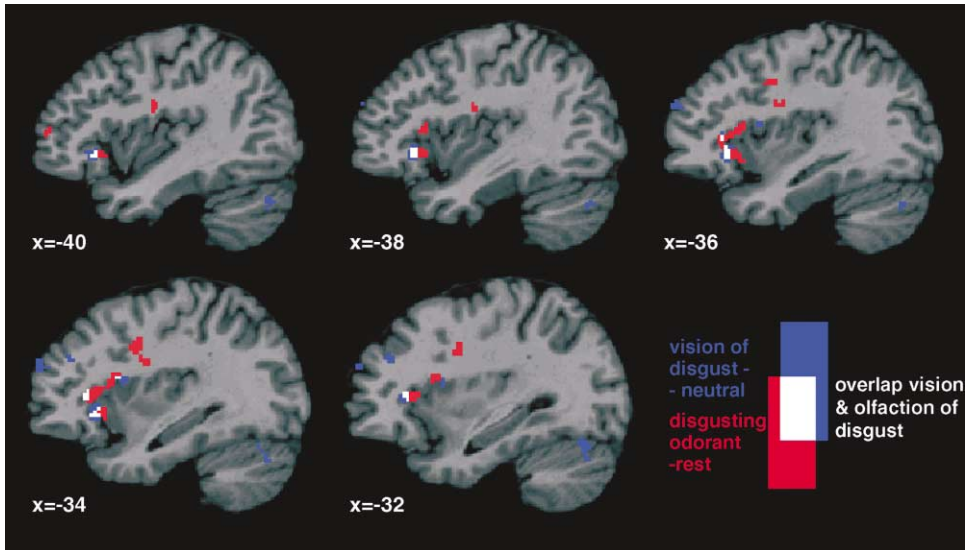
Figure 3. Illustration of the Overlap

Illustration of the overlap (white) between the brain activation during the observation (blue) and the feeling (red) of disgust. The olfactory and visual analysis were performed separately as random-effect analysis. The results are superimposed on parasagittal slices of a standard MNI brain.

sions were not restricted to the insula, but our data suggest that, among the affected structures, the insula was probably responsible for the symptomatology.

The Cingulate Cortex

Anatomically, the cingulate cortex is a very heterogeneous structure formed by a large number of cytoarchitectonic areas. It can be divided along the rostrocaudal axis into a posterior granular and an anterior agranular sector (Brodmann, 1909). Furthermore, it can be divided along the dorsoventral dimension into an old periallocortical area, adjacent to the corpus callosum (Brodmann areas, BA 33), a proisocortical region (BA 24, 25), and a paralimbic region on the upper bank of the cingulate sulcus and in the paracingulate gyrus (BA 32). Our activation is located in the anterior sector of the cingulate cortex and is relatively ventral, thus, most likely falling within the paracingulate gyrus.

The anterior cingulate cortex is considered to be important for the processing of painful stimuli. Single neuron studies in monkeys (Koyama et al., 1998) and humans (Lozano et al., 1995, and Hutchison et al., 1999) show neurons in the anterior cingulate cortex responding to painful stimulation. This finding was confirmed by neuroimaging studies in humans (Talbot et al., 1991; Casey et al., 1996; Vogt et al., 1996; Davis et al., 1997; Peyron et al., 2000, for a review). The anterior cingulate has also been shown to participate in the processing of aversive olfactory and gustatory stimuli (Zald et al., 1998b; Royet et al., 2000).

On the other hand, evidence for the activation of the same structure during the observation of aversive stimuli occurring to others is still very scarce. Only Hutchison et al. (1999) report that a single neuron in the anterior cingulate cortex of a patient responded both when the finger of the patient was pinpricked and when the patient observed the surgeon pinpricking himself. In the ab-

sence of further imaging studies demonstrating the activation of the anterior cingulate during the observation of the facial expressions of others, conclusions about the overlapping activation found in our study can only be tentative. In the light of the study of Hutchison et al. (1999), our data nevertheless suggest that the anterior cingulate might be implicated both in the experience and the observation of aversive stimuli, be they painful or disgusting.

Understanding Others by Matching Felt and Observed Emotions

The idea that we perceive emotions in others by activating the same emotion in ourselves is not new. It has been the explicit content of many theoretical papers and the tentative conclusion of many experimental studies (Phillips et al., 1997; Adolphs, 2002; Goldman and Gallese, 2000; Gallese, 2003; Calder et al., 2000; Carr et al., 2003). In the present study, by using disgusting olfactory stimulation, we evoked what is called "core disgust" (Rozin et al., 2000)—the most primitive and intimate feeling of disgust. The neural substrate of this core disgust overlapped considerably with the neural activation obtained during the passive viewing of another's facial expression of disgust. This finding is in accord with the above-mentioned data of Krolak-Salmon et al. (2003) showing that that the anterior ventral insula is activated by the observation of disgusted facial expressions and that electrical stimulation of the same location causes unpleasant sensations in the throat and mouth. Taken together, these findings demonstrate that observing someone else's facial expression of disgust automatically retrieves a neural representation of disgust. The fact that the anterior insula is necessary for our ability to feel disgust and recognize the same emotion in others is supported by neuropsychological studies (Calder et al., 2000, and Adolphs et al., 2003) showing that lesions

focused on the anterior insula lead to selective deficits in experiencing disgust and recognizing that emotion in others. Thus, the available empirical data strongly support the hot hypothesis of emotion recognition.

Our subjects passively observed the stimuli without any explicit task and without being aware of the aim of the study. This indicates that the anterior insula/inferior frontal gyrus and cingulate cortex activations we observed are the result of an *automatic* sharing, by the observer, of the displayed emotion. In the context of everyday life, this automaticity may explain why it is so hard to refrain from sharing a visceromotor response (e.g., vomiting) of others when observing it in them. It is likely, though, that our understanding of the emotions of others depends on multiple systems associated with different levels of processing of emotional stimuli. The "hot" activation we found in the present experiment is likely to be the evolutionary oldest form of emotion understanding. This "primitive" mechanism may protect monkeys and young infants from the food poisoning described in the Introduction, even before the evolution/development of sophisticated cognitive skills. In humans, cognitive routes toward the understanding of emotions are then probably added (see Frith and Frith, 1999). Thus, the hot hypothesis and the cold hypotheses we mentioned earlier should be seen as complementary. One may speculate, however, that a disturbance of this primitive mechanism might have important implications for social interactions.

The mirror-neuron matching system found in monkeys and humans shows that our internal representation of actions is triggered during the observation or listening of someone else's actions (Gallese et al., 1996; Rizzolatti et al., 1996; Kohler et al., 2002; see Rizzolatti et al., 2001, for a review). The present findings demonstrate that a similar mechanism may apply to emotions: seeing someone else's facial emotional expressions triggers the neural activity typical of our own experience of the same emotion—even when, as in our experiment, participants are not explicitly instructed to empathize with the actors they saw.

In conclusion, the present results suggest that there is a common mechanism for understanding the emotion in others and feeling the same emotions in ourselves. Furthermore, and most importantly, these findings suggest that a similar mechanism allows us to understand both the actions and the emotions of others, therefore providing a unifying perspective on the neural mechanisms underlying our capacity to understand the behavior of others.

Experimental Procedures

Subjects
Fourteen healthy right-handed male volunteers (20–27 years of age) screened for neurological and psychiatric antecedents participated in the experiment. Handedness was assessed by means of the Edinburgh questionnaire (Oldfield, 1971). All subjects had normal olfaction and a mean duration of breath cycle ranging from 3 to 6 s. The subjects participating in the study provided informed written consent, and the experiment was approved by the local ethics committee and conducted according to French regulations on biomedical experiments on healthy volunteers. Subjects were not informed about the aim of the study before the experiment but were informed after the study.

Experimental Design
The study was conducted as a block design, with four functional data acquisition runs: two visual runs followed by two olfactory runs.

Visual Runs
Visual runs followed a 24 s ON/3 s OFF block design, with three conditions: observation of neutral, disgusted, and pleased facial emotional expression (see Figure 1). Each block was repeated three times in each run and was composed of 3 s movies showing an actor leaning forward (∼1 s) to smell the content of a glass. The actor then leaned back slowly with either a neutral (neutral), pleased (pleasure), or disgusted (disgust) facial expression (∼2 s) (see Figure 1). Actors were recruited from a theater school in Marseille. The glass in front of them contained either pure water (neutral) or water with an added disgusting or pleasant odorant. This odorant was the content of "stinking balls" taken at the local toy store for the disgust and perfume for the pleasure condition. They were asked to display the emotion in a natural but clear way. Each emotion was filmed three times for each actor, and the most natural example was selected by one of the experimenters. Each block contained six movies of the same condition showing six different actors separated by a 1 s pause of black screen. Two consecutive blocks were separated by a 3 s pause of black screen. The order of the blocks was pseudorandomized and mirror imaged between the first and second run. The order of the two runs was inverted from subject to subject.

Olfactory Runs
Olfactory runs followed a 12 s ON/24 s OFF blocked design, with two experimental conditions: pleasant odorants (P) and disgusting odorants (D). Each run contained eight blocks of each experimental condition, separated by rest (R). In each run, the order of presentation of P and D conditions was pseudorandomized but identical for all subjects. The order of both runs was counterbalanced between subjects. Subjects were instructed to breathe regularly and to focus their attention on the odorants. They had their eyes and mouth closed throughout the runs. Since the mean duration of a breath cycle was from 3 to 5 s, two to four odorous stimulations were performed during an ON block. *Olfactory stimulation*: Odors were presented with an airflow olfactometer, which allowed synchronization of stimulation with breathing. The stimulation equipment was essentially the one used in a previous PET study (Royet et al., 1999, 2001), but adapted so as to avoid interference with the static magnetic field of the scanner (Royet et al., 2003). Briefly, compressed air (10 l/min) was pumped into the olfactometer and delivered continuously through a commercially available anesthesia mask. This masked was put in place before the beginning of the experiment and was therefore on the subjects face even during the visual runs. At the beginning of each inspiration, odors were injected into the olfactometer, which carried it to the subject's anesthesia mask. Breathing was recorded with the aid of a PVC foot bellows (Herga Electric Ltd, Suffolk, UK) held on the stomach with a judo belt. An operator monitored breathing and squeezed the odor bottle so as to flush the odor into the injection head during inspiration. *Odorous stimuli:* Twenty odorants were used for both olfactory functional runs. They were split into two sets of ten odorants as a function of perceived hedonicity and intensity ratings (Table 4) from data obtained in previous work (Royet et al., 1999). For the pleasant condition, ten odorants were selected so as to provide the highest hedonicity scores. For the unpleasant condition, ten odorants were selected for their particularly low hedonicity scores. To avoid an intensity effect, the mean intensity scores between the two conditions were kept as similar as possible [$F_{(1,18)} = 5.3$, $p > 0.03$], but as reported previously, odors selected to be the most unpleasant are generally perceived as more intense and more likely to evoke a stronger emotional reaction than the odors selected to be the most pleasant (Royet et al., 2003). The hedonicity scores indeed deviated more from neutral (i.e., 5) for the disgusting compared to the pleasant odorants. Accordingly, all our subjects described having felt strong disgust in reaction to the disgusting odorants but often reported that the pleasant odorants, while clearly perceived, were not as pleasant as the disgusting odorants were disgusting. Before scanning, subjects were trained not to move their heads or facial musculature during odorous stimulation. Despite strong

Table 4. List of Odorants Selected for Pleasant and Disgusting Conditions during Olfactory Runs

	Pleasant	Disgusting
1	passion fruit	valeraldehyde
2	lavender	ethyl-mercaptan[a]
3	apricot	hexane
4	anise	butyric acid
5	pear	tetrahydrothiophene[a]
6	caramel	ethyl-diglycol
7	coconut	isovaleric acid[a]
8	wild strawberry	furfuryl mercaptan
9	mint	onion
10	banana	iso amylphenyl acetate
Hedonicity		
Mean score (SD)	6.39 (0.55)	1.16 (0.45)
Score range	5.58–7.24	0.55–1.93
Intensity		
Mean score (SD)	5.91 (0.68)	6.88 (1.13)
Score range	4.69–6.62	4.95–8.25

[a] Odorant with high potency and of which the concentration was limited to 1%.

unpleasant and possible trigeminal sensations, the results from the realignment procedures confirm that the subjects did not move their heads in reaction to the odorants. Odorants were presented in white polyethylene squeeze bottles (100 ml) provided with a dropper (Osi, France). They were diluted in mineral oil so that 5 ml of odorous solution (10%) were prepared and adsorbed by compressed filaments of polypropylene. The concentration of the products with very high potency was limited to 1%.

fMRI Acquisition
Images were acquired using a 3T whole-body imager MEDSPEC 30/80 AVANCE (Brucker, Ettlingen, Germany) equipped with a circular polarized head coil. For each participant, we first acquired a high-resolution structural T1-weighted anatomical image (inversion-recovery sequence, $1 \times 0.75 \times 1.22$ mm) parallel to the bicommissural plane, covering the whole brain. For functional imaging, we used a T2*-weighted echo-planar sequence at 30 interleaved 3.5 mm thick axial slices with 1 mm gap (TR = 3000 ms, TE = 35 ms, flip angle = 80°, FOV = 19.2×19.2 cm, 64×64 matrix of 3×3 mm voxels).

fMRI Data Preprocessing
Data were preprocessed and analyzed using Statistical Parametric Mapping (SPM 99, Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk; Friston et al., 1995a). All functional volumes for each subject were realigned to the first volume acquired. Images were then spatially normalized (Friston et al., 1995b) to the Montreal Neurological Institute (MNI) standard brain and resampled to obtain images with a voxel size of $2 \times 2 \times 2$mm. All volumes were then smoothed with a 6 mm full-width half-maximum isotropic Gaussian kernel. This smoothing is necessary to fulfill the statistical assumptions of the random field analysis.

Random-Effect Statistical Data Analysis
Preprocessed data were analyzed subject-by-subject using the standard General Linear Model (GLM) approach of SPM99 with box-car predictors. Four t contrast maps were calculated: disgusting odorants – rest, pleasant odorants – rest, observation of disgust – neutral, and observation of pleasure – neutral, where "–neutral" refers to the observation of neutral facial expressions. Random-effects analyses were applied to extrapolate statistical inferences into the healthy population. This two-stage analysis (second-order analysis) accounted first for intrasubject (scan-to-scan) variance and second for between-subject variance. At the group level, a voxel-by-voxel single sample t test was then performed to test if the

contrast significantly differed from zero. Clusters were considered significant only if they were composed of at least 20 contiguous voxels, each of which having a p < 0.005 (uncorrected). Overlaps between different contrasts were obtained by transforming the filtered statistic three-dimensional maps into true-false maps of significant and nonsignificant voxels. Voxels were considered to be part of an "overlap" when they had a "true" value in both contrasts. Since we were considering results from a random-effect analysis (second-order analysis) a reliable estimate of the type I error of finding voxels of overlap is not currently available.

Direct Comparisons
Once we determined clusters activated both by disgusting odorants and by the observation of disgusted facial expressions, we tested within these clusters if the activation caused by disgust stimuli (be they odorants or facial expressions) was significantly larger than that determined by pleasure stimuli. Using the toolbox MarsBar (http://marsbar.sourceforge.net; M. Brett, J.-L. Anton, R. Valabregue, and J.-B. Poline, 2002, Region of interest analysis using an SPM toolbox, abstract), for each of the four clusters of Table 3 and for each subject, we evaluated the GLM used for the group analysis but considered the mean BOLD signal of the voxels composing each cluster instead of the voxel-by-voxel values used in the group analysis. This method yielded a single time series and a single set of GLM parameters for each cluster and subject. We then calculated the contrast values for disgusting odorants – pleasant odorants and for observation of disgust – observation of pleasure for each subject separately. Finally, we tested if these contrast values had a mean larger than zero using a one-sided t test with df = 13. This analysis was a random-effect analysis for ROI. The last two columns of Table 3 show the results.

Modified Conjunction Analyses
Conjunction analyses between two contrasts A and B have been described as a method to test if both contrasts are different from zero in a particular voxel (Price and Friston, 1997). Due to the implementation of the conjunction analysis in SPM99 (Price and Friston, 1997), the probability reported by such a conjunction analysis can pass a certain statistical threshold despite the fact that one of the contrasts would not be significant if tested alone. To exclude this possibility, we masked the results of the conjunction analysis between A and B (p < 0.005 and k = 20) with the results of the individual t test for the two contrasts A and B at p < 0.01. All these analyses were performed at the second level, i.e., on the contrast images obtained from the single subject analyses, and were therefore random-effect analyses.

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