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A differential neural response in obsessive–compulsive disorder patients with washing compared with checking symptoms to disgust

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ABSTRACT

Background. Patients with obsessive–compulsive disorder (OCD) have symptoms that predominantly concern washing (washers) or checking (checkers), or both. Functional neuroimaging has been used to identify the neural correlates of the urge to ritualize but has not distinguished between washing and checking symptoms in OCD. We used functional magnetic resonance imaging to compare the neural response to emotive pictures in washers and checkers.

Methods. In one of two 5-minute experiments, washers ($N = 7$), checkers ($N = 7$) and age-matched normal controls ($N = 14$) were scanned while viewing alternating blocks of normally disgusting (rated as disgusting by all subjects) and neutral pictures. In the other experiment, all patients and a normal subgroup ($N = 8$) viewed alternating blocks of washer-relevant (rated as more disgusting by washers than normal controls or checkers) and neutral pictures.

Results. In all subjects, normally disgusting pictures activated visual regions implicated in perception of aversive stimuli and the insula, important in disgust perception. Only in washers were similar regions activated by washer-relevant pictures. In checkers, these pictures activated fronto-striatal regions associated with the urge to ritualize in OCD. Normal controls were more similar in neural response to checkers than washers to these pictures. Both normal controls and checkers had frontal regions activated significantly more by washer-relevant than normally disgusting pictures, and had these regions activated significantly more than washers by washer-relevant pictures.

Conclusions. We demonstrate a differential neural response to washer-relevant disgust in washers and checkers: only washers demonstrate a neural response to washer-relevant disgust associated with emotion perception rather than attention to non-emotive visual detail.

INTRODUCTION

Recent studies of the neural correlates of experimentally-induced obsessive–compulsive symptoms, (i.e. the urge to ritualize) and concomitant anxiety, in patients with obsessive–compulsive disorder (OCD) have found increases in metabolism and blood flow in orbitofrontal cortex, anterior cingulate, striatum and thalamus (Rauch *et al.* 1984; McGuire *et al.* 1994; Breiter & Rauch, 1996; Breiter *et al.* 1996). Other studies have reported decreases in blood flow in similar structures after successful treatment (Saxena *et al.* 1998). OCD patients often have either mainly washing- or mainly checking-related symptoms, but may also show both types of symptom (Marks, 1987). Patients with compulsive washing (washers) tend to experience more disgust when perceiving supposed contaminants, e.g. rubbish bags, unclean

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bathrooms, than normal controls, or patients with compulsive checking (checkers) (Power & Dalgleish, 1997). In a positron emission tomography (PET) study (Rauch *et al.* 1998), increased regional blood flow was reported in the striatum in checkers, and in the anterior cingulate and orbitofrontal cortex in washers. These patients, however, were examined while performing a continuous performance task, involving serial presentations of visual cues and a motor response, rather than during the perception of stimuli relevant to their main symptom type.

Disgust is a basic emotion (Ekman, 1992; Phillips *et al.* 1998) evoked by body products such as blood, saliva, sweat, hair (Angyal, 1941; Rozin & Fallon, 1987). In normal subjects, the insula is activated by seeing facial expressions of disgust (Phillips *et al.* 1997; Sprengelmeyer *et al.* 1998), consistent with this region's role in gustatory processing (Yaxley *et al.* 1990). Studies have also demonstrated that visual regions are activated by aversive and disgusting visual stimuli, such as unpleasant scenes (Lane *et al.* 1999; Lang *et al.* 1998) and film excerpts (Reiman *et al.* 1997), and that the extrastriate cortical response to aversive stimuli may be modulated by limbic structures (Morris *et al.* 1998).

The present study compared OCD patients who were mainly washers or mainly checkers with normal controls while they viewed pictures of either normally disgusting scenes or scenes that particularly disgusted washers (washer-relevant pictures) using functional magnetic resonance imaging (fMRI) to identify the neural correlates of processing these stimuli.

We predicted the following.

1 All subjects would experience disgust and would show activation in visual cortical regions and the insula when viewing normally disgusting scenes.

2 Washers would also experience disgust and show activation in the same regions when viewing scenes that disgusted them but not the checkers or normal controls (washer-relevant pictures).

3 Checkers and normal controls would experience significantly less disgust than washers when viewing washer-relevant pictures, and, in response to these pictures, would show reduced activation in the regions activated by normally disgusting pictures.

METHOD

Stimuli

Thirty-five colour pictures of scenes found disgusting by normal controls (e.g. decaying food, cockroaches, wounds) and 39 pictures of neutral scenes (jewellery, pastoral scenes, household objects) were chosen from a standard set of stimuli (Lang *et al.* 1997). The neutral stimuli employed in the study included stimuli that were thought to be unrelated to the symptoms of the patients. Forty-one pictures of scenes that commonly evoke compulsive washing (washer-relevant pictures, e.g. urinals, sanitary material, unclean basins, unclean bathroom utensils, bags of rubbish) were made by the investigators. Each picture was rated by a separate group of normal volunteers from the Institute of Psychiatry in London for the level of visual detail or complexity on a four-point scale (1, low complexity; 4, very high complexity). From the original pictures, 20 normally disgusting pictures, 20 washer-relevant pictures and 27 neutral pictures were selected, such that the three groups of stimuli were matched for the level of visual complexity (see Appendix 1, p. 1050). More neutral pictures were selected in order to reduce the number of times they were repeated over the two fMRI experiments (below).

Subjects

Patients with a DSM-IV diagnosis of OCD were recruited from the Bethlem and Maudsley ($N = 14$) Hospitals, London. Subjects with past head injury or substance abuse were excluded from the study. Patients were selected if their symptoms were predominantly washing- and cleaning-related in theme ($N = 7$; four female; washers), or checking- and counting-related ($N = 7$; 3 female; checkers). Symptoms of the washers included excessive cleaning behaviour, avoidance of 'dirt', public transport or public buildings because of worry about contamination. Symptoms of the checkers included excessive tidying and checking behaviour, and excessive avoidance of mess, etc. Patients in whom both types of symptom were prominent were excluded from the study. A third group of normal controls ($N = 14$) was recruited from staff at the Institute of Psychiatry, London. Written, informed consent was obtained from all subjects after the procedure had been fully

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Table 1. *Subject details*

	Normal volunteers ($N = 14$)	Checkers ($N = 7$)	Washers ($N = 7$)
Age	31 (20–48)	34 (23–48)	31 (22–38)
Years of education	19 (15–22)	15 (12–18)	13 (10–17)
YBOCS		28 (21–34)	27 (18–37)
BDI		13 (0–27)	22 (1–45)
Spielberger State		50 (32–64)	52 (31–79)
Spielberger Trait		51 (46–59)	61 (42–75)
Duration of illness (years)		19 (7–35)	12 (1–21)
Medication*		4	7

Figures are mean values. Numbers in parentheses refer to the range.

YBOCS, Yale–Brown Obsessive–Compulsive Scale (moderate, marked and severe OCD: 16–23; 24–31; 32–40, respectively); BDI, Beck's Depression Inventory (mild depression $\geqslant 10$); Spielberger State and Trait (50th percentile score for both scales in normal adults in age groups 19–39 and 40–49 = 33–35).

* Four checkers were taking SSRI medication o.d. (fluoxetine 20 mg; fluoxetine 60 mg; fluoxetine 20 mg; and paroxetine 30 mg). Seven washers were taking SSRI or tricyclic medication: fluoxetine 40 mg; clomipramine 25 mg; fluoxetine 60 mg; fluoxetine 40 mg; sertraline 100 mg; fluoxetine 40 mg; lofepramine 70 mg).

explained, and prior to participation in the study. The three groups were matched for age and sex. Although there was a significant effect of diagnosis on years of education ($F(2, 25) = 16{\cdot}2$; $P < 0{\cdot}001$), this reflected the higher number of years of education of the normal controls compared with either of the two patient groups. At the time of scanning, washers and checkers had similar levels of OCD symptoms (as rated by the Yale–Brown OC Scale; Goodman *et al.* 1989), concomitant depression (Beck's Depression Inventory, BDI; Beck *et al.* 1961) and anxiety (Spielberger State and Trait Anxiety; Spielberger, 1983), although the washers had a higher trait anxiety mean score than the checkers (Table 1).

Procedure

There were two 5-minute experiments (Fig. 1). All subjects participated in Experiment 1. All patients and a subgroup of eight normal controls participated in Experiment 2.

Experiment 1

Normally disgusting and neutral pictures were presented on a screen to subjects in alternating 30 s blocks. Each block contained 10 pictures, each presented for 2 s, with a 1 s interstimulus interval (ISI). Five blocks of each type of picture (neutral or normally disgusting) were presented over five min. There were 20 different examples of each picture type; 10 were presented twice and 20 were presented once in a randomized order over the 5 blocks.

Experiment 2

The procedure was as for Experiment 1, except that 20 neutral pictures were contrasted with 20 washer-relevant pictures. The 20 neutral pictures comprised 13 of those used in Experiment 1 and 7 different pictures from the original set of 27 described above.

The starting order of blocks within each experiment (emotional or neutral block first) and of experiments (Experiment 1 or 2 first) were randomized across patients so that the same seven combinations of presentation orders of experiments and starting order of blocks in each experiment occurred in each patient group. The order of experiments and starting order of blocks in each experiment were counterbalanced over the eight normal controls participating in both experiments. Subjects were asked to view each picture and indicate whether it depicted an outdoor or indoor scene by pressing one of two buttons with their right thumb. This task was designed in order to ensure that subjects attended to the pictures, but did not become aware of the purpose of the study and then focus their attention on the emotional content of the pictures.

After scanning, subjects chose adjectives from three separate lists to rate the emotion experienced when viewing each picture in the scanner. The lists included adjectives related to disgust (e.g. 'disgusted', 'nauseous', 'repulsed'), fear (e.g. 'afraid', 'aghast', 'fearful') and anxiety (e.g. 'shaky', 'worried', 'uncomfortable'). Sub-

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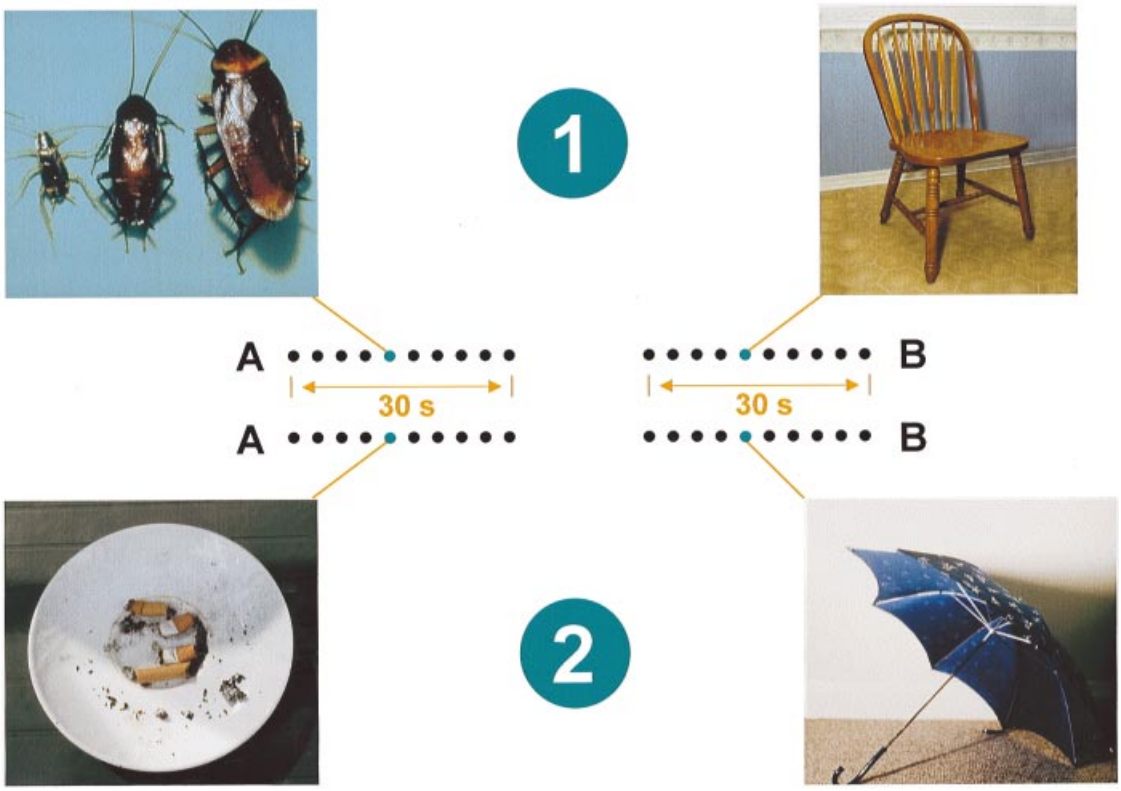


FIG. 1. Experimental design: there were two 5-min experiments (1 and 2), the order counterbalanced across subjects. In Experiment 1, subjects viewed alternating blocks of 30 s duration, in which were presented either 10 normally disgusting pictures (e.g. cockroaches, A) or 10 neutral pictures (e.g. chair, B). In Experiment 2, subjects viewed alternating blocks of 30 s duration, in which were presented either 10 washer-relevant pictures (e.g. ash and cigarettes in an ashtray, A) or 10 neutral pictures (e.g. umbrella, B). Each picture was presented for 2 s, with an interstimulus interval of 1 s.

jects also rated the intensity of each of the three emotions experienced on a scale of 0–8. The maximum total score for each emotion (disgust, fear and anxiety) for each picture was therefore 24, and for each set of 20 pictures, 480.

Image acquisition and analysis

Gradient echo echoplanar imaging (EPI) data were acquired on a GE Signa 1.5 T system (General Electric, Milwaukee, WI, USA) at the Maudsley Hospital, London. One hundred T_2-weighted images depicting BOLD contrast (Ogawa *et al.* 1990) were acquired over 5 min (for each task) at each of 14 near-axial non-contiguous 7 mm thick planes parallel to the intercommissural (AC–PC) line; TE 40 ms, TR 3 s, in-plane resolution 7 mm, interslice gap 0·7 mm. This EPI dataset provided complete coverage of the temporal lobes (including hippocampus and amygdala) and almost complete coverage of frontal, occipital and parietal lobes. (Simmons *et al.* 1999).

Following motion correction (Bullmore *et al.* 1999), periodic change in T2*-weighted signal intensity at the (fundamental) experimentally determined frequency of alternation between A and B conditions ($= 1/60$ Hz in both tasks) was estimated by an iterated least squares fit of a sinusoidal regression model to the fMRI time series observed at each voxel, and a standardized test statistic, the fundamental power quotient (FPQ), was obtained for each voxel (Bullmore *et al.* 1996). Parametric maps representing FPQ observed at each intracerebral voxel were constructed. In order to sample the distribution of FPQ under the null hypothesis that observed values of FPQ were not determined by experimental design (with few assumptions), the

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Table 2. *Picture ratings*

Type of picture	Normal controls	Washers	Checkers
Neutral			
D	0 (0–2)	1 (0–1)	1 (0–5)
F	0 (0–3)	1 (0–7)	7 (0–43)
A	1 (0–7)	8 (0–16)	5 (0–28)
Normally disgusting			
D	105 (0–315)	184 (7–410)	67 (8–192)
F	81 (0–341)	220 (7–421)	43 (9–182)
A	90 (2–322)	229 (47–416)	46 (0–168)
Washer-relevant			
D	12 (0–37)	107 (0–328)	24 (0–139)
F	2 (0–7)	101 (0–359)	16 (0–114)
A	5 (0–19)	105 (0–331)	19 (0–108)

Values refer to the mean value for the total score in each subject group for all pictures of each type on the disgust (D), fear (F) and anxiety (A) dimensions. Numbers in parentheses refer to the range of these values in each group.

99 images observed in each anatomical plane were randomly permuted and FPQ was estimated exactly as above in each permuted time series. This process was repeated 10 times, resulting in 10 permuted parametric maps of FPQ at each plane for each subject.

Observed and randomized FPQ maps were transformed into the standard space of Talairach & Tournoux (1988), and smoothed by a 2D Gaussian filter with full width half maximum = 11 mm. The median observed FPQ at each intracerebral voxel in standard space was tested against a critical value of the permutation distribution for median FPQ ascertained from the permuted FPQ maps (Brammer *et al.* 1997). Voxels with a significant mean power of response ($P \leqslant 0{\cdot}005$) to the stimuli presented in each experiment were depicted in red on a grey-scale template. The significance level was chosen in order to ensure that the maximum number of expected false-positive activated voxels did not exceed 40 per brain image (search volume approximately 12000 voxels).

To estimate the differences in mean FPQ between subject groups (controls, washers and checkers), and between experiments in each subject group, we fitted non-repeated and repeated measures analysis of variance (ANOVA) models, respectively, at each voxel of the observed FPQ maps in standard space. (Bullmore *et al.* 1999). 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.

RESULTS

Stimulus accuracy and emotional response ratings

All subjects were able to distinguish similarly well between outdoor and indoor scenes. Eleven of the normal volunteers, five washers and seven checkers completed rating scores on all pictures. The mean total scores on the disgust, fear and anxiety dimensions for the three main types of picture for washers, checkers and normal controls appear in Table 2. Multivariate analyses of variance performed for ratings for neutral, normally disgusting and washer-relevant scenes as within subject, and diagnosis as between-subject variables, revealed a significant effect of diagnosis (Wilks' lambda: $F(2, 20) = 13{\cdot}2$; $P < 0{\cdot}001$) and picture (neutral, normally disgusting or washer-relevant; Wilks' lambda: $F(2, 19) = 30{\cdot}3$; $P < 0{\cdot}001$) on score, and a near-significant effect of emotion (disgust, fear, anxiety; Wilks' lambda: $F(2, 19) = 2{\cdot}5$; $P = 0{\cdot}1$). There were significant interactions between picture and diagnosis (Wilks' lambda: $F(4, 38) = 5{\cdot}3$; $P = 0{\cdot}002$) and picture and emotion (Wilks' lambda: $F(4, 17) = 8{\cdot}3$; $P = 0{\cdot}001$), and a near-significant interaction between emotion and diagnosis (Wilks' lambda: $F(4, 38) = 2{\cdot}3$; $P = 0{\cdot}08$).

Univariate analyses of variance were employed to compare mean total scores for each emotion rating for each picture among the three groups. These tests revealed significant differ-

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Table 3(*a*). *Normal controls: generically activated brain regions to normally disgusting pictures*

Region (approximate Brodmann area)	Side	*x**	*y**	*z**	No. of voxels	*P*†
Lingual gyrus (18)	R	28	−73	−7	75	0·00003
	L	−28	−69	−2	25	0·00003
Cerebellum	R	−21	−73	−13	73	0·00003
Middle occipital gyrus (19)	R	28	−76	9	46	0·00003
	L	−40	−73	15	49	0·00003
Cuneus (18)	R	21	−73	20	46	0·00003
	L	−21	−73	26	31	0·00003
Middle temporal gyrus (37)	R	40	−60	4	19	0·00006
	L	−47	−63	9	37	0·00003
Superior temporal gyrus (38)	L	−43	7	7	18	0·00003
Inferior parietal lobule (40)	L	−50	−43	31	17	0·00003
Inferior temporal gyrus (19)	R	40	−69	−2	16	0·00003
Insula (anterior)	L	−43	7	−2	11	0·00009
		−36	20	4	9	0·0001
Transverse temporal gyrus (41)	R	40	−23	15	9	0·0003
Inferior frontal gyrus (44)	L	−36	13	20	5	0·00003

* The cluster with the largest number of voxels within each region is reported. Talairach coordinates refer to the voxel with the maximum FPQ (fundamental power quotient) in each cluster.

† All such 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 $P \leqslant 0{\cdot}005$.

ences among the groups on all three emotion ratings for the washer-relevant pictures ($F(2, 22) = 4{\cdot}6$; $P = 0{\cdot}02$; $F(2, 22) = 4{\cdot}3$; $P = 0{\cdot}03$; and $F(2, 22) = 5{\cdot}4$; $P = 0{\cdot}01$ for ratings of disgust, fear and anxiety, respectively), and on the rating for fear for the normally-disgusting pictures ($F(2, 22) = 6{\cdot}1$; $P = 0{\cdot}01$), but not for any of the other scores. Washers had higher ratings than controls and checkers in each of these cases.

Generic brain activation maps

The major brain regions activated in each GBAM and comparison between GBAMs are reported.

Activation associated with normally disgusting stimuli

In normal controls, these pictures activated predominantly visual regions, middle, superior and inferior temporal gyri, anterior insula and cerebellum, (Table 3(*a*) and Fig. 2A). Washers showed activation in visual areas, posterior cingulate gyrus, hippocampus, insula, frontal regions, superior and middle temporal gyri, the cerebellum and putamen. (Table 3(*b*) and Fig. 2A). Checkers showed activation in the cerebellum, visual areas, inferior, middle and superior temporal gyri, posterior cingulate gyri, insula, hippocampus, and frontal regions (Table 3(*c*) and Fig. 2A).

Differences in neural response to normally disgusting pictures in patients and normal controls

Washers v. *normal controls*

There was little significant difference in regions activated by normally disgusting pictures in washers and controls. Controls showed significantly more activation than washers in right visual areas (the right middle occipital gyrus and lingual gyrus) and bilateral middle temporal gyri, but not the insula. Washers did not show any significantly greater activation in response to these pictures than controls (search volume = 925 voxels; $P = 0{\cdot}01$; expected number of false positive activated voxels = 9; observed number of activated voxels = 38).

Checkers v. *normal controls*

There was no significant difference in activation between checkers and controls in response to normally disgusting pictures.

Washers v. *checkers*

There was no significant difference in activation between washers and checkers in response to normally disgusting pictures.

Activation associated with washer-relevant pictures

In normal controls, these pictures activated predominantly visual and frontal regions, the cerebellum, middle and inferior temporal gyri

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Table 3(*b*). *Washers: generically activated brain regions to normally disgusting pictures*

Region (approximate Brodmann area)	Side	*x**	*y**	*z**	No. of voxels	*P* †
Lingual gyrus (18/19)	R	15	−46	−2	52	0·00007
	L	−21	−80	−2	44	0·00003
Primary visual cortex (17)	R/L	0	−82	9	9	0·00004
Posterior cingulate gyrus (31)	R	15	−46	26	9	0·0002
Cuneus (19)	L	−25	−73	15	17	0·0006
Hippocampus	L	−21	−33	−2	15	0·0004
Medial frontal gyrus (6)	R	11	0	48	9	0·0005
Anterior cingulate gyrus (24)	R	11	17	26	8	0·0001
Superior temporal gyrus (22)	R	43	−52	20	8	0·0005
Cerebellum	R	21	−69	−18	7	0·0005
	L	−21	−39	−7	5	0·001
Fusiform gyrus (19)	R	32	−56	−7	6	0·001
Middle occipital gyrus (19)	L	−36	−76	4	5	0·00005
Middle temporal gyrus (37)	R	50	−56	4	2	0·002
	L	−47	−56	9	5	0·001
Postcentral gyrus (40)	R	50	−23	20	4	0·0004
Putamen	R	28	−20	−2	3	0·002
Precuneus (7)	R	11	−69	42	3	0·0007
Inferior frontal gyrus (44)	R	50	10	20	3	0·002
Insula	L	−40	−20	15	2	0·002
Middle frontal gyrus (46)	R	32	37	26	2	0·003

See footnotes to Table 3(*a*).

Table 3(*c*). *Checkers: generically activated brain regions to normally disgusting pictures*

Region (approximate Brodmann area)	Side	*x**	*y**	*z**	No. of voxels	*P*†
Cerebellum	R	17	−60	−13	8	0·00004
	L	−28	−76	−13	78	0·00001
Lingual gyrus (18)	R	25	−73	−7	11	0·00001
	L	−17	−76	−7	59	0·00001
Inferior occipital gyrus (18)	L	−36	−76	−2	52	0·00001
Precuneus (7)	R	4	−50	31	18	0·00001
	L	−17	−67	37	52	0·00001
Inferior temporal gyrus (19)	R	47	−67	−2	33	0·00001
Middle temporal gyrus (21/37)	R	47	−60	4	21	0·00001
	L	−50	−33	4	10	0·0001
Cuneus (17/18)	R	4	−73	31	14	0·00001
	L	−15	−89	4	21	0·00001
Posterior cingulate gyrus (23/30)	R	4	−37	26	9	0·00001
	L	−4	−52	20	19	0·00001
Middle occipital gyrus (19)	R	47	−67	−7	9	0·00001
	L	−28	−67	20	17	0·00001
Fusiform gyrus (18)	R	36	−67	−13	15	0·00001
Inferior frontal gyrus (44)	R	47	4	31	6	0·0003
	L	−43	7	31	15	0·00001
Inferior parietal lobule (40)	R	32	−39	42	5	0·0004
	L	−43	−46	31	13	0·0002
Superior temporal gyrus (22)	R	50	−30	20	10	0·0003
	L	−43	−52	26	6	0·0002
Insula	L	−40	0	9	9	0·0004
Hippocampus	R	7	−37	4	9	0·00001
Precentral gyrus (6)	L	−40	0	42	8	0·0002
Postcentral gyrus (40)	L	−43	−23	20	6	0·0002
Anterior cingulate gyrus (24)	R	17	33	15	5	0·0003

See footnotes to Table 3(*a*).

and the hippocampus (Table 4(*a*) and Fig. 2B). In washers, these pictures activated predominately the cerebellum and visual areas. Additional regions included the post-central gyrus, inferior parietal lobules, middle temporal gyrus, angular gyrus, the precentral gyrus, frontal regions and the insula. (Table 4(*b*) and Fig. 2B). In checkers, these pictures activated

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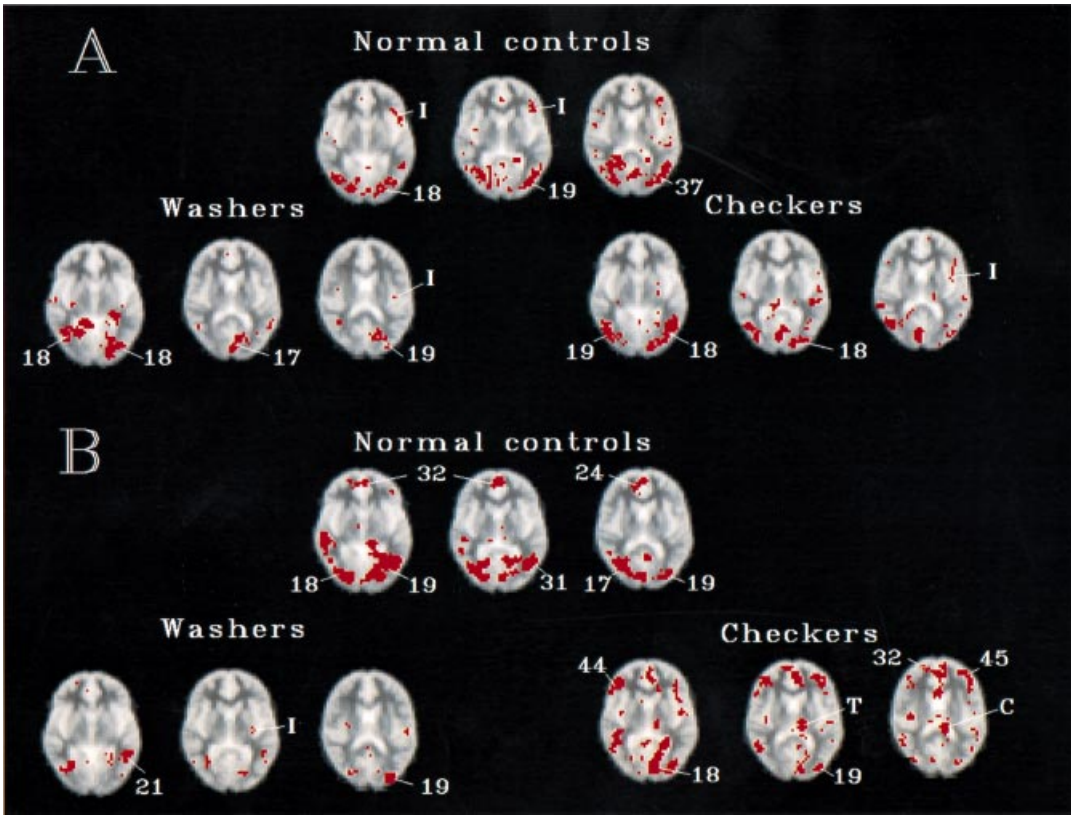


FIG. 2. Generic brain activation maps (GBAMs) in response to stimuli depicting normally disgusting (A) and washer-relevant pictures (B) in the normal controls, washers and checkers. The probability threshold for activation was $P \leqslant 0{\cdot}005$. For normal controls and checkers in A, three transverse slices are shown at 1·5 mm below (left), 4 mm above (middle) and 9·5 mm above (right) the transcallosal plane, and for washers in A, at 1·5 mm below (left), 9·5 mm (middle) and 15 mm above (right) this plane. For normal controls and washers in B, three transverse slices are shown at 1·5 mm below (left), 4 mm (middle) and 15 mm above (right) the transcallosal plane, and for checkers in B, at 4 mm above (left), 9·5 mm (middle) and 15 mm above (right) this plane. The left side of the brain is shown on the right side of the image and vice versa.

A For all three groups, activations are evident primarily in bilateral visual processing regions (lingual, middle and inferior occipital gyri, the cuneus and the inferior temporal gyrus BA 18, 19, primary visual cortex, BA 17 and the middle temporal gyrus, BA 37), in addition to the insula (I).

B Similar regions are shown in the washers (visual processing regions: middle occipital gyrus, BA 19, and middle temporal gyrus, BA 21, and the insula, I). In normal controls and checkers, activations are shown in frontal regions (anterior cingulate BA 24 and 32, and inferior frontal gyri, BA 44 and 45) and visual processing regions (lingual, middle and inferior occipital gyri, inferior temporal gyrus and the cuneus, BA 18, 19, 31 and primary visual cortex, BA 17). Additional activation is shown in the thalamus (T) and caudate nucleus (C) in checkers.

visual areas, the cerebellum, frontal regions, the caudate nucleus, thalamus, middle and superior temporal gyri, posterior cingulate and precentral gyri (Table 4(*c*) and Fig. 2B).

Differences in neural responses to washer-relevant pictures

Washers v. *normal controls*

Normal controls showed significantly greater activation to these pictures than washers in bilateral visual regions (bilateral lingual gyri, the right precuneus, the left occipital and superior occipital gyri), bilateral middle temporal gyri, the right hippocampus and the left inferior frontal gyrus. No areas were activated significantly more by these pictures in the washers compared with normal controls (search volume = 1956 voxels; $P = 0{\cdot}01$; expected number of false positive activated voxels = 19; observed number of activated voxels = 137).

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Table 4(*a*). *Normal controls: generically activated brain regions to washer-relevant pictures*

Region (approximate Brodmann area)	Side	*x**	*y**	*z**	No. of voxels	*P*†
Inferior temporal gyrus (19)	L	−36	−60	−2	120	0·000007
Precuneus (7/31)	R	25	−67	26	94	0·000007
	L	−21	−63	37	33	0·000007
Lingual gyrus (18)	R	28	−76	−7	93	0·000007
	L	−11	−63	4	26	0·00003
Middle temporal gyrus (19/39)	R	36	−69	20	78	0·000007
	L	−32	−67	26	23	0·0001
Cerebellum	R	28	−63	−13	76	0·000007
	L	−36	−63	−13	18	0·00007
Inferior parietal lobule (40)	L	−36	−46	48	71	0·000007
Cuneus (17)	R	7	−82	9	52	0·000007
Middle frontal gyrus (6/8)	L	−28	7	48	52	0·000007
Middle occipital gyrus (19/31)	R	36	−69	4	48	0·000007
	L	−40	−63	4	26	0·000007
Superior occipital gyrus (19)	R	21	−69	31	40	0·000007
Inferior occipital gyrus (18)	R	21	−82	−2	38	0·000007
Hippocampus	R	21	−10	−13	21	0·000007
Anterior cingulate gyrus (24/32)	R	4	39	9	19	0·00007
		7	37	15	13	0·00007
	L	−4	39	−7	9	0·000007
Inferior frontal gyrus (44)	L	−47	4	26	13	0·00007
Precentral gyrus (6)	R	47	0	31	12	0·00009
Superior temporal gyrus (42)	R	53	−26	20	8	0·00009
Posterior cingulate gyrus (23)	L	−4	−60	9	8	0·0001
Supramarginal gyrus (40)	L	−40	−63	31	7	0·0002
Medial frontal gyrus (11)	L	−7	37	−13	6	0·00002
Superior frontal gyrus (8)	R	25	17	48	5	0·0005

See footnotes to Table 3(*a*).

Table 4(*b*). *Washers: generically activated brain regions to washer-relevant pictures.*

Region (approximate Brodmann area)	Side	*x**	*y**	*z**	No. of voxels	*P* †
Cerebellum	R/L	0	−60	−18	70	0·00001
Cuneus (18)	L	−4	−82	26	31	0·00001
Postcentral gyrus (1–4)	L	−50	−26	37	24	0·00008
Inferior parietal lobule (40)	R	40	−50	42	5	0·002
	L	−28	−39	53	19	0·0002
Lingual gyrus (18)	R	17	−80	−13	16	0·0002
	L	−11	−86	−13	9	0·00003
Middle temporal gyrus (21)	L	−50	−46	−2	16	0·0001
Angular gyrus (39)	R	40	−52	37	16	0·00003
Middle occipital gyrus (19)	R	25	−69	20	7	0·0007
	L	−28	−80	15	15	0·00001
Precentral gyrus (6)	L	−36	0	26	15	0·00008
Inferior frontal gyrus (44)	L	−43	7	31	13	0·0003
Precuneus (7)	L	−15	−67	42	11	0·001
Fusiform gyrus (19/37)	R	32	−33	48	10	0·0003
	L	−28	−73	−13	5	0·0006
Medial frontal gyrus (9)	R	32	20	42	4	0·001
	L	−40	4	42	7	0·00003
Anterior cingulate gyrus (23/32)	R	21	43	−2	5	0·0007
	L	−21	−23	26	4	0·002
Supramarginal gyrus (40)	R	43	−52	31	5	0·0005
Posterior cingulate gyrus (31)	R	4	−39	37	5	0·002
Postcentral lobule (5)	R	15	−23	48	3	0·002
Superior frontal gyrus (8)	R	32	13	48	3	0·001
Insula	L	−32	−20	4	3	0·003

See footnotes to Table 3(*a*).

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Table 4(*c*). *Checkers: generically activated brain regions to washer-relevant pictures*

Region (approximate Brodmann area)	Side	*x**	*y**	*z**	No. of voxels	*P*†
Lingual gyrus (18)	R	7	−80	−7	127	0·00001
	L	−7	−76	4	71	0·00001
Cerebellum	R	7	−69	−13	28	0·00001
	L	−11	−69	−18	58	0·00001
Middle frontal gyrus (9)	R	47	13	37	17	0·00001
	L	−36	0	42	38	0·00001
Anterior cingulate gyrus (32)	R	4	23	37	35	0·00001
		21	39	15	6	0·0001
	L	−15	50	−2	18	0·00001
Caudate nucleus	R	4	13	15	35	0·0001
Medial frontal gyrus (9)	R	15	33	31	30	0·00001
	L	−17	37	31	26	0·00001
Middle temporal gyrus (39)	R	36	−60	26	30	0·00001
Inferior frontal gyrus (44)	R	43	26	4	23	0·00001
	L	−40	0	31	28	0·00001
Inferior frontal gyrus (46)	L	−36	37	20	25	0·00001
Inferior parietal lobule (40)	R	32	−56	42	23	0·00004
	L	−43	−30	31	5	0·0006
Inferior frontal gyrus (45)	R	43	26	15	22	0·00003
	L	−40	26	15	21	0·00001
Inferior frontal gyrus (47)	R	43	23	−2	21	0·00001
	L	−36	23	−7	6	0·00001
Medial frontal gyrus (8)	R	17	30	42	20	0·00001
Superior temporal gyrus (22)	R	40	−23	15	7	0·00003
	L	−43	−10	−2	20	0·00001
Precuneus (7)	R	7	−52	31	19	0·00001
Cuneus (19/31)	R	21	−67	37	18	0·00001
	L	−15	−63	9	16	0·0003
Posterior cingulate gyrus (23)	R	11	−39	26	18	0·00001
Superior occipital gyrus (19)	R	36	−67	31	17	0·00003
Precentral gyrus (4)	L	−28	−13	48	16	0·0002
Thalamus	L	−11	−26	9	15	0·00001
Medial frontal gyrus (10)	L	−21	43	−7	14	0·00001
Insula	L	−36	13	4	13	0·0003
Middle occipital gyrus (19)	L	−32	−80	9	8	0·00001
Superior frontal gyrus (8)	L	−17	13	48	5	0·00003

See footnotes to Table 3(*a*).

Checkers v. *normal controls*

Few areas were activated significantly more by these pictures in normal controls compared with checkers; left inferior and right middle temporal gyri, and the left inferior parietal lobule. No areas were activated significantly more by checkers compared with normal controls (search volume = 2712 voxels; $P = 0{\cdot}01$; expected number of false positive activated voxels = 27; observed number of activated voxels = 45).

Washers v. *checkers*

Checkers showed significantly greater activation to these pictures than washers in right frontal regions (inferior and medial frontal gyri and the anterior cingulate gyrus), the left thalamus and left caudate nucleus. No areas were activated significantly more by washers compared with checkers (search volume = 1685 voxels; $P = 0{\cdot}01$; expected number of false positive activated voxels = 16; observed number of activated voxels = 65).

Differences in neural response to normally disgusting and washer-relevant pictures

Normal controls

Normal controls did not show significantly greater activation to normally-disgusting than washer-relevant pictures in any regions. They had significantly more activation to washer-relevant than normally-disgusting pictures in bilateral visual regions (right occipital gyrus and left superior occipital gyrus), left frontal regions (left frontal and left inferior frontal gyri), the left middle temporal gyrus and bilateral posterior cingulate gyri (search volume = 1459 voxels; $P = 0{\cdot}01$; expected number of false positive activated voxels = 14; observed number of activated voxels = 60).

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Washers

There were some significant differences in activation to normally disgusting and washer-relevant pictures in the washers, but predominantly in visual regions in each comparison: to normally disgusting compared with washer-relevant pictures in the right lingual gyrus and right posterior cingulate gyrus (search volume = 893 voxels; $P = 0{\cdot}01$; expected number of false positive activated voxels = 8; observed number of activated voxels = 31), and to washer-relevant compared with normally disgusting pictures in the left inferior frontal gyrus and right fusiform gyrus (search volume = 893 voxels; $P = 0{\cdot}01$; expected number of false positive activated voxels = 8; observed number of activated voxels = 50).

Checkers

Checkers had significantly more activation to normally disgusting than washer-relevant pictures in the cerebellum and right inferior temporal gyrus, and significantly more activation to washer-relevant than normally disgusting pictures in frontal regions (right superior frontal gyrus, right medial frontal gyrus, right medial frontal gyrus and bilateral anterior cingulate gyri), and the left precentral gyrus (search volume = 2415 voxels; $P = 0{\cdot}01$; number of expected false positive activated voxels = 24; observed number of activated voxels = 104.

DISCUSSION

We aimed to distinguish washers from checkers on the basis of their neural response to pictures that disgusted washers more than checkers. We predicted that such pictures would be rated as more disgusting by washers than by checkers, and would activate the insula and visual regions to a greater extent in the former. We also predicted that all patients and normal controls would experience disgust when viewing normally disgusting pictures, and show insular and visual cortical activation.

As expected, washers, checkers and normal controls all rated the normally disgusting stimuli as disgusting. Washers rated them as much more disgusting, frightening and anxiety-evoking, than checkers, while controls were intermediate on these three dimensions (Table 2). All three groups showed insular activation with normally disgusting stimuli, again as expected (Fig. 2A), plus activation in the ventral pathway running from primary visual cortex to the inferior temporal gyri, which is involved in object perception (Ungerlieder & Mishkin, 1982). There was little significant difference in areas activated by these pictures amongst the three subject groups.

Turning to the washer-relevant pictures, washers rated these as more disgusting, frightening and anxiety-evoking than controls or checkers (Table 2). Unlike the washers, normal controls and checkers gave low ratings for disgust, fear and anxiety for the washer-relevant pictures. In both patient groups, these pictures activated visual regions and the insula. In checkers, however, there was prominent activation in frontal regions (prefrontal cortex and the anterior cingulate gyrus), the thalamus and striatum. Normal controls, similarly, had frontal regions activated by these pictures, in addition to visual cortical areas (Fig. 2B). Frontal regions were activated significantly more by washer-relevant pictures in normal controls and checkers than washers. The pictures also activated frontal regions significantly more than normally disgusting pictures in both normal controls and checkers.

As previous studies have linked increased fronto-striatal activation with the urge to ritualize in OCD (Rauch *et al.* 1984; McGuire *et al.* 1994; Breiter & Rauch, 1996; Breiter *et al.* 1996), our findings suggest that checkers and normal controls may have attended to the non-emotive visual details of these pictures, possibly evoking checking urges in the checkers, although we did not measure this. Unlike the normal controls and checkers, washers showed a similar pattern of visual cortical and insular activation to both types of picture, with some activation by washer-relevant pictures in frontal regions but not the striatum or thalamus. One possibility is that washers directed their attention to the emotive component of the washer-relevant pictures at the expense of the urge to ritualize.

Although we predicted that washers would have high ratings of disgust for both types of picture, they also had high ratings of fear and anxiety for the pictures. It is probable that the complex scenes depicted in the pictures employed in this study evoked a combination of negative emotions, and not disgust alone. It is clearly

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difficult to employ pictures of naturalistic scenes which evoke only one emotion. Our results suggest, however, that disgust is experienced at least to the same extent as fear by all subjects when viewing the normally disgusting pictures, and by washers to a greater extent than the checkers and normal controls when viewing the washer-relevant pictures.

Washers had higher ratings for disgust, fear and anxiety for the normally disgusting than the washer-relevant pictures. Their ratings for the washer-relevant pictures on all three dimensions were similar to those of the controls for the normally disgusting pictures, however. These findings suggest that washers were 'supersensitive' to the emotive content of both types of picture, experiencing more disgust, fear and anxiety to pictures of disgust than controls and checkers. Furthermore, the neural response to pictures of disgust may involve specific brain regions, regardless of the context (normal, or 'pathological') in which the emotional experience occurs.

Although the washers had a higher mean score for depression, and the checkers, a higher mean duration of illness, these differences were not significant. There were no significant differences between the two groups on trait and state anxiety scores, or on the severity of obsessive–compulsive symptomatology.

We have demonstrated that the experience of disgust, in addition to fear and anxiety, when viewing pictures of disgust is associated with activation in visual cortical regions and the insula. Washers rated both washer-relevant and normally disgusting pictures as disgusting, frightening and anxiety-provoking, and showed activation predominantly in visual regions, with additional activation in the insula, in response to these pictures. Our results also indicate, in normal controls and checkers, that as sensitivity to emotive aspects of the pictures decreased, with pictures rated as relatively non-disgusting, frightening and anxiety-provoking, activation increased in fronto-striatal regions, the brain regions associated with the experience of obsessive–compulsive symptoms. This was particularly evident in the checkers, who experienced low levels of emotion when viewing washer-relevant pictures, and showed a marked fronto-striatal response to these pictures.

To our knowledge, our study provides the first evidence for a distinction between the two main types of obsessive–compulsive symptom on the basis of the neural response to emotive visual stimuli. Future studies with larger numbers of patients measuring the urge to ritualize provoked by viewing emotive pictures will help to clarify the relationship between the experience of emotion and obsessive–compulsive symptoms. It would also be interesting to study the neural response in washers and checkers to pictures depicting scenes related to checking rather than washing. Finally, our results indicate that attention to emotive and non-emotive components of complex visual stimuli are associated with significantly distinct patterns of neural response.

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APPENDIX 1: Pictures employed in the study

Neutral			Normally disgusting			Potential contaminants	
Picture number*	Scene	Visual complexity rating	Picture number*	Scene	Visual complexity rating	Scene	Visual complexity rating
7550	Office	4	3530	Gun/mouth	3	Binbags	4
5500	Mushroom	3	1274	Cockroaches	3	Dirty razor	3
2270	Boy	3	3230	Patient	3	Rust	3
7130	Truck	3	3280	Dental work	3	Litter bins	1
1670	Cow	2	9050	Bodies/crash	3	Basins	2
7100	Hydrant	2	9600	Shipwreck	3	Toilet	2
7150	Umbrella	2	3261	Mutilation	3	Basin	2
7020	Fan	2	9921	Body/rescue	3	Dirty plate	2
7010	Basket	2	9433	Dead man	3	Urinals	1
5990	Sky	2	1931	Shark attack	2	Tampon	1
7050	Hairdryer	2	1930	Shark attack	2	Dirty plate	3
7000	Rolling pin	2	2720	Urinating	2	Litter	3
2200	Adult	2	2750	Tramp	2	Binbags	3
7235	Chair	2	9300	Dirty toilet	2	Condom	2
6150	Outlet	2	9405	Injured hand	2	Condom	2
2190	Man	3	9340	Litter	2	Cigarette ash	2
5201	Trees	3	3071	Mutilation	2	Unmade bed	3
5800	Leaves	3	3010	Mutilation	2	Dirty grate	3
5390	Boats	3	3170	Baby-tumour	2	Litter bin	2
5780	Bay	3	9253	Dead body	2	Litter bins	1
7090	Book	1					
5982	Sky	1					
1600	Horse	3					
7185	Block	3					
5991	Sky	3					
5250	Sky	3					
7187	Counters	1					

* Numbers from the International Affective Picture System (Lang *et al.* 1997).

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