

This is a repository copy of *Neural responses to facial and vocal expressions of fear and disgust*.

White Rose Research Online URL for this paper:
<http://eprints.whiterose.ac.uk/1320/>

Article:

Phillips, ML, Young, AW orcid.org/0000-0002-1202-6297, Scott, SK et al. (7 more authors) (1998) Neural responses to facial and vocal expressions of fear and disgust. *Proceedings of the Royal Society B: Biological Sciences*. pp. 1809-1817. ISSN 1471-2954

<https://doi.org/10.1098/rspb.1998.0506>

Reuse

Unless indicated otherwise, fulltext items are protected by copyright with all rights reserved. The copyright exception in section 29 of the Copyright, Designs and Patents Act 1988 allows the making of a single copy solely for the purpose of non-commercial research or private study within the limits of fair dealing. The publisher or other rights-holder may allow further reproduction and re-use of this version - refer to the White Rose Research Online record for this item. Where records identify the publisher as the copyright holder, users can verify any specific terms of use on the publisher's website.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

Neural responses to facial and vocal expressions of fear and disgust

M. L. Phillips^{1*}, A. W. Young², S. K. Scott³, A. J. Calder³, C. Andrew⁴, V. Giampietro⁵, S. C. R. Williams⁴, E. T. Bullmore^{1,5}, M. Brammer⁵ and J. A. Gray⁶

¹*Department of Psychological Medicine, King's College School of Medicine and Dentistry and Institute of Psychiatry, 103 Denmark Hill, London SE5 8AZ, UK*

²*Department of Psychology, University of York, Heslington, York YO1 5DD, UK*

³*Applied Psychology Unit, 15 Chaucer Road, Cambridge CB2 2EF, UK*

⁴*Neuroimaging Unit, ⁵Brain Image Analysis Unit, and ⁶Department of Psychology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, UK*

Neuropsychological studies report more impaired responses to facial expressions of fear than disgust in people with amygdala lesions, and vice versa in people with Huntington's disease. Experiments using functional magnetic resonance imaging (fMRI) have confirmed the role of the amygdala in the response to fearful faces and have implicated the anterior insula in the response to facial expressions of disgust. We used fMRI to extend these studies to the perception of fear and disgust from both facial and vocal expressions. Consistent with neuropsychological findings, both types of fearful stimuli activated the amygdala. Facial expressions of disgust activated the anterior insula and the caudate-putamen; vocal expressions of disgust did not significantly activate either of these regions. All four types of stimuli activated the superior temporal gyrus. Our findings therefore (i) support the differential localization of the neural substrates of fear and disgust; (ii) confirm the involvement of the amygdala in the emotion of fear, whether evoked by facial or vocal expressions; (iii) confirm the involvement of the anterior insula and the striatum in reactions to facial expressions of disgust; and (iv) suggest a possible general role for the perception of emotional expressions for the superior temporal gyrus.

Keywords: fear; disgust; neural substrate; fMRI; facial expression; vocal expression

1. INTRODUCTION

There has been continuing debate over the existence of separate human emotions (Darwin 1872; Cannon 1927; Oatley & Johnson-Laird 1987; Gray 1990; Davidson 1992*b*; Ekman 1992; Lang *et al.* 1992). One theory proposes a small number of basic emotions (including sadness, happiness, anger, surprise, fear and disgust), each characterized by a distinctive facial expression, physiology and evolutionary history (Ekman *et al.* 1972). In support of this theory, neuropsychological studies of patients with lesions to the amygdala (Adolphs *et al.* 1994, 1995; Young *et al.* 1995; Calder *et al.* 1996), and of patients with Huntington's disease, involving damage principally to frontostriatal regions (Sprengelmeyer *et al.* 1996), have demonstrated a double dissociation in that the former show more impaired responses to facial expressions of fear than disgust, and the latter show more impaired responses to expressions of disgust than fear. This dissociation between brain regions subserving responses to facial expressions of fear and disgust has been confirmed in recent experiments using functional magnetic resonance imaging (fMRI). These experiments have shown activation in the amygdala in response to the

facial expression of fear but not disgust (Breiter *et al.* 1996; Morris *et al.* 1996; Whalen *et al.* 1998), whereas facial expressions of disgust evoked particularly strong activation in the anterior insula, perhaps reflecting the role of this structure in the perception of disgusting oral stimuli (Phillips *et al.* 1997).

These studies have relied on the use of visual stimuli, particularly facial expressions, in the examination of the neural substrate underlying perception of different emotions. Few studies have used non-visual stimuli (Imaizumi *et al.* 1997; Scott *et al.* 1997; Zald & Pardo 1997), and there has been no functional imaging study using stimuli from different modalities to investigate the possibility of a modality-independent neural substrate underlying perception of a specific emotion. We therefore aimed to investigate this by examining cerebral blood oxygenation changes induced in six individuals by facial and vocal expressions of fear and disgust.

2. MATERIALS AND METHODS

(a) *Subjects*

Six right-handed, male volunteers (mean age, 37 years (range 25–43 years); mean IQ estimate, 120) participated in four experiments in the same testing session. Exclusion criteria included history of brain injury and past and current psychiatric

*Author for correspondence (spmampl@iop.bpmf.ac.uk).

illness. Informed consent was obtained from the subjects after the nature and possible consequences of the experiments were explained.

(b) *Experimental design*

There were four 5-min experiments in total. Each experiment had a similar design, comprising five cycles of periodic alternation between 30-s epochs of emotional (A) and neutral (B) stimuli. In two experiments, subjects were presented with black-and-white grey-scale images depicting prototypical facial expressions of either fear (experiment 1) or disgust (experiment 2), contrasted with a neutral baseline expression. These stimuli were from a standard series (Ekman & Friesen 1976) depicting prototypical facial expressions of the six basic emotions, fear, disgust, anger, sadness, surprise and happiness, in addition to a neutral expression. These can be computer-transformed to create different intensities of each facial expression (Calder *et al.* 1997). As 100% neutral facial expressions (muscles relaxed) from this series can appear cold and threatening, because of the convention to signal approval in normal social interactions, we used a mildly happy expression (75% neutral, 25% happy) as the neutral baseline (figure 1). During each epoch (A or B), eight different standard faces (identities) from the Ekman–Friesen series displaying an emotional (fear or disgust) or neutral facial expression were each presented for 3 s, with an interstimulus interval of 0.75 s.

In the other two experiments, the subjects heard non-verbal vocal sounds classified as expressing either fear (experiment 3) or disgust (experiment 4), contrasted with sounds classified as mildly happy. Non-verbal vocal sounds displaying the basic emotions above have been used in a previous study investigating perception of emotion from auditory stimuli in a patient with bilateral lesions of the amygdala (Scott *et al.* 1997). These stimuli were recorded from two native English speakers (one male and one female), who were requested to generate a range of non-verbal sounds corresponding to basic emotions, including mild happiness, fear and disgust. The stimuli used in this study comprised the following: a range of different screams for fear, a range of sounds of retching for disgust, and different sounds of laughter and gasping for mild happiness. The vocal expressions were recorded on to digital audiotape (DAT) in a sound-protected environment, and digitized at 22 kHz. These were presented to six judges for categorization. Sounds recognized with 90% or greater accuracy were used in the study. In total, eight different sounds for each emotional expression (fear, disgust and mild happiness) were presented to subjects. During each epoch (A or B), eight different sounds expressing an emotional (fear or disgust) or 'neutral' (mild happiness) sound were each presented for 3 s, with an interstimulus interval of 0.75 s, using software used for the presentation of the facial stimuli.

During presentation of the sounds, and during the inter-stimulus intervals in the two experiments with visual stimuli, the subjects viewed a central white cross on a black background.

The subjects were requested to decide the sex of each face or voice and press one of two buttons accordingly with the right thumb. The subjects were not informed that the purpose of the study was to examine the neural response to emotional stimuli. This sex-decision task has been used in previous studies investigating the neural response to emotional stimuli (Morris *et al.* 1996; Phillips *et al.* 1997) and allows an identical task and response across the four experiments. These studies have shown that the neural response to facial expressions of emotion does



Figure 1. Faces from the standard set of Ekman & Friesen (1976). Examples of faces depicting 100% neutral (a), 100% disgust (b) and 100% fear (c) are demonstrated, along with an example of a stimulus depicting a mildly happy expression (75% neutral and 25% happy) (d) used as the emotionally neutral baseline condition in both experiments using facial stimuli.

not depend on explicit instructions to attend to the emotional content of such stimuli.

The order of presentation of stimuli within each condition, the first presentation (A or B) for each experiment, and the presentation order of all experiments were counterbalanced across the subjects. In order to familiarize the subjects with the stimuli to be used in the subsequent experiments, each subject was presented with similar stimuli before the scanning procedure. To allow for practise with the button box, subjects were presented with practise stimuli (eight 100% neutral facial expressions or eight of the neutral baseline non-verbal sounds) before scanning.

Accuracy of judgement of sex for all visual stimuli was near 100%: for facial expressions of fear versus mildly happy expressions, the mean was 99% (range 95–100%); for facial expressions of disgust versus mildly happy expressions, the mean was 99% (range 98–100%). For vocal expressions of fear and disgust, the mean accuracy of judgement of sex was slightly lower: 85% (range 51–99%) and 73% (range 54–93%), respectively.

(c) *Image acquisition and analysis*

Echoplanar magnetic resonance brain images were acquired using a 1.5 Tesla GE Sigma system (General Electric, Milwaukee, WI) retrofitted with Advanced NMR hardware (ANMR, Woburn, MA) using a standard head coil. One hundred T2*-weighted images depicting BOLD contrast (Ogawa *et al.* 1990) were acquired over 5 min (for each experiment) at each of 14 near-axial, non-contiguous 5 mm-thick planes parallel to the

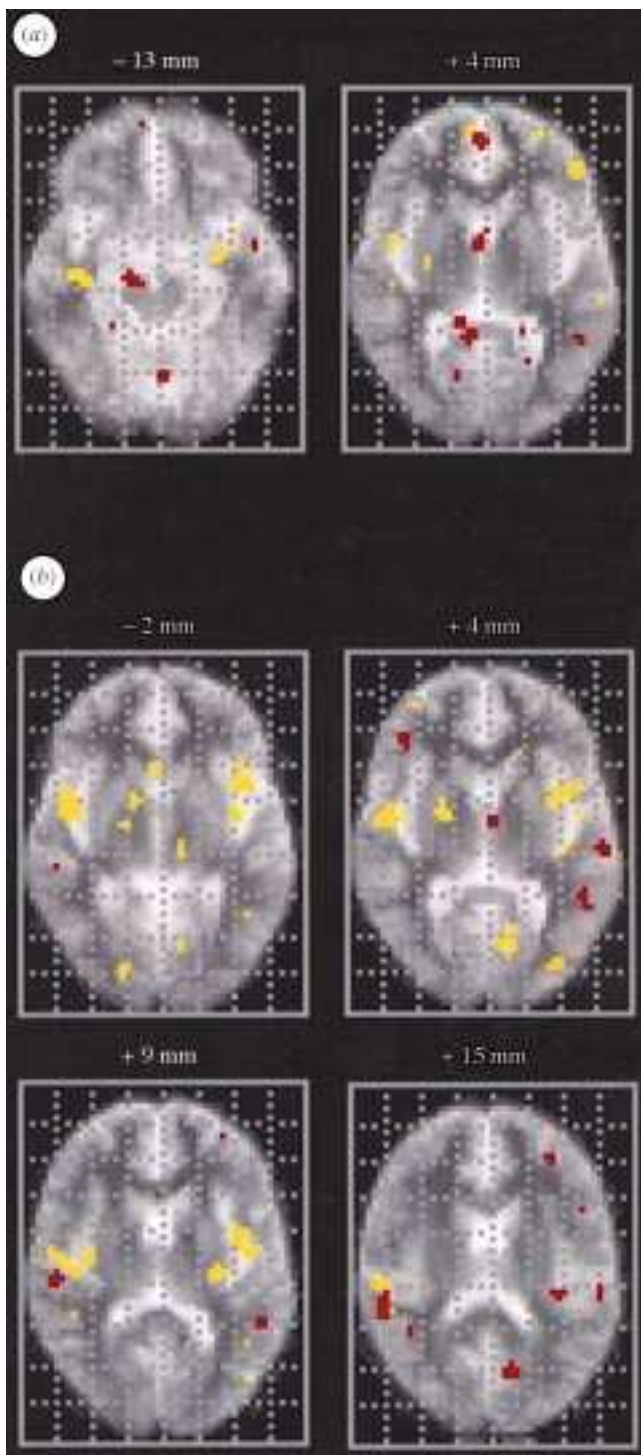


Figure 2. (a) Foci of generic brain activation in six right-handed normal male subjects during perception of facial and vocal expressions of fear. The grey-scale template was obtained by voxel-by-voxel averaging of the individual inversion recovery EPI images of all six subjects, following transformation into Talairach space. The transverse sections are at 13 mm below (left) and 4 mm above (right) the trans-callosal line. The right side of the brain is shown on the left side of each panel, and vice versa. Voxels activated at $p < 0.004$ by perception of visual expressions of fear (yellow) are demonstrated in the left amygdala, right middle temporal gyrus (BA 21) (left), and right medial frontal cortex (BA 10), right middle temporal gyrus (BA 21) and left dorsolateral prefrontal cortex (BA 45) (right). Voxels activated at $p < 0.004$ by perception of vocal expressions of fear (red) are demonstrated in the right amygdala/hippocampus (left), and

intercommissural (AC-PC) line, providing whole-brain coverage: TE, 40 ms; TR, 3 s; in-plane resolution, 3 mm; interslice gap, 0.5 mm. An inversion recovery EPI data set was also acquired at 43 near-axial 3 mm-thick planes parallel to the AC-PC line to facilitate registration of fMRI data sets to the standard stereotactic space of Talairach & Tournoux (1988): TE, 80 ms; TI, 180 ms; TR, 16 s; in-plane resolution, 3 mm; number of signal averages, 8.

The periodic change in T2*-weighted signal intensity at the (fundamental) experimentally determined frequency of alternation between A and B conditions was estimated by pseudo-generalized least-squares fit of a sinusoidal regression model to the movement-corrected fMRI time-series at each voxel. Maps of the squared amplitude of a sinusoidal function at the AB frequency divided by its standard error, the fundamental power quotient (FPQ), were constructed (Bullmore *et al.* 1996). Each observed time-series was randomly permuted ten times, and FPQ estimated as above in each randomized time-series, to generate ten randomized maps of FPQ for each subject in each anatomical plane. To construct generic brain activation maps which robustly identified voxels that showed the significant power of response on average over all subjects under each condition, observed and randomized parametric maps of FPQ estimated in each individual were first transformed into the stereotactic space of Talairach & Tournoux and smoothed by a Gaussian filter with full width at half maximum of 11 mm. The median observed value of FPQ was then computed at each voxel in standard space, and its statistical significance was tested by reference to the null distribution of median FPQ computed from the identically smoothed and spatially transformed randomized maps. For a one-tailed test of size $p = 0.004$, the critical value was the $100 \times (1 - p)$ th percentile of this randomization distribution of median response. Voxels at which the null hypothesis was refuted were coloured and superimposed on a grey-scale template image to form a generic brain-activation map (GBAM) (Brammer *et al.* 1997).

Differences between the neural response to facial expressions of fear and disgust, and between the neural response to vocal expressions of fear and disgust, were tested using two planned comparisons (or contrasts). For the first contrast, the comparison was between the experiment investigating the response to facial

Figure 2 (continued) right medial frontal cortex (BA 32), thalamus and right hippocampus (right). (b) Foci of generic brain activation in six right-handed normal male subjects during perception of facial and vocal expressions of disgust. The transverse sections are at 2 mm below (top left), 4 mm above (top right), 9 mm above (bottom left) and 15 mm above (bottom right) the trans-callosal line. Voxels activated at $p < 0.004$ by perception of facial expressions of disgust (yellow) are demonstrated in the left anterior and mid-insula, right superior temporal gyrus (BA 22), the right caudate nucleus and globus pallidus and right middle occipital cortex (BA 18) (top left), left anterior insula, right superior temporal gyrus (BA 22), right putamen, left middle occipital cortex (BA 18) and inferior posterior temporal gyrus (BA 37) (top right), bilateral insulae and left putamen (bottom left). Voxels activated at $p < 0.004$ by vocal expressions of disgust (red) are demonstrated in the left thalamus, left superior temporal gyrus (BA 22) and right dorsolateral prefrontal cortex (BA 45) (top right), bilateral superior temporal gyri (BA 42 and 22) (bottom left), bilateral superior temporal gyri (BA 42), left rostral prefrontal cortex (BA 32/46), and left posterior cingulate gyrus (BA 23/31) (bottom right).

expressions of fear compared with the neutral baseline faces, and the experiment investigating the response to facial expressions of disgust and the neutral baseline faces. This contrast aimed to identify voxels that were activated in response to facial expressions of fear to a significantly greater degree than to facial expressions of disgust, and vice versa. For the second contrast, the comparison was between the experiment investigating the response to vocal expressions of fear compared with the mildly happy sounds, and the experiment investigating the response to vocal expressions of disgust and the mildly happy sounds. This experiment aimed to identify voxels that were activated to a greater degree in response to vocal expressions of fear compared with disgust, and vice versa.

To estimate the differences between experimental conditions in mean FPQ, we fitted the following repeated-measures analysis of variance (ANOVA) model at each voxel of the observed FPQ maps in standard space: $FPQ_{i,j} = \beta_0 + \beta_j E + e_{i,j}$. Here, $FPQ_{i,j}$ denotes standardized power in the i th individual under the j th experimental design, β_0 is the overall mean FPQ, $\beta_0 + \beta_j$ is the mean FPQ under the j th experimental design, E is a dummy variable coding experimental design, and $e_{i,j}$ is a residual quantity unique to the i th individual. The null hypothesis of zero difference in mean FPQ between experiments was tested by comparing the coefficient β_j to critical values of its non-parametrically ascertained null distribution. To do this, the elements of E were randomly permuted ten times at each voxel, β_j was estimated at each voxel after each permutation, and these estimates were pooled over all intracerebral voxels to sample the permutation distribution of β_j . For a two-tailed test of size $p=0.05$, the critical values were the $100 \times p/2$ and $100 \times (1 - p/2)$ th percentile values of the permutation distribution. Because of the repeated-measures nature of the data, the permutation procedure was constrained so that if the FPQ observed in the i th individual in one experiment was randomly assigned a code of 1 in the permuted variable E , then the FPQ observed in the same individual under the other experimental condition was automatically assigned a code of -1 (Edgington 1980; Bullmore *et al.* 1998). Differences in mean FPQ between conditions were tested for significance only at those voxels which were generically activated by one or both of the conditions considered independently, thereby substantially reducing the search volume or number of tests conducted.

3. RESULTS

Generic activation was demonstrated in the left amygdala for perception of facial expressions of fear, and in the right amygdala–hippocampal region for perception of fearful sounds (figure 2a). Both facial and vocal expressions of fear activated the superior temporal gyrus (Brodmann areas (BA) 22 and 42), inferior posterior temporal gyrus (BA 37), middle temporal gyrus (BA 21), and medial frontal cortex (BA 10 and 32). (See table 1a for details of generic brain-activation foci in response to fearful face expressions, and table 1b for corresponding details of the response to fearful sounds.)

In response to presentation of facial expressions of disgust, we demonstrated activation in the left anterior insula, bilateral putamen, right globus pallidus and right caudate nucleus (striatal structures previously implicated in the response to facial expressions of disgust (Phillips *et al.* 1997)), and superior, middle and inferior posterior temporal gyri (BA 22 and 42, 21, 37, respectively). Vocal

expressions of disgust activated bilateral superior temporal gyri (BA 42 and 22), rostral prefrontal cortex (BA 32/46), dorsolateral prefrontal cortex (BA 45) and thalamus. (figure 2b and table 2a,b).

A one-way repeated-measures analysis of variance with facial emotion (fear and disgust) as the factorial effect of interest revealed significantly greater mean power of response to facial expressions of fear, compared with disgust, in the left dorsolateral prefrontal cortex (BA 45), right hippocampus, left angular gyrus (BA 39), right inferior posterior temporal gyrus (BA 37), right superior temporal gyrus (BA 22/42), right middle temporal gyrus (BA 21), left medial frontal cortex (BA 10/32), right putamen and left amygdala. The following brain regions showed significantly greater mean power of response to facial expressions of disgust compared with fear: left anterior insula, right superior temporal gyrus (BA 42; in a region superior to that for fear versus disgust), bilateral parahippocampal gyri, right putamen (in a region anterior and superior to that for fear versus disgust), left middle occipital cortex (BA 18), and right globus pallidus (search volume = 322 voxels; $p=0.05$; expected number of false positive-activated voxels = 16; observed number of suprathreshold voxels = 100; table 3a,b).

A one-way repeated measures analysis of variance with vocal emotion (fear and disgust) as the factorial effect of interest revealed significantly greater mean power of response to vocal expressions of fear compared with disgust in the right hippocampus, left posterior cingulate gyrus (BA 23/30), right middle occipital cortex (BA 19), right anterior cingulate gyrus (BA 24), right medial frontal cortex (BA 32), right caudate nucleus and right middle temporal gyrus (BA 21). The following brain regions showed significantly greater mean power of response to vocal expressions of disgust compared with fear: left middle occipital cortex (BA 19), left posterior cingulate gyrus (BA 31; in a region superior to that for fear versus disgust), right dorsolateral prefrontal cortex (BA 45), right superior temporal gyrus (BA 22/42) and left thalamus (search volume = 304 voxels; $p=0.05$; expected number of false positive-activated voxels = 15; observed number of suprathreshold voxels = 112; table 4a,b).

4. DISCUSSION

Overall, these findings provide further evidence for the differential localization of the neural substrates underlying perception of visual displays of fear and disgust, and confirm the involvement of the amygdala in the emotion of fear. The amygdala was activated to a significantly greater extent by facial expressions of fear compared with facial expressions of disgust (table 3a), and was also activated by auditory expressions of fear (figure 2a). Furthermore, the right hippocampus was activated to a significantly greater extent by both facial and vocal expressions of fear compared with those of disgust (tables 3a and 4a), which indicates a possible role of the hippocampus in perception of fearful stimuli (Gray 1982). Other studies investigating the neural response to emotional stimuli have used non-facial or non-visual stimuli, including emotive film clips (Lane *et al.* 1997; Paradiso *et al.* 1997), unpleasant (although not specifically

Table 1. (a) Facial expressions of fear and (b) vocal expressions of fear: main generically activated brain regions

region (approximate Brodmann area)	side	x^a	y^a	z^a	number of activated voxels ^b
<i>(a) Facial expressions</i>					
anterior insula/superior temporal gyrus (22)	R	43	6	-2	17
superior temporal gyrus (22)	R	46	-3	4	4
middle temporal gyrus (21)	R	40	-19	-13	9
		58	-31	-2	5
		46	-31	-7	3
dorsolateral prefrontal cortex (45)	L	-43	31	4	7
amygdala	L	-29	-8	-13	6
angular gyrus (39)	L	-40	-61	26	5
inferior posterior temporal gyrus (37)	R	43	-50	-7	5
putamen	R	40	-56	-2	4
medial frontal cortex (10)	R	14	17	-2	3
	R	6	50	4	3
<i>(b) Vocal expressions</i>					
inferior posterior temporal gyrus (37)	R	23	-53	-7	20
caudate nucleus	R/L	0	8	9	13
medial frontal cortex (32)	R	3	44	4	12
middle occipital cortex (19)	L	-17	-50	-2	11
middle temporal gyrus (21)	R	38	-25	-7	11
	L	-40	-17	-7	9
superior temporal gyrus (42)	L	-52	-31	15	10
	R	23	-31	15	8
		35	-25	15	6
hippocampus	R	6	-44	4	10
anterior cingulate gyrus (24)	R	6	25	-2	8
amygdala/hippocampus	R	12	-19	-13	7
thalamus	R	3	-3	4	6
		6	-31	15	4

^aTalairach coordinates refer to the voxel with the maximum FPQ (fundamental power quotient) in each regional cluster.

^bAll activated voxels were identified by a one-tailed test of the null hypothesis that median FPQ is not determined by experimental design. The probability threshold for activation was $p \leq 0.004$.

disgusting) odours (Zald & Pardo 1997) and spoken words (Imaizumi *et al.* 1997), but have not aimed to compare the neural response to emotional stimuli presented in two different sensory modalities.

The results also confirm the importance of the anterior insula, and the caudate nucleus and putamen, in the perception of facial expressions of disgust (figure 2*b*); the involvement of the latter is expected from the neuropsychological findings in Huntington's disease (Sprenghelmeyer *et al.* 1996). The anterior insula in particular was activated to a significantly greater extent by facial expressions of disgust compared with fear (table 3*b*), confirming the findings of a previous study (Phillips *et al.* 1997). Neither the anterior insula nor striatum, however, was significantly activated by auditory stimuli expressing the emotion of disgust (sounds of retching, etc.). Further studies with different

materials will be needed to determine whether there is no supramodal neural response to disgust; all we can do at present is to note that (in contrast to our results for fear), we did not find such a region for disgust even though the facial expressions were derived from a well-validated set and the sounds we used could be readily identified by control subjects. The anterior insula has an important role in feeding-related functions, including taste processing and vomiting; the insular cortex is also implicated in the receptive aspects of language perception (Augustine 1996). Activation of the anterior insula specifically in response to facial expressions of disgust may therefore reflect the role of this structure in perception of oral gestures, in particular those related to expulsion or spitting out of unpleasant substances. Future research investigating the neural response to facial displays of disgust and aversive gustatory stimuli within

Table 2. (a) *Facial expressions of disgust and (b) vocal expressions of disgust: main generically activated brain regions*

region (approximate Brodmann area)	side	x^a	y^a	z^a	number of activated voxels ^b
<i>(a) Facial expressions</i>					
middle temporal gyrus (21)	R	43	0	-13	19
superior temporal gyrus (22)	R	46	3	-2	17
anterior mid-insula	R	49	-6	4	14
	L	35	-11	9	16
		-38	-3	9	16
		-38	6	4	14
		-40	6	-2	14
		-35	-3	-2	5
middle occipital cortex (18)	L	-9	-67	4	10
	R	20	-81	-2	4
putamen	R	23	-6	4	7
	L	-26	-19	9	7
hippocampus/amygdala	R	17	-19	-13	6
superior temporal gyrus (42)	R	26	-11	-18	4
inferior posterior temporal gyrus (37)	R	55	-25	15	6
	L	-32	-78	4	5
globus pallidus	R	14	0	-2	4
caudate nucleus	R	6	14	-2	4
<i>(b) Vocal expressions</i>					
middle occipital cortex (19)	L	-29	-67	31	16
	R	9	-67	31	8
superior temporal gyrus (42)	R	55	-33	15	9
		52	-22	9	6
	L	-32	-28	15	4
		-52	-25	15	3
posterior cingulate gyrus (31)	L	-9	-64	15	7
		-3	-47	26	3
superior temporal gyrus (22)	L	-55	-22	4	6
		-43	-44	4	6
		-46	-44	9	4
dorsolateral prefrontal cortex (45)	R	40	28	4	5
thalamus	L	-3	-8	4	4
rostral prefrontal cortex (32/46)	L	-26	36	15	3

^aTalairach coordinates refer to the voxel with the maximum FPQ (fundamental power quotient) in each regional cluster.

^bAll activated voxels were identified by a one-tailed test of the null hypothesis that median FPQ is not determined by experimental design. The probability threshold for activation was $p \leq 0.004$.

the same individuals will help to clarify the extent to which this is the case.

The only region activated by all four types of emotional stimuli was the superior temporal gyrus. Facial and vocal expressions of fear and facial expressions of disgust also activated middle and inferior posterior temporal gyri. Previous studies have linked the sulcus between the superior and middle temporal gyri with perception of social signals from the face, including facial expressions (Kanwisher *et al.* 1997) and eye and mouth movements (Puce *et al.* 1998), and the superior temporal gyrus with word perception (Wise *et al.* 1991; Demonet *et al.* 1994; Fiez *et al.* 1996). Activation of the superior temporal gyrus in this study may therefore reflect its role

in deciphering emotional content from facial and vocal stimuli, and in emotional behaviour in general.

Other regions were activated by visual and vocal expressions of fear and disgust. Limbic structures, including the anterior cingulate, have been implicated in the response to threatening stimuli (Morris *et al.* 1998). In the current study, anterior and posterior cingulate gyri were activated by vocal expressions of fear and disgust, respectively. Regions implicated previously in the response to emotive visual stimuli, including inferior posterior temporal gyrus and middle occipital cortex (Phillips *et al.* 1997), were activated by both visual and vocal stimuli. Activation of these regions in response to emotive vocal stimuli may reflect

Table 3. Brain regions demonstrating a greater mean power of response (a) to facial expressions of fear compared with disgust, and (b) to facial expressions of disgust compared with fear

region (approximate Brodmann area)	side	x^a	y^a	z^a	number of activated voxels	probability ^b
<i>(a) Response to facial expressions of fear compared with disgust</i>						
dorsolateral prefrontal cortex (45)	L	-43	33	4	7	0.00009
hippocampus	R	43	-17	-13	6	0.002
angular gyrus (39)	L	-43	-61	26	5	0.003
inferior posterior temporal gyrus (37)	R	43	-50	-7	3	0.008
superior temporal gyrus (42/22)	R	49	-31	-7	3	0.001
middle temporal gyrus (BA 21)	R	40	-56	-2	3	0.007
medial frontal cortex (10/32)	L	-26	47	4	2	0.01
putamen	R	29	-14	4	2	0.002
		17	17	-2	2	0.02
amygdala	L	-29	-11	-13	1	0.02
<i>(b) Response to facial expressions of disgust compared with fear</i>						
anterior insula	L	-35	0	9	11	0.009
		-43	8	-2	3	0.02
superior temporal gyrus (42)	R	52	-22	15	5	0.01
parahippocampal gyrus	L	-17	-22	-18	4	0.002
putamen	R	20	-36	-7	2	0.0007
	R	23	0	4	2	0.02
middle occipital cortex (18)	L	-9	-67	-2	2	0.001
globus pallidus	R	17	-11	-2	2	0.005
		14	0	-2	2	0.004

^aTalairach coordinates refer to the voxel with the maximum difference in FPQ (fundamental power quotient) between experimental conditions in each regional cluster.

^bDifferentially activated voxels were identified by a one-way analysis of variance with the factorial effect of interest being facial emotion: fear versus disgust (in *(a)*), and facial emotion: disgust versus fear (in *(b)*). The probability threshold was $p=0.05$. The probability of the maximum difference in FPQ between conditions is shown for each regional cluster.

the role of these structures in the response to emotional stimuli *per se*.

It is interesting that many of the brain regions activated during presentation of facial and vocal expressions were right-sided. Previous studies have provided evidence for the role of the right hemisphere in the perception of negative emotion, including fear and disgust, and the left hemisphere in the perception of positive emotion, including happiness (Davidson & Fox 1982; Davidson 1992a; Adolphs *et al.* 1996). The predominance of right-sided activation in this study may therefore reflect the role of the right hemisphere in the perception of negative emotion *per se*.

Although we demonstrated some activation in the putamen for facial expressions of fear, and in the caudate nucleus for vocal expressions of fear, a greater number of activated voxels was demonstrated in these regions for facial expressions of disgust. Similarly, we demonstrated some activation in the right amygdala/hippocampus in the response to facial expressions of disgust, but a greater number of activated voxels in the amygdala region in the response to fearful stimuli of both modalities. Our find-

ings therefore support the presence of a differential neural response to facial stimuli expressing fear and disgust, and confirm the role of the amygdala in the emotion of fear, whether evoked by facial or vocal expressions. Our results also confirm the involvement of the anterior insula and the striatum in reactions to facial expressions of disgust. In addition, our findings indicate a role of the hippocampus in perception of fearful stimuli, and a possible general role in perception of emotional stimuli for the superior temporal gyrus. In evolutionary terms, this would suggest that it is important that our ability to recognize and respond to a potentially harmful stimulus (one displaying fear or disgust) is appropriate and rapid, irrespective of the type of sensory information (visual or auditory) initially obtained from the stimulus. The superior temporal gyrus is perhaps involved in the mediation of the overall response to such emotional stimuli, whereas more specialized neural substrates are important in the appraisal of different types of danger: the amygdala and hippocampus in the detection of physical threat (one sign of which is the display of fear by others), and frontostriatal regions in the evaluation of risk of

Table 4. *Brain regions demonstrating a greater mean power of response (a) to vocal expressions of fear compared with disgust, and (b) to vocal expressions of disgust compared with fear*

region activated Brodmann area)	side	x^a	y^a	z^a	number of activated voxels	probability ^b
<i>(a) Response to vocal expressions of fear compared with disgust</i>						
hippocampus	R	38	-22	-7	8	0.003
Posterior cingulate gyrus (23/30)	L	-12	-58	9	5	0.01
middle occipital cortex (19)	R	26	-53	-7	9	0.01
anterior cingulate gyrus (24)	R	3	28	-2	4	0.01
medial frontal cortex (32)	R	6	44	4	3	0.008
caudate nucleus	R	20	-28	15	2	0.02
middle temporal gyrus (21)	R	55	-8	-2	2	0.007
<i>(b) Response to vocal expressions of disgust compared with fear</i>						
middle occipital cortex (19)	L	-32	-67	31	15	0.01
posterior cingulate gyrus (31)	L	-9	-61	15	5	0.01
		-3	-47	26	3	0.006
dorsolateral prefrontal cortex (45)	R	40	31	4	4	0.01
superior temporal gyrus (22/42)	L	-55	-19	4	4	0.004
	R	52	-22	9	3	0.01
		52	-31	15	3	0.02
thalamus	L	-3	-11	4	2	0.02

^aTalairach coordinates refer to the voxel with the maximum difference in FPQ (fundamental power quotient) between experimental conditions in each regional cluster.

^bDifferentially activated voxels were identified by a one-way analysis of variance with the factorial effect of interest being vocal emotion: fear versus disgust (in *(a)*), and vocal emotion: disgust versus fear (in *(b)*). The probability threshold was $p=0.05$. The probability of the maximum difference in FPQ between conditions is shown for each regional cluster.

contamination and disease (one sign of which is the display of disgust by others).

E.T.B. is supported by the Wellcome Trust. We thank Professor A. S. David and Dr H. Critchley for advice and helpful comments on the manuscript, and Dr A. Simmons and C. Long for technical support.

REFERENCES

- Adolphs, R., Tranel, D., Damasio, H. & Damasio, A. 1994 Impaired recognition of emotion in facial expressions following bilateral damage to the human amygdala. *Nature* **372**, 669-672.
- Adolphs, R., Tranel, D., Damasio, H. & Damasio, A. R. 1995 Fear and the human amygdala. *J. Neurosci.* **15**, 5879-5891.
- Adolphs, R., Damasio, H., Tranel, D. & Damasio, A. R. 1996 Cortical systems for the recognition of emotion in facial expressions. *J. Neurosci.* **16**, 7678-7687.
- Augustine, J. R. 1996 Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Res. Rev.* **22**, 229-244.
- Brammer, M., Bullmore, E. T., Simmons, A., Williams, S. C. R., Grasby, P. M., Howard, R. J., Woodruff, P. W. R. & Rabe-Hesketh, S. 1997 Generic brain activation mapping in functional magnetic resonance imaging: a nonparametric approach. *Magn. Reson. Imaging* **15**, 763-770.
- Breiter, H. C., Etcoff, N. L., Whalen, P. J., Kennedy, W. A., Rauch, S. L., Buckner, R. L., Strauss, M. M., Hyman, S. E. & Rosen, B. R. 1996 Response and habituation of the human amygdala during visual processing of facial expression. *Neuron* **17**, 875-887.
- Bullmore, E. T., Brammer, M. J., Williams, S. C. R., Rabe-Hesketh, S., Janot, N., David, A. S., Mellers, J. D. C., Howard, R. & Sham, P. 1996 Statistical methods of estimation and inference for functional MR image analysis. *Magn. Reson. Med.* **35**, 261-277.
- Bullmore, E. T., Brammer, M. J., Rabe-Hesketh, S., Curtis, V. A., Morris, R. G., Williams, S. C. R., Sharma, T., Murray, R. M. & McGuire, P. K. 1998 Methods for diagnosis and treatment of stimulus correlated motion in generic brain activation studies using fMRI. *Hum. Brain Mapp.* (In the press.)
- Calder, A. J., Young, A. W., Rowland, D., Perrett, D. I., Hodges, J. R. & Etcoff, N. L. 1996 Facial emotion recognition after bilateral amygdala damage: differentially severe impairment of fear. *Cogn. Neuropsychol.* **13**, 699-745.
- Calder, A. J., Young, A. W., Rowland, D. & Perrett, D. I. 1997 Computer-enhanced emotion in facial expressions. *Proc. R. Soc. Lond. B* **264**, 919-925.

- Cannon, W. B. 1927 The James-Lange theory of emotions: a critical examination and an alternative theory. *Am. J. Psychol.* **39**, 106–124.
- Darwin, C. 1872/1965 *The expression of the emotions in man and animals*. University of Chicago Press.
- Davidson, R. J. 1992a Anterior cerebral asymmetry and the nature of emotion. Special issue: the role of frontal lobe maturation in cognitive and social development. *Brain Cogn.* **20**, 125–151.
- Davidson, R. J. 1992b Prolegomenon to the structure of emotion: gleanings from neuropsychology. *Cogn. Emotion* **6**, 245–268.
- Davidson, R. J. & Fox, N. A. 1982 Asymmetrical brain activity discriminates between positive and negative affective stimuli in human infants. *Science* **218**, 1235–1236.
- Demonet, J. F., Price, C., Wise, R. & Frackowiak, R. S. 1994 A PET study of cognitive strategies in normal subjects during language tasks. influence of phonetic ambiguity and sequence processing on phoneme monitoring. *Brain* **117**, 671–82.
- Edgington, E. S. 1980 *Randomisation tests*. New York: Dekker.
- Ekman, P. 1992 An argument for basic emotions. *Cogn. Emotion* **6**, 169–200.
- Ekman, P. & Friesen, W. V. 1976 *Pictures of facial affect*. Palo Alto, CA: Consulting Psychologists Press.
- Ekman, P., Friesen, W. V. & Ellsworth, P. 1972 *Emotion in the human face: guidelines for research and integration of findings*. New York: Pergamon.
- Fiez, J. A., Raichle, M. E., Balota, D. A., Tallal, P. & Petersen, S. E. 1996 Activation of posterior temporal regions during auditory word presentation and verb generation. *Cerebr. Cortex* **6**, 1–10.
- Gray, J. A. 1982 *The neuropsychology of anxiety*. New York: Oxford University Press.
- Gray, J. A. 1990 Brain systems that mediate both emotion and cognition. *Cogn. Emotion* **4**, 269–288.
- Imaizumi, S. (and 11 others) 1997 Vocal identification of speaker and emotion activates different brain regions. *NeuroReport* **8**, 2809–2812.
- Kanwisher, N., McDermott, J. & Chun, M. 1997 The fusiform face area: a module in human extrastriate cortex specialized for face perception. *J. Neurosci.* **17**, 4302–4311.
- Lane, R. D., Reiman, E. M., Ahern, G. L., Schwartz, G. E. & Davidson, R. J. 1997 Neuroanatomical correlates of happiness, sadness and disgust. *Am. J. Psychiat.* **154**, 926–933.
- Lang, P. J., Bradley, M. M. & Cuthbert, B. N. 1992 A motivational analysis of emotion: reflex-cortex connections. *Psychol. Sci.* **3**, 44–49.
- Morris, J. S., Frith, C. D., Perrett, D. I., Rowland, D., Young, A. W., Calder, A. J. & Dolan, R. J. 1996 A differential neural response in the human amygdala to fearful and happy facial expressions. *Nature* **383**, 812–815.
- Morris, J. S., Friston, K. J., Buchel, C., Frith, C. D., Young, A. W., Calder, A. J. & Dolan, R. J. 1998 A neuromodulatory role for the human amygdala in processing emotional facial expressions. *Brain* **121**, 47–57.
- Oatley, K. & Johnson-Laird, P. N. 1987 Towards a cognitive theory of emotions. *Cogn. Emotion* **1**, 29–50.
- Ogawa, S., Lee, T. M., Kay, A. R. & Tank, D. W. 1990 Brain magnetic resonance imaging with contrast dependent blood oxygenation. *Proc. Natn. Acad. Sci. USA* **87**, 8868–8872.
- Paradiso, S., Robinson, R. G., Andreasen, N. C., Downhill, J. E., Davidson, R. J., Kirchner, P. T., Watkins, G. L., Boles Ponto, L. L. & Hichwa, R. D. 1997 Emotional activation of limbic circuitry in elderly normal subjects in a PET study. *Am. J. Psychiat.* **154**, 384–389.
- Phillips, M. L. (and 10 others) 1997 A specific neural substrate for perceiving facial expressions of disgust. *Nature* **389**, 495–498.
- Puce, A., Allison, T., Bentin, S., Gore, J. & McCarthy, G. 1998 Temporal cortex activation in humans viewing eye and mouth movements. *J. Neurosci.* **18**, 2188–2199.
- Scott, S. K., Young, A. W., Calder, A. J., Hellowell, D. J., Aggleton, J. P. & Johnson, M. 1997 Impaired auditory recognition of fear and anger following bilateral amygdala lesions. *Nature* **385**, 254–257.
- Sprengelmeyer, R., Young, A. W., Calder, A. J., Karnat, A., Lange, H., Homburg, V., Perrett, D. I. & Rowland, D. 1996 Perception of faces and emotions: loss of disgust in Huntington's disease. *Brain* **119**, 1647–1665.
- Talairach, J. & Tournoux, P. 1988 *Co-planar stereotaxic atlas of the human brain*. Stuttgart: Thieme.
- Whalen, P. J., Rauch, S. L., Etcoff, N. L., McInerney, S. C., Lee, M. B. & Jenike, M. A. 1998 Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. *J. Neurosci.* **18**, 411–418.
- Wise, R., Hadar, U., Howard, D. & Patterson, K. 1991 Language activation studies with positron emission tomography. *Ciba Found. Symp.* **163**, 218–228 (discussion, pp. 228–234).
- Young, A. W., Aggleton, J. P., Hellowell, D. J., Johnson, M., Brooks, P. & Hanley, J. R. 1995 Face processing impairments after amygdalotomy. *Brain* **118**, 15–24.
- Zald, D. H. & Pardo, J. V. Emotion, olfaction, and the human amygdala: amygdala activation during aversive olfactory stimulation. *Proc. Natn. Acad. Sci. USA* **94**, 4119–4124.

As this paper exceeds the maximum length normally permitted, the authors have agreed to contribute to production costs.

