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ORIGINAL ARTICLE

To discard or not to discard: the neural basis of hoarding symptoms in obsessive-compulsive disorder

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Preliminary neuroimaging studies suggest that patients with the 'compulsive hoarding syndrome' may be a neurobiologically distinct variant of obsessive-compulsive disorder (OCD) but further research is needed. A total of 29 OCD patients (13 with and 16 without prominent hoarding symptoms) and 21 healthy controls of both sexes participated in two functional magnetic resonance imaging experiments consisting of the provocation of hoarding-related and symptom-unrelated (aversive control) anxiety. In response to the hoarding-related (but not symptom-unrelated) anxiety provocation, OCD patients with prominent hoarding symptoms showed greater activation in bilateral anterior ventromedial prefrontal cortex (VMPFC) than patients without hoarding symptoms and healthy controls. In the entire patient group ($n=29$), provoked anxiety was positively correlated with activation in a frontolimbic network that included the anterior VMPFC, medial temporal structures, thalamus and sensorimotor cortex. Negative correlations were observed in the left dorsal anterior cingulate gyrus, bilateral temporal cortex, bilateral dorsolateral/medial prefrontal regions, basal ganglia and parieto-occipital regions. These results were independent from the effects of age, sex, level of education, state anxiety, depression, comorbidity and use of medication. The findings are consistent with the animal and lesion literature and several landmark clinical features of compulsive hoarding, particularly decision-making difficulties. Whether the results are generalizable to hoarders who do not meet criteria for OCD remains to be investigated.
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Introduction

Compulsive hoarding, the acquisition of and inability to discard a large number of possessions that appear to be useless and have no apparent value, poses a formidable challenge in understanding and treating obsessive-compulsive disorder (OCD). Extreme forms of this behavior can be severely disabling and even life threatening. Compulsive hoarders have a high prevalence of comorbid personality disorders, social phobia and pathological grooming behaviors, have reduced insight into their illness and respond poorly to conventional treatments.[1–3] This has motivated a substantial increase in research into this condition, including its neural correlates.

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Recent human lesion studies suggest that damage to the ventromedial prefrontal cortex (VMPFC), including the frontal pole, may lead to abnormal hoarding behaviors that were not present before the lesion occurred.[4–9] In light of these findings, Anderson *et al.*[9] speculated that these brain regions are involved in modulating subcortically driven predispositions to hoard. This idea is based on the animal literature, which suggests that hoarding behavior is mediated by subcortical limbic structures including the nucleus accumbens, amygdala, hippocampus, thalamus and hypothalamus.[10–12]

Recent functional neuroimaging studies have begun to examine the neural correlates of hoarding behaviors in healthy and psychiatric populations. In the first such study, Mataix-Cols *et al.*[13] scanned a group of healthy subjects while they were asked to imagine discarding their possessions. This procedure was aided with the presentation of pictures of the items to be discarded (for example, old newspapers, toys, empty food containers). Interestingly, healthy

individuals rated this activity as somewhat anxiety-provoking and primarily activated ventral prefrontal and paralimbic regions including the orbitofrontal cortex (BA11).

Two recent functional imaging studies have examined the neural correlates of abnormal hoarding behavior in OCD patients. Saxena *et al*.[14] found that 12 OCD patients with predominant hoarding symptoms showed reduced glucose metabolism in the dorsal anterior cingulate cortex and increased metabolism in the right sensorimotor cortex, compared with 33 non-hoarding OCD patients. In addition, across all OCD patients ($n = 45$), the severity of hoarding was negatively correlated with metabolism in the former region and positively correlated with metabolism in the latter region. Using functional magnetic resonance imaging (fMRI) and the above-mentioned symptom provocation procedure,[13] Mataix-Cols *et al*.[15] studied the neural correlates of hoarding symptoms in a consecutive sample of 16 OCD patients. Both patients and controls activated a similar network of brain regions in response to symptom provocation but, compared to healthy controls, OCD patients showed greater activation in left precentral (BA4/6) and fusiform (BA37) gyri, and in right orbitofrontal cortex (BA11). Furthermore, in the patient group, subjective anxiety during symptom provocation was significantly correlated with activation in the left precentral gyrus (sensorimotor cortex). However, only 50–56% of patients in this study endorsed hoarding symptoms on the Yale-Brown Obsessive-Compulsive scale (Y-BOCS) Symptom Checklist[16] and their Savings Inventory–Revised (SI-R) scores (mean = 28.2) were substantially lower than in other studies involving OCD hoarders (mean = 53.7[17]). Therefore, these results require replication in a specifically selected sample of patients with more prominent hoarding symptoms.

In a small pilot study, we have recently found that OCD hoarders ($n = 10$), relative to OCD non-hoarders and healthy controls, had impaired performance on the Iowa Gambling Task, a laboratory task of decision-making, accompanied by flattened skin conductance responses during performance on this task, whereas they had normal performances on the Wisconsin Card Sorting Test.[18] These findings are consistent with the hypothesis of VMPFC involvement in compulsive hoarding and also agree with the clinical observations and questionnaire studies that have led Frost and colleagues[1,19] to postulate that difficulties in decision-making are landmark features of the 'compulsive hoarding syndrome'.

This symptom provocation study builds upon previous work by our group[13,15] and aimed to examine the neural substrates of hoarding symptoms in OCD. To achieve this, we recruited new samples of OCD patients with ($n = 13$) and without ($n = 16$) prominent hoarding symptoms and healthy volunteers ($n = 21$) and studied their patterns of brain activity during the provocation of both hoarding-related and symptom-unrelated anxiety using a previously validated symptom provocation paradigm.[13,15,20] Based on previous animal and human lesion studies, and the above functional neuroimaging and neuropsychological studies, we hypothesized that compared with healthy controls and non-hoarding OCD patients, OCD hoarders would show greater subjective anxiety, greater activation in VMPFC and limbic regions[13,15] and reduced activation in dorsal prefrontal regions[14] during symptom provocation. We also predicted that the three groups would show comparable subjective anxiety and neural responses during the generally aversive control experiment.

Materials and methods

Participants

A total of 31 OCD patients were recruited from the Cognitive-Behavioral Therapy Unit at the Bethlem Royal Hospital in London, United Kingdom. They were at various stages of treatment but all were symptomatic at the time of the study. Axis I and Axis II diagnoses were made according to *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV) criteria by trained psychiatrists or nurse therapists using the Structured Clinical Interview for DSM-IV.[21,22] Patients with comorbid diagnoses were not excluded provided that OCD was the main problem for which treatment was sought. Exclusion criteria were brain injury, any neurological condition, psychosis, substance abuse, and use of antipsychotics (except as augmentation strategy). Two non-hoarding OCD patients were excluded from the final analyses due to faulty data acquisition and signs of brain atrophy, respectively, yielding a final sample of 29 patients (11 inpatients and 18 outpatients). Twenty-one healthy volunteers of similar demographic characteristics were recruited among ancillary staff at the Institute of Psychiatry, King's College London and the local community. A brief screening interview ruled out any history of neurological or psychiatric disorder in this group.

None of the subjects had participated in our initial studies[13,15] but the same individuals took part in parallel experiments in our laboratory, which will be published separately.

This study was approved by The Ethics Committee (Research) of the Maudsley Hospital and Institute of Psychiatry and all participants signed a written informed consent form prior to their participation.

Measures

Global OCD severity was assessed with the 10-item Y-BOCS[16]. Types of OCD symptoms were ascertained using the Y-BOCS Symptom Checklist.[16] The severity of hoarding symptoms was examined by the SI-R[17], a 23-item self-administered questionnaire requesting a response on a 0–4 scale (range 0–92). Factor analytical studies have identified three factors that correspond to the three hypothesized domains of compulsive hoarding: acquisition, difficulty discarding and clutter.[17,23] The severity of other OCD symptom

dimensions was assessed with the Obsessive-Compulsive Inventory–Revised (OCI-R[24]), a well-validated self-administered measure of OCD symptoms. Each of its subscales (washing, checking, order, hoarding, neutralizing and obsessing) consists of three items measured on a 0–4 scale (score range 0–12).

Depression and state anxiety were assessed with the Beck Depression Inventory (BDI[25]) and the state subscale of the State Trait Anxiety Inventory (STAI-S[26]), respectively. The Vividness of Visual Imagery Questionnaire[27] was administered to assess the participants' visual imagery abilities.

Selection of hoarding and non-hoarding groups

Patients who endorsed lifetime hoarding symptoms on the Y-BOCS Symptom Checklist and scored above the group median on the SI-R (SI-R > 30) formed the hoarding group ($n = 13$); the remaining 16 patients formed the non-hoarding group. This method ensured that patients in the hoarding group had prominent and disabling hoarding symptoms. Their mean SI-R score was 51.4 (s.d. = 13.5, range 35–75), which is comparable to that reported by OCD hoarders in other studies.[17,28]

Symptom provocation paradigm

We used a paradigm that had reliably provoked OCD symptoms in previous studies by our group.[13,15,20] All subjects participated in two, 6-min fMRI experiments in which they viewed 10, 20-s alternating blocks of emotional and neutral pictures. The order in which the two experiments were conducted was fully counterbalanced, as was the order of the emotional and neutral conditions within each experiment.

For experiment 1 (hoarding), 50 color pictures depicting objects commonly hoarded by patients were obtained with a standard digital camera. Three clinicians with experience in OCD treatment had previously listed the most common items that their patients reported hoarding. In addition, the pictures were rated by several patients (unrelated to this study) to ensure that they would be anxiety-provoking (data not shown). Examples of these pictures include old magazines/newspapers, empty food containers, clothes and toys. For experiment 2 (aversive control), 50 color pictures of scenes rated as highly disgusting and anxiety-provoking by healthy subjects were obtained from the International Affective Picture System (IAPS[29]). These included scenes of mutilated bodies/wounds, small animals (snakes, spiders, cockroaches and rats) and body products. Finally, 50 pictures of neutral or mildly positive scenes (for example, furniture, nature scenes, urban landscapes, household items, pets, families) were also selected from the IAPS and used as control stimuli in both experiments.

The final set of 150 pictures were selected after an independent group of nine healthy volunteers (unrelated to the study) had rated an originally larger pool of pictures according to their level of visual complexity, anxiety and disgust on a 0–3 scale (0 = nil, 3 = high). Pictures that were too simple/complex were excluded as were hoarding-related pictures that were rated as aversive/disgusting by healthy individuals. The final 150 stimuli were well matched regarding visual complexity and, as intended, the aversive pictures induced more anxiety and disgust than the other two types of pictures (data not shown).

Prior to the presentation of each set of pictures, subjects were played a prerecorded voice file by means of high-fidelity pneumatic headphones, asking them to imagine being in a particular situation while looking at the scenes they were about to see (for example, for hoarding: 'Imagine that these objects belong to you and that you must throw them away forever;' for aversive control: 'Imagine that you must come into contact with what is shown in the pictures'). After each set of pictures were presented, another prerecorded sound file of the question 'How anxious do you feel?' was played and the subjects rated their subjective anxiety on a Likert-style scale (0 = no anxiety to 8 = extreme anxiety).

Image acquisition

Gradient-echo echo-planar (EPI) images were acquired on a GE Sigma 1.5 T neuro-optimized MR system (General Electric, Milwaukee WI, USA) at the Maudsley Hospital, London. A total of 100 T2* weighted whole-brain volumes depicting blood oxygen level dependent (BOLD) contrast[30] and consisting of 16 slices oriented according to the bicomissural plane (thickness 7 mm, 0.7 mm gap) were acquired over 6 min for each of the two experiments (repetition time (TR) = 2.0 s; echo time (TE) = 40 ms; field of view = 24 cm; flip angle = 70; 64×64 matrix). This EPI dataset provided almost complete brain coverage.

In each 20 s stimulus presentation block, subjects viewed either 10 provocative or 10 neutral pictures. Each picture was presented for 1950 ms, with an interstimulus interval of 50 ms. Ten whole-brain volumes were acquired during each block. Each block was preceded by an 8-s period during which the subjects listened to a sound file containing instructions pertinent to that stimulus block. Four 'dummy volumes' were excited during this 8-s period using exactly the same radio frequency envelope and gradient slice selection parameter, with the same TR of 2 s to allow the magnetization to reach an equilibrium amplitude prior to the next period of data acquisition. The frequency-encoding gradient was turned off during this period to minimize acoustic noise and ensure that the instructions were heard clearly by the subjects. Each block was followed by a further 8-s period (four volumes) of complete silence during which subjects were asked to rate their level of anxiety. The four volumes before and the four volumes after each block were modeled in the analyses and treated as a nuisance variable.

Individual brain activation maps were coregistered to a structural scan with the following acquisition parameters: TE = 40 ms, TR = 3000 ms, field of view = 24 cm, image resolution = 128×128, number of

slices = 43, slice thickness = 3.0 mm, inter-slice gap = 0.3 mm, number of signal averages = 8.

Data analysis

The fMRI data were analyzed with software developed at the Institute of Psychiatry (XBAM), using a nonparametric approach to minimize assumptions. Data were first corrected for subject motion[31] and then smoothed using a Gaussian filter (full-width at half-maximum 7.2 mm) chosen to improve signal-to-noise ratio over the spatial neighborhood of each voxel. Responses to the experimental paradigms were then detected by time series analysis using a linear model in which each component of the experimental design was convolved separately with two γ variate functions (peak responses at 4 and 8 s, respectively) to permit variability in the hemodynamic delay. The method of Friman *et al.*[32] was used to constrain model fits to those deemed physiologically plausible. Following computation of the model fit, a goodness of fit statistic was computed. This consisted of the ratio of the sum of squares of deviations from the mean image intensity due to the model (over the whole time series) to the sum of squares of deviations due to the residuals (SSQ ratio). This addresses the problem inherent in the use of the F-statistic that the residual degrees of freedom are often unknown in fMRI time series due to the presence of colored noise in the signal. Following computation of the observed SSQ ratio at each voxel, the data were permuted by the wavelet-based method described and extensively characterized in Bullmore *et al.*,[33] which permits the data-driven calculation of the null distribution of SSQ ratios under the assumption of no experimentally determined response. This distribution can then be used to threshold the activation maps at any desired type I error rate. In addition to the SSQ ratio, the percentage BOLD change was also calculated from the model fit at each voxel.

The detection of activated regions was extended from voxel to cluster level using the method described in detail by Bullmore *et al.*[33] The observed

Table 1 Demographic and clinical characteristics of 29 OCD patients with and without prominent hoarding symptoms and 21 healthy controls

Variable	*Hoarding OCD* (n = *13*)	*Non-hoarding OCD* (n = *16*)	*Healthy control* (n = *21*)	*Statistic (d.f.)*	P-*value*
Women, *n* (%)	8 (61.5)	6 (37.5)	12 (57.1)	$\chi^2 = 2.0$ (2)	0.360
Right-handed, *n* (%)	12 (92.3)	14 (87.5)	20 (95.2)	$\chi^2 = 0.7$ (2)	0.690
Age (years)	39.6 (9.1)	33.5 (11.6)	30.6 (8.4)	F = 3.5 (2.47)	0.039[a]
Education (years)	14.2 (2.6)	12.9 (2.8)	16.2 (2.7)	F = 6.9 (2.47)	0.002[b]
Y-BOCS obsessions	13.2 (3.5)	14.5 (3.1)	—	F = 1.2 (1.27)	0.279
Y-BOCS compulsions	12.9 (2.6)	13.9 (5.2)	—	F = 0.4 (1.27)	0.523
Y-BOCS total	26.0 (5.9)	28.4 (7.8)	—	F = 0.8 (1.27)	0.372
SI-R total	51.4 (13.5)	13.6 (10.0)	14.7 (11.8)	K–W $\chi^2 = 26.3$ (2)	< 0.001[c]
SI-R (discarding)	19.1 (4.3)	4.6 (4.1)	5.3 (4.2)	K–W $\chi^2 = 27.2$ (2)	< 0.001[c]
SI-R (clutter)	18.8 (7.5)	4.1 (5.7)	3.6 (4.6)	K–W $\chi^2 = 23.8$ (2)	< 0.001[c]
SI-R (acquisition)	13.5 (3.0)	4.9 (3.4)	5.8 (4.2)	K–W $\chi^2 = 21.5$ (2)	< 0.001[c]
OCI-R hoarding	6.6 (3.2)	1.4 (2.1)	1.3 (2.2)	F = 22.1 (2.47)	< 0.001[c]
OCI-R washing	4.9 (3.4)	5.8 (4.6)	0.7 (1.5)	F = 12.8 (2.47)	< 0.001[d]
OCI-R checking	5.9 (3.4)	5.8 (4.6)	1.1 (1.5)	F = 13.0 (2.47)	< 0.001[d]
OCI-R order	5.6 (3.3)	6.6 (4.1)	1.5 (1.8)	F = 13.7 (2.47)	< 0.001[d]
BDI	22.8 (9.5)	21.2 (10.8)	3.9 (3.9)	K–W $\chi^2 = 29.8$ (2)	< 0.001[d]
STAI-S	55.2 (9.4)	40.7 (12.6)	31.2 (10.1)	F = 19.9 (2.46)	< 0.001[e]

Abbreviations: BDI, beck depression inventory; OCD, obsessive-compulsive disorder; OCI-R, obsessive compulsive inventory–revised; SI-R, savings inventory–revised; STAI-S, state subscale of the state trait anxiety inventory; Y-BOCS, Yale-Brown obsessive compulsive scale.

One patient in non-hoarding OCD group had missing data in the following variables: SI-R, OCI-R washing, OCI-R checking, OCI-R order and STAI-S.

Values are given in means (standard deviations) unless otherwise specified.

[a]*Post hoc* LSD test: high hoarding = low hoarding ($P = 0.099$), high hoarding > control ($P = 0.011$), low hoarding = control ($P = 0.369$).

[b]*Post hoc* LSD test: high hoarding = low hoarding ($P = 0.239$), high hoarding < control ($P = 0.036$), low hoarding < control ($P = 0.001$).

[c]*Post hoc* Man–Whitney *U*-test: high hoarding > low hoarding ($P < 0.001$), high hoarding > control ($P < 0.001$), low hoarding = control ($P > 0.5$).

[d]*Post hoc* Man–Whitney *U*-test: high hoarding = low hoarding ($P > 0.4$), high hoarding > control ($P < 0.001$), low hoarding > control ($P \leqslant 0.001$).

[e]*Post hoc* LSD test: high hoarding > low hoarding ($P = 0.001$), high hoarding > control ($P < 0.001$), low hoarding > control ($P = 0.013$).

and randomized SSQ ratio data for each individual were transformed into standard space of Talairach and Tournoux,[34] and group maps of activated regions were computed using the median observed and randomized SSQ ratio data as described by Brammer *et al*.[35] Permutation methods and median statistics were employed to allow exact computation of *P*-values with minimal assumptions and the minimization of outlier effects. The hierarchical method of analysis used above also allows separate treatment of intra- and inter-individual variance. After extension of inference from voxel to cluster level,[36] the resulting cluster maps were thresholded to give <1 expected type I error cluster per whole-brain volume to make interpretation of maps as intuitive as possible.

For each level of the task, comparison of responses between groups was performed by fitting the data at each intracerebral voxel at which all subjects have nonzero data using a linear model of the type:

$Y = a + bX + e$,

where Y is the vector of BOLD effect sizes for each individual, X is the contrast matrix for the particular inter-group contrasts required, a is the mean effect across all individuals in the various groups, b is the computed group difference and e is a vector of residual errors. The model is fitted by minimizing the sum of absolute deviations rather than the sums of squares to reduce outlier effects. The null distribution of b is computed by permuting data between groups (assuming the null hypothesis of no effect of group membership) and refitting the above model 50 times at each voxel and combining the data over all intracerebral voxels. Group difference maps at any desired voxel or cluster-wise type I error rate can then be computed by appropriate thresholding of this null distribution.

To control for the effect of potentially confounding variables such as age, years of education, sex (dummy-coded as 1–2), depression (BDI) and state anxiety (STAI-S) on the results, we repeated all the above whole-brain analyses introducing these variables as covariates. We also used a functionally derived region of interest (ROI) approach (extracting the percent change in BOLD signal in the regions identified in the above whole-brain analyses) to further examine the potential effects of comorbidity and medication on the results.

Finally, whole-brain correlation analyses controlling for the above confounding variables were performed to examine the association between provoked anxiety and brain activation during the hoarding experiment. For each significantly correlated cluster, the percent BOLD change of each participant was plotted against his/her corresponding anxiety score and when correlations were clearly due to extreme values, they were considered nonsignificant.

Results

Demographic and clinical variables

There was a nonsignificantly greater proportion of women in the hoarding group (61.5%) than in the non-hoarding OCD group (37.5%). Hoarders were slightly older than the non-hoarding and control groups and both patient groups were less educated than the controls. The hoarding and non-hoarding OCD groups had comparable Y-BOCS severity scores, which were in the moderate-to-severe range. As

Table 2 Additional Axis I and Axis II disorders in the hoarding and non-hoarding OCD groups and number of patients in each group taking medications and their mean doses in mg per day

	Hoarding OCD (n = *13*)	*Non-hoarding OCD* (n = *16*)
Axis I disorders		
Major depressive disorder	3	3
Dysthymic disorder	2	4
Social phobia	1	2
Hypochondriasis	1	1
Generalized anxiety disorder	1	0
Specific phobia	1	0
Panic disorder with agoraphobia	0	1
Posttraumatic stress disorder	0	1
Anorexia nervosa	0	1
Axis II disorders		
Avoidant personality disorder	5	2
Obsessive-compulsive personality disorder	4	1
Dependent personality disorder	3	1
Depressive personality disorder	3	1
Negativistic personality disorder	2	1
Schizoid personality disorder	1	0
Antisocial personality disorder	0	1
Medications		
Fluoxetine	$n = 5$ (36 ± 16.7)	$n = 3$ (40 ± 20)
Paroxetine	$n = 3$ (40 ± 17.3)	$n = 3$ (50 ± 10)
Clomipramine	$n = 2$ (100 ± 70.7)	—
Sertraline	—	$n = 2$ (125 ± 35.4)
Venlafaxine	—	$n = 2$ (150)
Fluvoxamine	—	$n = 1$ (100)
Citalopram	$n = 1$ (40)	—
Amytriptiline	—	$n = 1$ (30)
Diazepam	$n = 2$ (6 ± 1.4)	—
Temazepam	$n = 1$ (5–10)	—
Lithium	—	$n = 1$ (1200)
Thyroxine	$n = 1$ (150)	—
Zopiclone	$n = 1$ (3.75)	—

Abbreviation: OCD, obsessive-compulsive disorder.

expected, hoarders had significantly higher scores on the SI-R and the OCI-R hoarding subscale but both patient groups showed comparable levels of other OCD symptoms (washing, checking, symmetry/order) and depression (BDI), which were significantly higher than those of the control group. Both patient groups had significantly higher scores on the STAI-S than the controls. OCD hoarders also had higher STAI-S scores than the non-hoarding patients (Table 1).

The two patient groups had a comparable mean number of additional Axis I disorders (hoarding = 1.0, s.d. = 1.2; non-hoarding = 0.6, s.d. = 0.7; $F(1,27) = 1.5$, $P = 0.224$) but the hoarders tended (nonsignificantly) to have more Axis II psychopathology (hoarding = 1.4, s.d. = 2.1; non-hoarding = 0.4, s.d. = 0.8; $F(1,27) = 2.8$, $P = 0.114$) (Table 2).

As seen in Table 2, a similar proportion of patients in both OCD groups were on medication at the time of the study (hoarding: $n = 11$, 84.6%; non-hoarding: $n = 12$, 75.0%; $\chi^2(1) = 0.40$, $P = 0.525$).

Verification of the symptom provocation procedure

There were no differences between hoarders (mean = 42.3, s.d. = 20.7), non-hoarders (mean = 31.9, s.d. = 17.9) and controls (mean = 36.1, s.d. = 13.1) in visual imagery abilities ($F(2,47) = 1.4$, $P = 0.263$). The hoarding group rated the hoarding-related stimuli as more anxiety-provoking than the other two groups ($F(2,47) = 8.1$, $P = 0.001$; both *post hoc* LSD tests $P \leqslant 0.002$), which did not differ from one another ($P > 0.7$). On the other hand, generally aversive/disgusting IAPS pictures were rated as highly anxiogenic by all three groups, with no statistically significant differences between them ($F(1,46) = 1.7$, $P = 0.191$) (Figure 1).

Within the patient group, correlation analyses revealed statistically significant correlations between the two hoarding measures and the mean level of provoked anxiety during hoarding experiment (SI-R: Spearman's $\rho = 0.56$, $P = 0.002$; OCI-R hoarding: $\rho = 0.54$, $P = 0.002$). Other OCD symptoms were not correlated with subjective anxiety during this experiment (smallest $P = 0.25$). The results remained unchanged when Y-BOCS severity scores were entered as a covariate. Furthermore, SI-R and OCI-R hoarding scores did not correlate with subjective anxiety during the aversive control experiment ($P = 0.25$ and $P = 0.85$, respectively). Thus, the provocation procedure was effective and highly symptom specific.

Generic brain activation maps

Hoarding experiment. All three groups demonstrated widespread activations in ventral prefrontal, paralimbic and dorsal prefrontal brain regions including bilateral visual regions, cerebellum, ventrolateral, dorsolateral and dorsomedial prefrontal regions, anterior insula and temporal cortex (Table 3). However, some brain regions were uniquely activated in each group. Only hoarders activated a large cluster in the frontal pole (BA10; peak activation $z = 0$, $y = 63$, $z = 4$; 134 voxels) extending ventrally to the anterior part of the orbitofrontal cortex (BA11) and dorsally to the medial frontal gyrus (BA9). Additional regions activated in the non-hoarding group were the putamen and caudate nucleus. Finally, additional regions activated in the control group were the striatum, left thalamus and a large bilateral cluster in the VMPFC (peak activation $z = 14$, $y = 44$, $z = -13$; 146 voxels) including the orbitofrontal cortex (BA11) and the anterior cingulate gyrus (BA24/32).

Aversive control experiment. All three groups showed similar widespread activations in emotion-related regions including anterior insula, ventrolateral

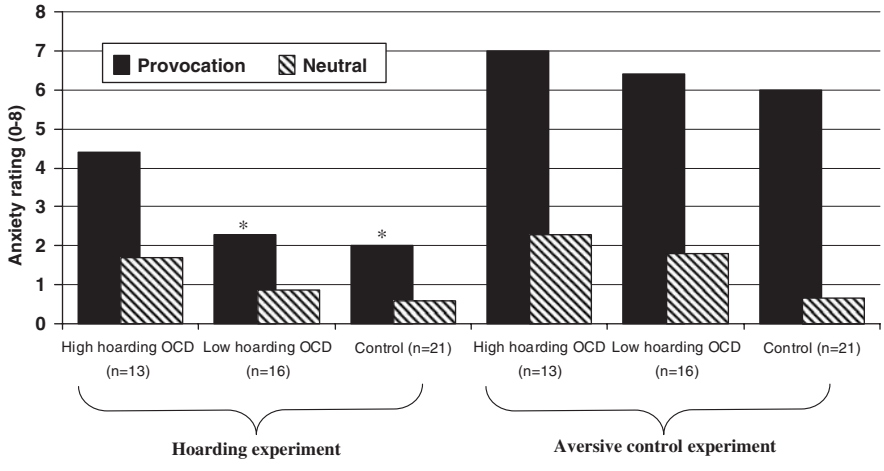

Figure 1 Subjective discomfort ratings during provoked and neutral conditions in obsessive-compulsive disorder (OCD) patients with and without prominent hoarding symptoms and healthy controls. Asterisks represent statistically greater subjective anxiety scores among hoarders compared to non-hoarders and healthy controls in the hoarding experiment only (see text).

Table 3 Hoarding experiment: brain regions significantly activated during the provocation of hoarding-related anxiety by group

Brain regions (approximate BA)	x	y	z	*No. of voxels*
Hoarding OCD (n = 13)[a]				
Bilateral frontal pole (10/11/9)	0	63	4	134
Right inferior frontal gyrus (44/45), ventrolateral prefrontal cortex (47) and insula	43	19	15	125
Left precentral gyrus (6), inferior frontal gyrus (44/45), ventrolateral prefrontal cortex (47) and insula	−54	−4	20	244
Left inferior (20) and middle (21) temporal gyri	−51	−15	−24	51
Right visual regions (17/18/19/39/40) and cerebellum	33	−78	−13	274
Left visual regions (18/19/20/39/40) and cerebellum	−47	−59	−29	352
Non-hoarding OCD (n = 16)[b]				
Bilateral medial frontal gyrus (8/6)	4	30	37	69
Right middle frontal gyrus (46/9/8), inferior frontal gyrus (44), insula, putamen and caudate nucleus	47	30	26	252
Left middle frontal (9/44/45) and precentral (6) gyri	−36	19	42	114
Left middle (21) and superior (22) temporal gyri	−58	−7	−13	56
Right visual regions (18/19/37/40/7) and cerebellum	33	−78	9	496
Left visual regions (18/19/40/7) and cerebellum	−26	−89	−7	647
Healthy controls (n = 21)[a]				
Bilateral orbitofrontal cortex (11), anterior cingulate gyrus (24/32), right insula and caudate nucleus	14	44	−13	146
Bilateral medial frontal (8) and anterior cingulate gyri (32)	0	19	42	222
Right inferior frontal (44/45) and middle frontal (9) gyri	47	11	26	159
Left inferior frontal gyrus (44/45), precentral gyrus (6), ventrolateral prefrontal cortex (47) and insula	−51	11	31	304
Left thalamus and caudate nucleus	−11	11	4	93
Left middle (21) and superior (22) temporal gyri	−54	−19	−13	69
Right visual regions (18/19/21/7) and cerebellum	29	−78	−15	658
Left visual regions (18/19/39/40/7) and cerebellum	−29	−81	−13	811

Abbreviations: BA, Brodmann area; OCD, obsessive-compulsive disorder.
Talairach coordinates refer to the voxels with the maximum change in % BOLD signal in each cluster.
[a]Voxel- and cluster-wise *P*-values were conservatively set at 0.02 and 0.01, respectively, yielding a total number of false positives <1.
[b]Voxel- and cluster-wise *P*-values were conservatively set at 0.02 and 0.0075, respectively, yielding a total number of false positives <1.

prefrontal cortex, inferior frontal gyrus, visual regions and cerebellum (Table 4).

Between-group comparisons

Hoarding experiment. Using a highly stringent significance test (adjusted voxel- and cluster-wise *P*-value, yielding <1 false-positive cluster), hoarding OCD patients demonstrated significantly greater activations than non-hoarding patients and controls in a large bilateral cluster situated in the anterior parts of the VMPFC (BA11/10) (Table 5 ; Figure 2a). In addition, the cerebellum was significantly more activated bilaterally in the hoarding compared with the control group.

Healthy controls demonstrated significantly greater activation than the two patient groups in a small cluster located in the left orbitofrontal cortex (BA 11), situated more ventrally and posteriorly than the above frontopolar cluster (Table 5; Figures 2b and c). No regions were activated to a greater extent in the non-hoarding OCD patients relative to the other two groups.

To examine the effects of potentially confounding variables on the above findings, we next performed whole-brain analyses of covariance controlling for age, years of education, sex (dummy-coded as 1–2), depression (BDI) and state anxiety (STAI-S). All findings remained significant (data not shown).

To examine the potential effects of comorbidity, we first repeated the above whole-brain analyses of variance (ANOVAs) including patients without other Axis I disorders only (nine hoarders versus five non-hoarders). The results showed that hoarders had showed greater activations in the frontal pole (BA11/10; peak $x=0$, $y=67$, $z=-7$; 252 voxels) and in the following additional regions: left medial temporal lobe (including uncus, parahippocampal gyrus and

Table 4 Aversive control experiment: brain regions significantly activated during the presentation of aversive/disgusting pictures by group

Brain regions (approximate BA)	x	y	z	*No. of voxels*
Hoarding OCD (n = 13)				
Bilateral anterior cingulate (24/32) and medial frontal (6/8) gyri	4	4	42	80
Right inferior frontal gyrus (44/45), precentral gyrus (6), ventrolateral prefrontal cortex (47) and insula	43	11	20	247
Left inferior frontal gyrus (44/45), precentral gyrus (6), ventrolateral prefrontal cortex (47) and insula	−43	7	26	310
Bilateral thalamus, posterior cingulate gyrus (29/23) and hippocampus	0	−15	4	291
Left inferior parietal lobule (40)	−54	−26	31	47
Right visual regions (18/19/37/7) and cerebellum	36	−63	−29	295
Left visual regions (18/19/37/7) and cerebellum	−43	−63	−24	441
Bilateral cerebellum	0	−70	−40	55
Non-hoarding OCD (n = 16)				
Bilateral medial frontal gyrus (9/10)	−4	59	26	87
Right inferior frontal gyrus (44/45), precentral gyrus (6), ventrolateral prefrontal cortex (47) and insula	43	15	20	313
Left inferior frontal gyrus (44/45), precentral gyrus (6), ventrolateral prefrontal cortex (47) and insula	−36	4	26	151
Right visual regions (18/19/37/7) and cerebellum	47	−59	−18	864
Left visual regions (18/19/37/7) and cerebellum	−29	−85	−2	841
Healthy controls (n = 21)				
Bilateral anterior cingulate (32/24) and medial frontal (6/8) gyri	0	15	42	107
Bilateral medial frontal gyrus (9/8)	0	48	26	103
Right inferior frontal gyrus (45/44), precentral gyrus (6), ventrolateral prefrontal cortex (47) and insula	43	41	4	329
Left inferior frontal gyrus (45/44), precentral gyrus (6), ventrolateral prefrontal cortex (47) and insula	−43	0	31	336
Bilateral thalamus and putamen, left caudate nucleus	4	−11	4	142
Right visual regions (18/19/7/40) and cerebellum	43	−67	−13	751
Left visual regions (18/19/7/39/40) and cerebellum	−47	−59	−24	802

Abbreviations: BA, Brodmann area; OCD, obsessive-compulsive disorder.
Voxel- and cluster-wise *P*-values were conservatively set at 0.02 and 0.01, respectively, yielding a total number of false positives <1.
Talairach coordinates refer to the voxels with the maximum change in % BOLD signal in each cluster.

amygdala/hippocampus complex; peak $x=-25$, $y=-4$, $z=-29$; 117 voxels), left ventrolateral/inferior frontal cortex extending to the superior temporal gyrus (BA47/44/45/38; peak $x=-47$, $y=19$, $z=-7$; 63 voxels) and thalamus/brain stem (peak $x=0$, $y=-22$, $z=4$; 44 voxels). Using a functional ROI approach, we next extracted the percent change in BOLD signal in the above frontopolar cluster and performed an ANOVA entering Axis I and Axis II comorbidity (coded as yes/no) as an independent factor. The main comorbidity and group by comorbidity interaction effects were all nonsignificant (data not shown).

Because different drugs may have different effects on brain function, we next repeated the whole-brain analyses excluding patients who were taking drugs other than selective serotonin reuptake inhibitors (SSRIs) (leaving 6 hoarders versus 8 non-hoarders). Again, the frontopolar cluster remained significant (BA11/10; peak $x=-4$, $y=67$, $z=-13$; 246 voxels). In addition, a cluster in the left ventrolateral/inferior frontal cortex extending to the superior temporal and the pre-central gyri was also significantly more activated in the hoarding than the non-hoarding group (BA47/44/45/38/6); peak $x=-43$, $y=33$, $z=-13$; 126 voxels). Finally, using a functional ROI approach, we entered medication use (coded as yes/no) as a factor in the ANOVA. The main medication and group by medication interaction effects were all nonsignificant (data not shown).

Aversive control experiment. There were few statistically significant differences between the 3 groups in this experiment. Hoarders showed significantly less activation in cerebellum and visual areas than non-hoarders and healthy controls. Non-hoarders

Table 5 Hoarding experiment: differences in neural responses between OCD hoarders ($n=13$), non-hoarding OCD patients ($n=16$) and healthy controls ($n=21$)

Brain regions (approximate BA)	x	y	z	*No. of voxels*
Hoarding OCD > non-hoarding OCD[a]				
Bilateral ventral frontal pole (11/10)	−4	67	−13	116
Hoarding OCD > healthy control[b]				
Bilateral ventral frontal pole (11/10)	0	67	−13	99
Right cerebellum	43	−63	−35	68
Left cerebellum	−47	−59	−29	35
Healthy control > hoarding OCD[c]				
Left orbitofrontal cortex (11)	−14	48	−18	15
Healthy control > non-hoarding OCD[a]				
Left orbitofrontal cortex (11)	−7	44	−18	34

Abbreviations: BA, Brodmann area; OCD, obsessive-compulsive disorder.
Talairach coordinates refer to the voxels with the maximum change in % BOLD signal in each cluster.
[a]Voxel- and cluster-wise *P*-values were conservatively set at 0.05 and 0.0075, respectively, yielding a total number of false positives <1.
[b]Voxel- and cluster-wise *P*-values were conservatively set at 0.05 and 0.01, respectively, yielding a total number of false positives <1.
[c]Voxel- and cluster-wise *P*-values were conservatively set at 0.05 and 0.005, respectively, yielding a total number of false positives <1.

demonstrated significantly greater activations in cerebellum and visual areas than controls (Table 6).

Planned correlation analyses (hoarding experiment only)

In the whole patient group ($n=29$), the level of provoked anxiety during the hoarding experiment significantly correlated with activation in the anterior VMPFC (BA10/11; $x=-4$, $y=52$, $z=-18$; 19 voxels), bilateral medial temporal structures (uncus, hippocampus, parahippocampal gyrus, extending to the amygdala and ventral striatum on the right side), left thalamus, bilateral pre- and postcentral gyri (BA6/4), right ventrolateral prefrontal cortex (BA47/10) and bilateral cerebellum. There were also significant negative correlations in widespread cortical and subcortical regions, including the left dorsal anterior cingulate gyrus (BA24), bilateral temporal cortex (BA21), bilateral dorsolateral/medial prefrontal regions (BA32/8/10/46), basal ganglia and various parieto-occipital regions (Table 7; Figure 3). These correlations remained highly significant after controlling for age, years of education, the remaining OCI-R subscales (washing, checking, ordering), overall OCD severity (Y-BOCS), depression (BDI) and state anxiety (STAI-S).

Discussion

This study investigated the neural correlates of hoarding symptoms in OCD. We compared the neural responses of 13 OCD patients with prominent and disabling hoarding symptoms, 16 OCD patients without hoarding symptoms and 21 healthy controls on a well-validated symptom provocation paradigm.[13,15,20] As predicted, hoarders felt significantly more anxious during symptom provocation than did non-hoarders and controls. Furthermore, in the entire OCD sample ($n=29$) the degree of provoked anxiety during the experiment was exclusively predicted by the severity of hoarding but not other types of OCD symptoms.

During the provocation of hoarding-specific anxiety, all 3 groups demonstrated a similar pattern of widespread activations in ventral prefrontal and limbic regions, thus replicating our initial report.[13] However, formal between-group comparisons found that hoarders demonstrated greater activation than non-hoarders and controls in a large bilateral cluster in the anterior VMPFC (BA11/10). This was independent from potentially confounding variables such as age, sex, education, comorbidity, use of medication, state anxiety and depression, which were all controlled for in various whole-brain and ROI *post hoc* analyses.

Whole-brain correlation analyses in the entire OCD group ($n=29$) confirmed and extended this finding; the level of provoked anxiety during the hoarding experiment correlated with activation in the anterior VMPFC and also in a wider neural network including bilateral medial temporal lobe structures (uncus, parahippocampal gyrus, hippocampus-amygdala extending to ventral striatum on the right), left thalamus, bilateral pre- and postcentral gyri, right ventrolateral prefrontal cortex and bilateral cerebellum. These correlations remained significant after statistically controlling for age, sex, education, overall OCD severity (Y-BOCS), state anxiety and depression.

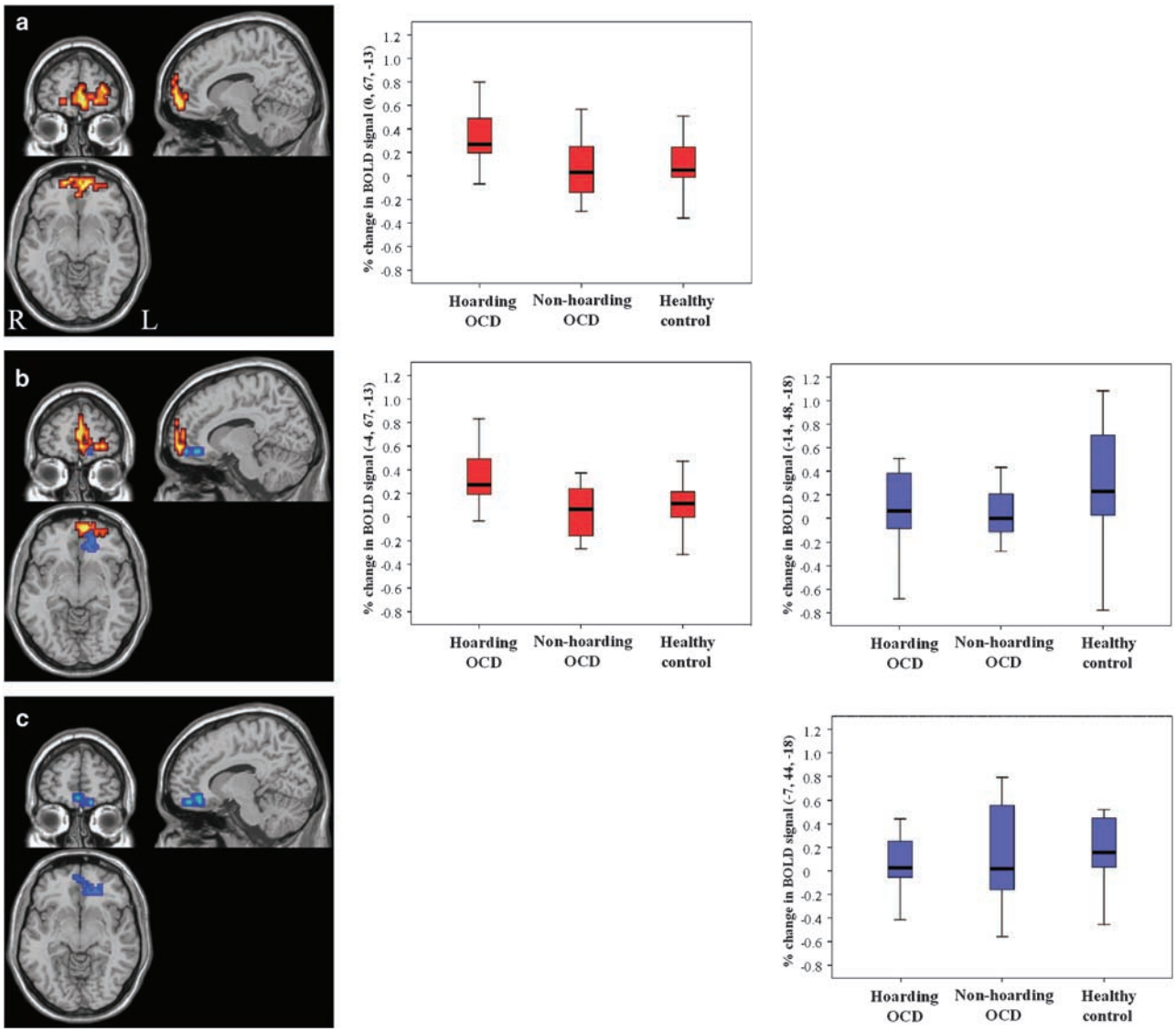

Figure 2 Brain regions significantly more activated in hoarders than in non-hoarders and controls (shown in red in (**a**) and (**b**)), and in healthy controls more than in hoarders and non-hoarders (shown in blue in (**b**) and (**c**)) during symptom provocation. The functional data are superimposed on a high-resolution anatomical template using the MRIcro software.[37] The left side of the brain appears on the right side of the image. The box plots depict the percent change in blood oxygen level dependent (BOLD) response in each group. In each box plot, the horizontal lines represent the group median, the box represents the quartiles and the whiskers the extreme values in each group.

The brain regions associated with compulsive hoarding in this study are anatomically very close to those associated with hoarding behaviors in the animal literature[10–12] and in human lesion studies.[4–9] Although it is plausible that hoarding behaviors caused by brain lesions may be phenomenologically and etiologically distinct from obsessive-compulsive hoarding, our results seem to suggest that they share similar neural substrates. That is, dysfunction in these brain regions (regardless its cause) seems to be associated with abnormal hoarding behaviors.

The specific function of these brain regions in compulsive hoarding is unclear but several of their key roles have been identified that are consistent with the clinical presentation of the disorder. Both lesion and neuroimaging studies suggest that the VMPFC, amygdala and nucleus accumbens are part of a neural network that is crucial for advantageous decision-making.[38–43] The current psychological model of compulsive hoarding emphasizes information processing deficits including decision-making.[1] Indeed, deciding what to keep and what to discard can be an extremely difficult task for these patients. We have recently reported that compulsive hoarders experience difficulties on a laboratory-based task of decision-making, the Iowa Gambling Task, despite intact performance on other neuropsychological tests.[18] It is therefore possible that the strong correlation between

Table 6 Aversive control experiment: differences in neural responses between OCD hoarders ($n=13$), non-hoarding OCD patients ($n=16$) and healthy controls ($n=21$)

Brain regions (approximate BA)	x	y	z	*No. of voxels*
Hoarding OCD < non-hoarding OCD[a]				
Right cerebellum and visual regions (18/19)	33	−85	−18	243
Left cerebellum and visual regions (17/18/19)	−36	−74	−35	223
Hoarding OCD < healthy control[b]				
Right cerebellum and visual regions (18/19/37)	26	−81	−18	185
Non-hoarding OCD > healthy control[b]				
Left cerebellum and visual regions (17)	−36	−74	−35	295

Abbreviations: BA, Brodmann area; OCD, obsessive-compulsive disorder.
Talairach coordinates refer to the voxels with the maximum change in % BOLD signal in each cluster.
[a]Voxel- and cluster-wise *P*-values were conservatively set at 0.05 and 0.01, respectively, yielding a total number of false positives <1.
[b]Voxel- and cluster-wise *P*-values were conservatively set at 0.05 and 0.0075, respectively, yielding a total number of false positives <1.

hoarding-related anxiety and activation in this neural network reflects greater difficulties among hoarders to decide upon the value or importance of the objects they were instructed to discard.

It is important to note that the ventromedial prefrontal cluster associated with hoarding in this study is situated somewhat anteriorly to the regions typically implicated in neuroimaging studies of decision-making. However, recent meta-analytical studies[44,45] suggest there may be an anterior-posterior functional distinction in the human orbitofrontal cortex, whereby the value of more complex and abstract reinforcers, such as monetary gain and loss, are represented more anteriorly and simpler reinforcers, such as taste or pain, are represented more posteriorly in the orbitofrontal cortex. Consistent with this anterior-posterior division, OCD hoarders showed increased activation in frontopolar regions when they were required to evaluate the 'hypothetical' future value of the presented objects or the consequences of discarding them.

The observed positive correlations between hoarding-related anxiety and activation in bilateral pre- and postcentral gyri replicate our previous fMRI study[15] and are likely to reflect the sensorimotor component of hoarding-related anxiety. Interestingly, in the resting state PET study by Saxena *et al.*,[14] the severity of compulsive hoarding also correlated with increased metabolism in sensorimotor cortex. This brain region has a crucial role in the visual processing of emotional material.[46]

Based on a previous PET study[14] we predicted that hoarders would show reduced activation in the dorsal anterior cingulate gyrus during symptom provocation. This hypothesis was partially confirmed. Both hoarding and non-hoarding patients showed significantly lower activation than healthy controls in a small cluster in the orbitofrontal cortex extending posteriorally to the cingulate gyrus. This cluster (peak activation: $x=-14$, $y=48$, $z=-18$) was more ventral and anterior to the one identified by Saxena *et al.*[14]($x=2$, $y=22$, $z=20$). Hoarding and non-hoarding patients showed comparably low activations in this region. This finding was not predicted and its significance is difficult to interpret, especially because activation in this region did not correlate with measures of hoarding, other OCD symptoms, overall OCD severity, anxiety or depression. However, in support of Saxena *et al.*'s findings, the degree of provoked anxiety in the hoarding experiment was negatively correlated with activation in the dorsal anterior cingulate gyrus (BA24; $x=-14$, $y=26$, $z=15$). This region has been implicated in a variety of cognitive functions including adaptive decision-making, that is, the ability to evaluate the outcome of choices, positive or negative, which have been voluntarily chosen,[47] which would be consistent with the clinical presentation of compulsive hoarding.

Hoarding-related anxiety also correlated inversely with activation in bilateral dorsal prefrontal regions, basal ganglia, temporal cortex and parieto-occipital regions. Clearly, more research is needed to understand the precise functional significance of these findings but the negative correlations with dorsal prefrontal-striatal and parietal regions could reflect deficient emotional regulation mechanisms in compulsive hoarding[48] and would also be consistent with difficulties in planning,[49] another important feature of this syndrome.[50] Interestingly, only non-hoarding patients activated regions of the basal ganglia during symptom provocation and the degree of provoked anxiety correlated inversely with activation in this region in the entire sample ($n=29$). Because the basal ganglia have been consistently implicated in non-hoarding OCD, our finding adds to the idea that the neural systems underlying compulsive hoarding are distinct from those implicated in other forms of OCD.

Table 7 Significant whole-brain correlations between provoked anxiety during the hoarding experiment and brain activation in the entire patient group ($n = 29$)

	x, y, z	*Cluster size*	*Cluster-wise* P-*value*
Positive correlations			
Left ventral frontal pole (BA10/11)	−4, 52, −18	19	0.000049
Right uncus (BA28), extending to hippocampus, parahippocampal gyrus (BA28/36), amygdala and ventral striatum	18, −11, −29	55	0.000049
Left hippocampus, extending to parahippocampal gyrus (BA36/28), uncus (BA28) and pons	−18, −11, −24	31	0.000049
Left thalamus	−4, −4, −2	34	0.000049
Left precentral gyrus (BA6/4)	−40, 0, 20	34	0.000049
Left precentral gyrus (BA4)/postcentral gyrus (BA1/2)	−32, −19, 48	29	0.000049
Right precentral gyrus (BA6)	51, 0, 42	22	0.000049
Right ventrolateral prefrontal cortex (BA47)/middle frontal gyrus (BA10)	47, 41, −2	21	0.000049
Left middle frontal gyrus (BA9)	−22, 44, 26	21	0.000049
Dorsal mid-cingulate gyrus (BA32/24)/medial frontal gyrus (BA6)	0, 7, 42	16	0.000049
Left cerebellum/brain stem	−4, −37, −35	10	0.000537
Right cerebellum	4, −52, −2	7	0.002
Right inferior parietal lobule (BA40)	58, −33, 26	6	0.00322
Negative correlations			
Right middle temporal gyrus (BA21)/posterior insula	43, −7, −13	74	0.000048
Left middle temporal gyrus (BA21)/posterior insula	−43, −11, −2	12	0.000048
Right medial frontal gyrus (BA32/8), superior and middle frontal gyrus (BA8)	18, 22, 37	48	0.000048
Right middle frontal gyrus (BA10/9/46)	22, 41, 9	44	0.000048
Left middle frontal gyrus (BA8)	−29, 22, 53	16	0.001450
Right middle frontal gyrus (BA8)	43, 18, 42	9	0.001209
Left anterior cingulate gyrus (BA24)/caudate nucleus	−14, 26, 15	23	0.000048
Right thalamus (pulvinar region)	22, −22, −7	13	0.000048
Left subgenual cingulate gyrus (BA25), extending to ventral striatum, putamen, caudate nucleus	−7, 11, −18	10	0.000048
Right anterior insula/putamen/caudate nucleus	25, 22, −7	9	0.000242
Right inferior parietal lobule (BA40)	−47, −48, 31	14	0.000048
Right fusiform gyrus (BA19)/cerebellum	22, −82, −13	29	0.000048
Left precuneus (BA7)/cuneus (BA19)	−4, −67, 31	26	0.000048
Right precuneus (BA7/19)	25, −67, 42	17	0.000048
Right inferior temporal gyrus (BA20)	43, −26, −29	9	0.000048
Left lingual (BA18) and inferior occipital gyrus (BA18)	−26, −81, −7	9	0.000048
Left fusiform gyrus (BA19)	−18, −81, −13	9	0.001064
Left inferior occipital gyrus (BA18)	−11, −96, −7	6	0.001982

As predicted, the 3 groups reported similar levels of anxiety and neural response during the aversive (symptom-unrelated) control experiment, indicating that the above findings were not a mere reflection of exaggerated neural responses to generally emotive stimuli in the hoarding group but rather syndrome-specific neural correlates. Interestingly, while hoarders showed greater activity in the cerebellum during the hoarding experiment, they showed reduced activation in this structure during the aversive control experiment. The reasons for this are unclear and will require further investigation.

Two methodological issues need to be considered when interpreting the results of this study. First, because all our hoarders met diagnostic criteria for OCD and had other OCD symptoms, the current results may not be generalizable to mono-symptomatic hoarders or hoarders who do not meet criteria for OCD. Whether these different types of hoarders are etiologically different is unclear and more research is needed. The second methodological consideration relates to the use of standardized stimuli rather than individually tailored stimuli. Arguably, the latter would have been more relevant and anxiety-provoking to the hoarding patients. However, this would be at the expense of experimental control. We therefore decided to use previously-validated standardized stimuli[13,15,20] to ensure that identical experimental stimuli are presented to all subjects (including controls), and therefore inter-individual differences

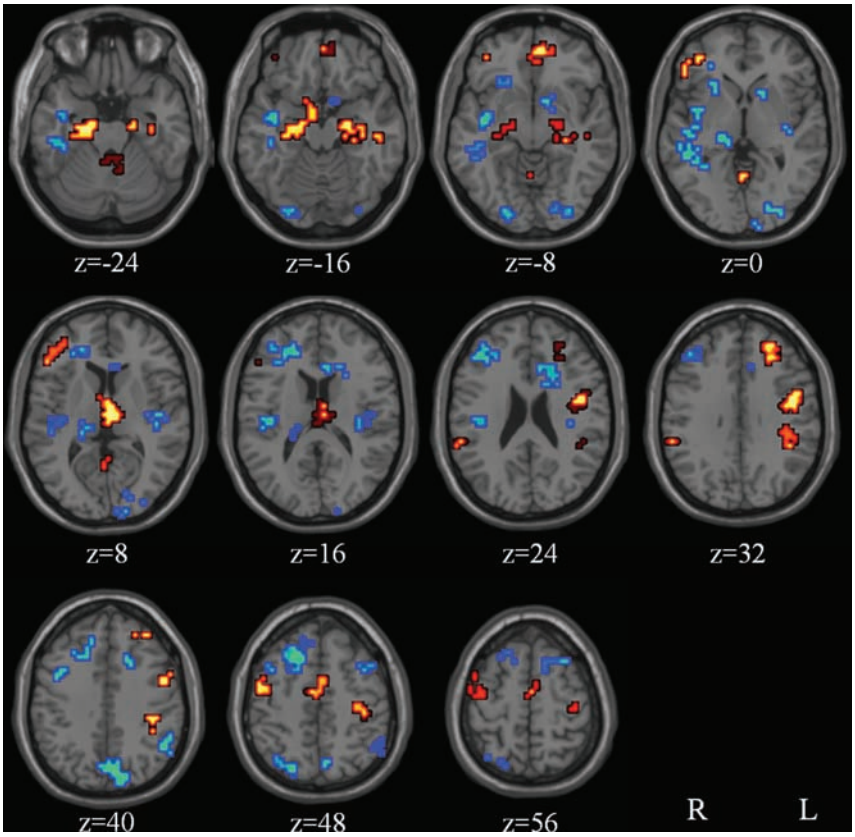

Figure 3 Significant positive (red) and negative (blue) correlations between provoked anxiety and brain activation during symptom provocation in the entire obsessive-compulsive disorder (OCD) group ($n = 29$). The functional data are superimposed on a high-resolution anatomical template using the MRIcro software.[37] R, right; L, left.

in brain activation cannot be attributed to the experience of different stimuli.

Our study had several limitations. The hoarding sample was small and we did not exclude patients with other Axis I or II disorders provided OCD was the main diagnosis. However, there were comparable levels of comorbidity in the hoarding and non-hoarding groups, and the effects of state anxiety and depression were statistically controlled for. Furthermore, when we repeated the analyses excluding patients with comorbid Axis I disorders, the results remained largely unchanged, although this analysis was underpowered. Most patients were medicated at the time of the study but there was no difference in the proportion of medicated patients in the hoarding and non-hoarding groups, medication had been stable for at least 6 weeks before the scan, and all patients were symptomatic at the time of the scan despite being on medication. The results remained largely unchanged when the analyses were repeated excluding patients taking medications other than SSRIs. However, replication of the results in a drug-free sample would be desirable.

In summary, hoarding symptoms in OCD are associated with dysfunction in a frontolimbic network previously associated with hoarding behavior in animal and human lesion studies. These findings may represent the neurophysiological substrate of the well-documented decision-making difficulties in compulsive hoarding.[1] Negative correlations in brain regions that are important for emotional regulation and planning are also consistent with the clinical features of this syndrome. Overall, the results support the notion of a multidimensional model of OCD, whereby this disorder is a compendium of multiple potentially overlapping syndromes rather than a unitary disease entity.[2]

Acknowledgments

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