Disgust and the insula: fMRI responses to pictures of mutilation and contamination

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Received 10 July 2004; accepted 12 August 2004

Although previous functional brain imaging studies have found that the insula responds selectively to facial expressions of disgust, it remains unclear whether the insula responds selectively to disgust-inducing pictures. In this fMRI study, healthy volunteers viewed pictures of contamination, human mutilation, attacks and neutral scenes during scanning, and then rated pictures for the 'basic' emotions. The anterior insula responded to contamination and mutilation but not attacks, while the ventral visual areas responded to attacks and mutilations more strongly than contamination. The above activations were predicted by disgust and arousal ratings respectively. Additionally, mutilations uniquely activated the right superior parietal cortex. These results support selective disgust processing at the insula, and suggest distinct neural responses to contamination and mutilation. *NeuroReport* 15:2347–2351 © 2004 Lippincott Williams & Wilkins.

Key words: Arousal; Disgust; Emotions; Fear; fMRI; Horror; Insula; Visual cortex

INTRODUCTION

Although case reports [1–3] and functional imaging studies using pictures of facial expressions [4,5] suggest that the insula may selectively process disgust, recent studies using affective pictures are in disagreement. An insula response to disgust-inducing pictures was reported in a study of obsessive-compulsive disorder (OCD) patients [6], but two subsequent studies of healthy controls found equal activation of the insula to both disgust- and fear-inducing pictures [7,8]. Recently, we extended the previous OCD study [6] by adding fear-inducing pictures [9], and found greater insula activation for disgust-inducing pictures than fear-inducing pictures in both healthy volunteers and patients with OCD. Noting that the former studies [7,8] used pictures of contamination (e.g. spoiled food and body products) and mutilations (e.g. injuries and corpses) to induce disgust, whereas ours used only pictures of contamination, we designed a study to test separately the effects of these two types of pictures.

Schienle *et al.* suggest that a shared affective pathway is sufficient to explain the insular response to affective pictures [7]. The insula has been associated with a range of functions, including visceral and gustatory processing [10], autonomic regulation [11], and self-generated affective experiences [12]; thus a general affective or disgust-specific role for the insula are both plausible. The current study re-examines these alternatives using 3 T fMRI to compare the neural responses to pictures of contamination, mutilation and threat and to neutral pictures. In addition to performing standard exploratory analysis using statistical activation maps, we examine the neural responses within selected regions of interest (ROIs), and test their correlation with dimensional and categorical affective ratings.

MATERIALS AND METHODS

Subjects: Eight healthy volunteers (four female) aged 20–26 years gave written informed consent in accordance with a protocol approved by the Institutional Review Board at the University of Florida. According to self-report, seven were right-handed, and one was left-handed. The volunteers denied taking any psychiatric medication at the time of the scan and gave no history of psychiatric or neurological disorders.

Stimuli: Pictures were selected from the International Affective Picture System (IAPS) [13] and were divided into four categories: contamination, mutilation, fear and neutral. Contamination pictures depicted of scenes associated with poor hygiene or poisons (e.g. spoiled food, bodily waste, garbage, pollution); mutilation pictures showed human injuries or disease (e.g. murder victims, traffic accidents, tumors, birth defects); fear pictures showed imminent attacks (e.g. humans with guns or knives, dogs, snakes); and neutral pictures depicted various scenes with low arousal and medium pleasure ratings [14] (e.g. landscapes, household tools, non-threatening animals).

Stimulus presentation: The pictures were presented using an Integrated Functional Imaging System (IFIS, MRI Devices, Inc., Waukesha, WI) in synchronization with the start of each scan. Each participant viewed the three emotion categories in separate, randomly ordered runs, in order to avoid fatigue. Each run consisted of six alternating emotional and neutral picture blocks (21 s long), interspersed with 9 s fixation blocks. Each block contained 14 pictures selected randomly (without replacement) from the list for that category, and each picture was presented for one second, followed by 0.5 s of fixation. Participants were instructed to view the pictures passively, keep their eyes open, and to avoid repressing or exaggerating their emotional response.

Paper responses: After scanning, each participant rated 15 randomly chosen pictures on a scale from 1 to 5 (5 being the most intense emotion) for each of the following 'basic' emotions: happiness, sadness, fear, anger, disgust and surprise [15]. Dimensional ratings were taken from the normative set provided with the IAPS [14]. These were ratings from 1 to 9 for pleasure, arousal, and dominance, with 9 indicating the viewer felt most pleasant, most aroused, and most dominant respectively. Finally, each participant completed a 32-item questionnaire designed to indicate their sensitivity to disgust [16].

Image acquisition: MR images were acquired using a 3 T Allegra system (Siemens, Munich, Germany). 3D anatomical images were acquired using a standard MPRAGE sequence with a 240 mm square field of view at 256 × 256 pixel resolution in the axial plane, and 160 slices of 1.0–1.4 mm thickness. Functional data were acquired using gradient echo-planar imaging (EPI) sensitive to blood oxygen level-dependent (BOLD) signal (TR=3000 ms, TE=30 ms, flip angle=90°, FOV=240 mm, matrix=64 × 64). Twenty-four slices were collected in the axial plane with 6 mm thickness and 0 mm gap. Each functional run lasted 3 min 9 s and consisted of 63 volumes, the first two of which were discarded before analysis due to their T1 saturation.

Data analysis: Data were analyzed using BrainVoyager v. 4.9.6 (Brain Innovations, Maastricht, Holland). The functional images from each participant were co-registered with the 3D anatomic images and both were normalized to Talairach space. The resulting 3D functional data then underwent motion correction and linear trend removal.

Voxel-wise statistical activation maps were generated using a general linear model (GLM) in which the predictors were estimated hemodynamic responses to each emotional condition. Contrasts between predictors were used to calculate the relative contribution of each condition to the variance in the BOLD signal. Unless otherwise stated, the statistical threshold was set to $p<0.05$ with Bonferroni correction for multiple comparisons, and the minimum cluster size was 100 mm^3.

Region of interest (ROI) analyses were performed within selected clusters of significantly activated voxels. Within each ROI, the BOLD responses for each condition were visualized using time-locked averaging of the percentage signal change relative to fixation. A GLM was calculated for the mean signal from the ROI, and the modeled amplitude of each predictor (the beta weight) was used to describe the size of the hemodynamic response. Unlike the statistical activation value, which reflects how well the model fits the data, the beta weight describes the BOLD response, which is assumed to be proportional to neural activation [17].

RESULTS

Paper responses: All three emotional conditions were rated as evoking significantly less pleasure, more arousal, and more dominance than neutral according to the mean IAPS scores for each picture set [14] (Table 1). Mutilation was less pleasant than contamination and fear, and contamination was less arousing than fear and mutilation. The fear condition elicited higher fear ratings than the other three conditions and the contamination and mutilation conditions each elicited higher disgust ratings than fear and neutral. (For all the above comparisons $p<0.001$, corrected for multiple comparisons.)

The mean ± s.d. disgust sensitivity score was 13.4 ± 4.0 (males 13.3 ± 3.4, females 13.6 ± 5.2). The mean for American adults is approximately 16 (males 14, females 18) [16].

Functional imaging data: Exploratory statistical activation maps were generated by contrasting each emotional condition with neutral using the GLM. Figure 1 illustrates clusters of activation seen in the anterior insula and occipito-temporal cortex (OTC). See Table 2 for a full list of activated regions.

The anterior insula was activated bilaterally in both the contamination and mutilation conditions. No significant activation was found in the insula for the fear condition at the threshold of $p<0.05$ corrected. The extent of activation in the OTC increased from contamination to fear to mutilation. Activation for mutilation extended into the midline occipital cortex and posterior cingulate and was additionally seen in the thalamus, ventral striatum, superior parietal cortex and several prefrontal regions (Table 2). No significant signal changes were found at the amygdala due to susceptibility artifact.

Comparisons between emotions revealed no unique activation for contamination or fear, but mutilation condition activated the right superior parietal cortex. The contrasts contamination *vs* fear and mutilation *vs* fear each showed activation in the left anterior insula at a threshold of $p<0.0001$ uncorrected, but this did not achieve the stricter threshold of $p<0.05$ corrected. The contrast mutilation *vs* contamination + fear revealed a unique activation of the right superior parietal cortex.

Figure 2 illustrates working ROIs. The insula ROI was derived from the contrast contamination + mutilation *vs* neutral and the OTC ROI from the contrast mutilation + fear *vs* neutral. The left and right ROIs were combined for analysis. The right superior parietal activation above was included.

Time-locked averaging of the BOLD signal across conditions (Fig. 3a–c) showed a phasic response to all picture

Table 1. Affective ratings.

Rating	Contamination	Mutilation	Fear	Neutral
Pleasure	3.2 ± 0.8	1.9 ± 0.6	3.0 ± 0.8	5.6 ± 0.9
Arousal	4.9 ± 0.8	6.3 ± 0.7	6.3 ± 0.9	3.4 ± 1.0
Dominance	4.7 ± 0.6	3.3 ± 0.6	3.3 ± 0.7	6.0 ± 0.6
Happy	1.2 ± 0.7	1.0 ± 0.0	1.0 ± 0.0	1.6 ± 0.9
Sad	1.3 ± 0.6	2.4 ± 1.3	1.3 ± 0.5	1.0 ± 0.0
Fearful	1.4 ± 0.8	1.6 ± 0.9	2.7 ± 1.0	1.1 ± 0.2
Angry	1.1 ± 0.3	1.4 ± 0.6	1.6 ± 1.0	1.0 ± 0.0
Disgusted	2.6 ± 1.0	3.2 ± 1.3	1.5 ± 1.0	1.1 ± 0.2
Excited	1.3 ± 0.5	1.6 ± 0.9	2.0 ± 1.3	1.2 ± 0.4

Pleasure, arousal and dominance ratings are out of nine, and were taken from the IAPS data. The remaining ratings are out of five, and were obtained from subjects in the current study.

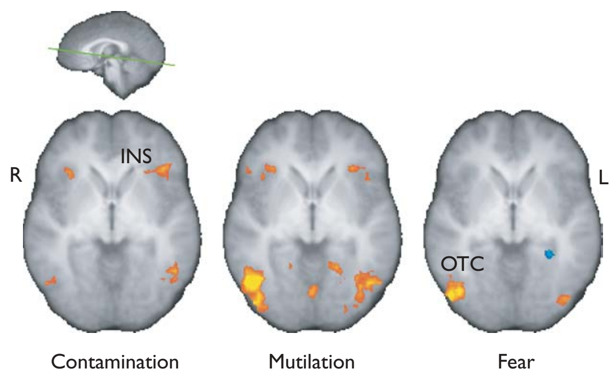

Fig. 1. Statistical activation maps showing contrasts between each emotional condition and neutral. Contamination and mutilation caused activation of the anterior insula (INS). The occipito-temporal cortex (OTC) responded to all three emotional conditions, but comparatively weakly to contamination. Red/yellow: emotion > neutral, blue: neutral > emotion. Green line in inset shows slice angle (8° from ACPC). Threshold: $p < 0.05$, corrected for multiple comparisons, minimum cluster size 100 mm^3.

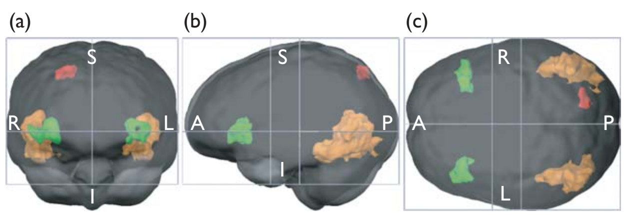

Fig. 2. Glass brain showing ROIs at the insula (green), occipito-temporal cortex (orange) and right superior parietal cortex (red), from the front (**a**), left (**b**) and top (**c**). Talairach co-ordinates (x, y, z, in mm): left insula: −36, 25, 1; right insula: 37, 22, 1; left OTC: −39, −61, −5; right OTC: 44, −61, −5; right superior parietal: 21, −72, 48. The contrasts from which these ROIs were selected are described in Materials and Methods: data analysis. Internal axes denote the anterior and posterior commissures. L = left, R = right, A = anterior, P=posterior, S=superior, I=inferior.

conditions (including neutral) in the OTC that was enhanced in the emotional conditions: the enhancement was smallest for contamination, greater for fear, then greatest for mutilation. At the insula, viewing neutral pictures evoked no change in signal, but contamination and mutilation again caused a phasic increase. Viewing fear pictures caused a small response, although this failed to reach the threshold for statistical significance during the exploratory analysis (Fig. 1). Signal in the right superior parietal cortex increased in response to mutilation pictures, but was indistinguishable from neutral during the other conditions.

The widespread activation for mutilation pictures (Fig. 1) may reflect the high affective arousal ratings for these pictures, particularly the amplitude of the signal increases in the OTC; also, activity in the anterior insula suggested a relationship with the disgust rating. We therefore tested the correlations between picture ratings and BOLD signal change, represented by beta weight. Since the experimental design did not include comprehensive picture ratings for each subject, the ratings were pooled across subjects. Arousal rating predicted signal change in the OTC (r^2=0.98, $p < 0.05$) and disgust rating marginally predicted signal change in the anterior insula (r^2=0.85, p=0.08; Fig. 3d,e). The complementary correlations were not significant: disgust rating and occipito-temporal signal change: r^2=0.61, p=0.22; arousal rating and insula signal change: r^2=0.28, p=0.47. Occipito-temporal signal change was also predicted by ratings for happiness, pleasure and dominance, but these were each correlated with the arousal rating (respectively, r^2=0.97, 0.85 and 0.999, $p < 0.05$, p=0.08 and p=0.0005), suggesting that these ratings are confounded with a common factor. The disgust rating did not correlate significantly with any other ratings. Each subject's disgust sensitivity score was compared with that individual's signal change in the OTC and insula for each emotional condition, but no significant correlations were found.

DISCUSSION

This study investigated the neural responses to two potentially different types of disgust. Contrary to two previous studies comparing disgust- and fear-inducing pictures [7,8], we found that disgust significantly activated the insula while fear did not. We also found distinct neural responses to viewing pictures of contamination and mutilation. Specifically, viewing pictures of mutilation caused greater activation of the OTC, and unique activation of the right superior parietal cortex. The most compelling evidence for a specific response to disgust in the insula is found in the correlations between disgust rating and insula response, and arousal rating and occipito-temporal response (Fig. 3d,e). These suggest a double dissociation between the insula, processing information related to disgust, and the OTC, processing general affective arousal. These findings are compatible with the existence of a common affective pathway, but suggest that this simple model is insufficient to explain activity at the insula.

Since the insula responded to both mutilation and contamination, the data presented here are insufficient to explain the absence in two previous studies [7,8] of a specific insular response to disgust in terms of the effect of combining pictures of contamination and mutilation. It is possible that our small (and statistically non-significant) insula response to fear was because our pictures evoked less fear than those of the other two studies, but the fear ratings for our fear picture set (2.7 out of 5, equivalent to 4.8 out of 9) are close to those of Schienle *et al.* and Stark *et al.* (5.5 and 4.8 out of 9, respectively). If we are to accept the interpretation that activity in the insula reflects a shared affective system, then our study should have shown greater activity in the insula to fear than to contamination, since the fear pictures were rated as more arousing and less pleasant. One possible explanation is that 1.5 T MRI is not sufficiently sensitive to BOLD effects to detect the relatively small differences between the fear and disgust responses at the insula that are detectable at 3 T.

The unique activation of the right superior parietal cortex by mutilation pictures is an interesting new finding that should be further explored by future studies. A previous case study proposed a parietal pathway for processing acted-out emotions [3]. This pathway may be more responsive to mutilation pictures if the viewer processes them by mentally re-enacting the bodily condition of the victim in the picture. This view is further supported by studies locating mirror neurons for bodily actions in the parietal cortex [18]. An interesting question for further

Table 2. Clusters of significant activation.

Region	Side	BA	Size	x	y	z	t (478)
Fear > neutral							
OTC	R	37	4314	46	−62	−4	8.72
OTC	L	37	2855	−42	−64	−3	7.96
Parahippocampal gyrus*	L	36	219	−26	−39	−3	−6.58
Contamination > neutral							
Insula	R	13	571	31	20	2	6.56
Insula/frontal operculum	L	13, 47	1650	−38	27	0	7.69
Middle frontal gyrus	R	46	119	44	17	23	6.18
OTC	L	37	1909	−45	−55	−8	7.36
OTC	R	37	554	45	−49	−10	6.7
Mutilation > neutral							
Cerebellum			136	1	−72	−24	6.18
Insula	L	13	526	−33	22	1	6.5
Insula/frontal operculum	R	13, 47	1614	39	22	−1	7.38
Medial frontal gyrus	R	8	248	5	40	36	6.6
Middle frontal gyrus*	R	10/46	134	33	46	13	−6.07
Midline occipital		17–19, 29–31	6818	0	−67	9	8.19
OTC	L	37	8419	−38	−61	−10	9.96
OTC	R	37	14555	42	−60	−7	11.31
Parahippocampal gyrus	R	36	290	19	−52	0	6.09
Parahippocampal gyrus	L	36	844	−19	−52	−3	7.44
Precentral gyrus	R	6	481	45	−3	35	6.29
Superior frontal gyrus†		9	2165	−4	57	30	8.72
Superior frontal gyrus	L	8	144	−11	24	57	6.54
Cuneus	L	19	279	−8	−89	33	6.35
Cuneus and precuneus	R	19	8924	25	−69	39	9.6
Cuneus and precuneus	L	19	1132	−23	−76	32	6.36
Intra-parietal sulcus	L	7	151	−30	−55	38	6.12
Thalamus	L		109	−6	−15	13	5.93
Ventral striatum	R		108	21	0	−4	6.64

Only clusters > 100 voxels shown. BA=Brodmann's Area. Size=number of 1 mm^3 voxels. x, y and z refer to Talairach co-ordinates. OTC=occipito-temporal cortex.
*Decrease relative to neutral.
†This cluster may not reflect neural activity because it is partly outside the brain and its shape corresponds to the anterior sagittal sinus.

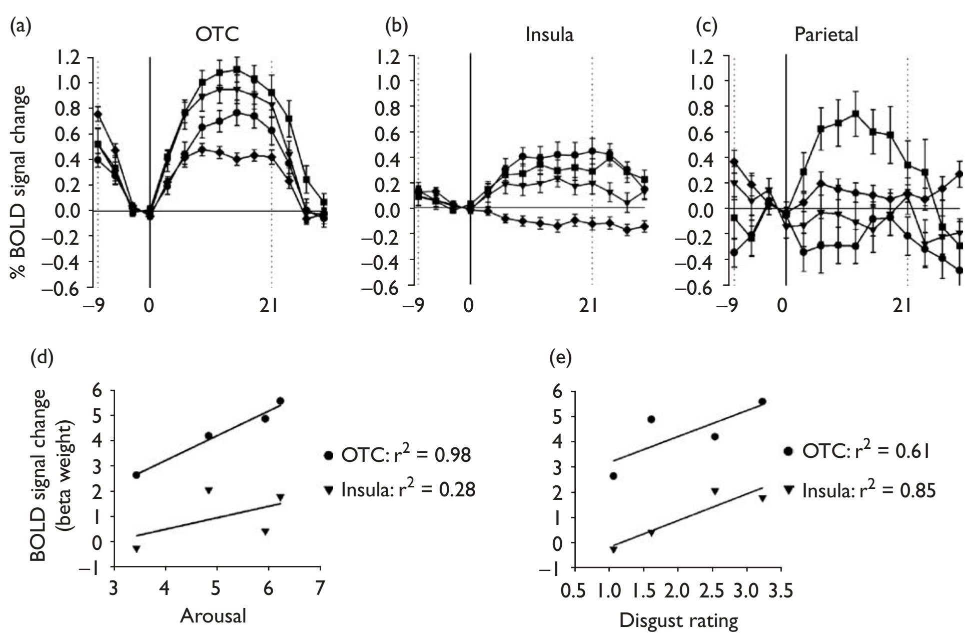

Fig. 3. (**a–c**) Time-locked averaged BOLD responses at the OTC (a), insula (b) and right superior parietal cortex (c). (a) There is a visual response to all conditions, but this is enhanced in the emotional conditions. (b) The insula did not respond to neutral pictures, but showed the greatest response to contamination pictures. The small response to fear pictures did not reach significance in the exploratory analysis (Fig. 1). (c) The superior parietal ROI responded only to mutilation pictures. ● =contamination, ■=mutilation, ▼=fear, ◆=neutral. Solid vertical lines indicate start of picture block, dotted vertical lines indicate start of fixation block, with values in seconds. (**d**,**e**) Emotion ratings plotted against modeled BOLD response amplitude (Beta weight). ● =occipito-temporal cortex, ▼=anterior insula. Arousal predicted ventral visual activity (d), whereas disgust predicted activity in the anterior insula (e).

study is whether mutilation pictures evoke a distinct emotion, for example horror. McNally suggested that horror is a blend of disgust and fear, and it is interesting to note that mutilation may be viewed for pleasure in art or entertainment [19].

We recognize several limitations of this study. Since we were unable to image the amygdala, we had to use occipito-temporal activation as a proxy for the amygdala response. Although in this study, activity in the insula was not correlated with affective arousal, the insula influences autonomic arousal [11], and we cannot rule out the insula's influence on occipito-temporal activity. The affective ratings of our picture sets may be confounded with other features unique to each set, such as the lack of human faces in the contamination set, or the abundance of the color red in the mutilation set. Future studies should use imaging parameters able to image the amygdala, take physiological measures of arousal (such as heart rate and skin conductance) and specifically account for possible confounds during selection of picture sets. (It should be noted that not all studies report confirmation of proper amygdala imaging, and that artifact is common at higher magnetic fields, i.e. 3 T [20]).

CONCLUSION

Our findings suggest that the OTC and the insula process different affective information, as reflected by arousal and disgust ratings respectively. Modulation of occipito-temporal activity by feelings of arousal is well modeled by the concept of a shared affective network processing basic affective dimensions. However, the apparently disgust-specific activity in the insula supports the idea that emotional categories may have distinct neural representations. We also suggest that future studies consider contamination and mutilation pictures separately. Whether mutilation pictures evoke a distinct emotion (perhaps horror) is a question best answered by future research.

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Acknowledgements: Funding for this study was provided by the National Alliance for Schizophrenia and Depression (NARSAD).