ORIGINAL ARTICLE

Neural Mechanisms of Decision Making in Hoarding Disorder

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Context: Hoarding disorder (HD), previously considered a subtype of obsessive-compulsive disorder (OCD), has been proposed as a unique diagnostic entity in *DSM-5*. Current models of HD emphasize problems of decision-making, attachment to possessions, and poor insight, whereas previous neuroimaging studies have suggested abnormalities in frontal brain regions.

Objective: To examine the neural mechanisms of impaired decision making in HD in patients with well-defined primary HD compared with patients with OCD and healthy control subjects (HCs).

Design: We compared neural activity among patients with HD, patients with OCD, and HCs during decisions to keep or discard personal possessions and control possessions from November 9, 2006, to August 13, 2010.

Setting: Private, not-for-profit hospital.

Participants: A total of 107 adults (43 with HD, 31 with OCD, and 33 HCs).

Main Outcome Measures: Neural activity as measured by functional magnetic resonance imaging in which actual real-time and binding decisions had to be made about whether to keep or discard possessions.

Results: Compared with participants with OCD and HC, participants with HD exhibited abnormal activity in the anterior cingulate cortex and insula that was stimulus dependent. Specifically, when deciding about items that did not belong to them, patients with HD showed relatively lower activity in these brain regions. However, when deciding about items that belonged to them, these regions showed excessive functional magnetic resonance imaging signals compared with the other 2 groups. These differences in neural function correlated significantly with hoarding severity and self-ratings of indecisiveness and "not just right" feelings among patients with HD and were unattributable to OCD or depressive symptoms.

Conclusions: Findings suggest a biphasic abnormality in anterior cingulate cortex and insula function in patients with HD related to problems in identifying the emotional significance of a stimulus, generating appropriate emotional response, or regulating affective state during decision making.

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CURRENT MODELS OF hoarding disorder (HD)—defined as the excessive acquisition of and inability to discard objects, resulting in debilitating clutter[1]—identify various deficits in cognitive processes, as well as maladaptive beliefs and behavioral patterns, as relevant underlying mechanisms.[2-4] Specific cognitive impairments noted in patients with HD include impaired attention,[5,6] impaired verbal and nonverbal recall,[7] and impaired categorization and decision-making ability.[8,9] Maladaptive beliefs include perfectionism and fears of making wrong decisions,[10,11] fears of wasting or losing important information,[12] and emotional or anthropomorphic attachment to possessions.[13] The disorder is characterized by marked avoidance of decision making about possessions. Patients with HD are frequently characterized by poor insight about the severity of their condition,[14,15] leading to resistance of attempts by others to intervene. Such impairments might suggest abnormalities in frontal cortical regions and the anterior cingulate cortex (ACC), which are involved with executive functions, such as decision making and categorization,[16-18] and temporal regions that are associated with memory, categorization, and attachment of affective or motivational significance to stimuli.[19,20]

Four studies have used neuroimaging technology to examine regional brain function associated with hoarding. Positron emission tomography research reveals that patients with obsessive-compulsive disorder (OCD) with hoarding symptoms have lower resting state glucose metabolism in the posterior cingulate and cuneus than do healthy control subjects (HCs) and lower glucose metabolism in the dorsal ACC than do patients with OCD without hoarding symptoms.[21] Functional magnetic resonance imaging (fMRI)

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reveals that patients with OCD (mostly patients with OCD without hoarding symptoms) asked to imagine discarding an item experience greater activity in the left precentral gyrus and right medial orbitofrontal cortex (OFC) than do HCs,[22] and patients with OCD with hoarding symptoms experience greater activation in the ventromedial prefrontal cortex than do patients with OCD without hoarding symptoms and HCs using the same task.[23] During actual decision making about real possessions, patients with HD experience greater activity in the left lateral OFC and parahippocampal gyrus than do HCs.[24]

Thus, results to date implicate frontal and temporal regions thought to underlie problems of decision making, attachment, reward processing, impulse control, self-awareness, and emotion regulation. However, substantial differences in population and methods across these studies preclude clear generalization of conclusions. The objective of the present study is to provide a clearer examination of the neural mechanisms of impaired decision making that are specific to HD. Unlike previous research, the present study recruited patients with well-defined primary HD and compared them with patients with OCD and HCs using a unique fMRI task in which actual, real-time, and binding decisions had to be made about whether to keep or discard possessions. We predicted that, compared with patients with OCD and HCs, patients with HD would experience increased hemodynamic activity in the frontal and temporal cortical regions, including the ventromedial prefrontal cortex, OFC, ACC, and parahippocampal gyrus, when deciding whether to discard their own possessions. No such differences were predicted when participants were deciding whether to discard control items that did not belong to them. We further predicted that fMRI measures in the aforementioned regions of interest (ROIs) would reveal a unique relationship to hoarding symptom severity, independent of severity of OCD or depressive symptoms.

METHODS

STUDY PARTICIPANTS

Forty-three patients with HD, 31 patients with OCD, and 33 HCs participated in the study and provided written informed consent. The patients with HD were recruited using advertisements for people with "clutter problems" or "hoarding" and from the existing patient group at a clinic specializing in HD treatment. The patients with OCD were recruited using advertisements seeking people with OCD, and the HCs were recruited using advertisements for a brain imaging study. All the assessments were conducted by well-trained postdoctoral fellows or postgraduate research assistants. Participants were classified as having HD if they met the clinical criteria outlined by Frost and Hartl[25] and proposed for *DSM-5*,[26] hoarding was their primary diagnosis as defined by Clinical Severity Ratings on the Anxiety Disorders Interview Schedule for *DSM-IV*,[27] the Clinician's Global Impression[28] rating was "moderately ill" or above, and symptom duration was 1 year or longer. One potential participant with comorbid HD and OCD was excluded from the study, given the study aim of comparing HD and OCD. Where there were questions about the severity of hoarding, symptom severity was confirmed via home visit or analysis of current photographs of living space. The patients with OCD met diagnostic criteria for a primary diagnosis of (nonhoarding) OCD, had at least moderate symptom severity as evidenced by a Clinician's Global Impression rating of moderately ill or above, and had at least 1 year of symptom duration. The HD or OCD participants were excluded if they had a history of psychotic disorder, neurologic disorder, substance abuse, or serious suicidal ideation. Healthy controls were excluded if they met criteria for a current or past Axis I or Axis II disorder, had a history of neurologic disorders, or were taking psychiatric medications. Participants who were unsuitable for fMRI (eg, those with severe claustrophobia, pregnancy, or metal implants) were excluded.

OUTCOME MEASURES

Demographic information, including self-reported race and ethnicity, was collected via questionnaire. The HD diagnoses were made using the Hoarding Rating Scale–Interview,[29] a semistructured interview that assesses the severity of clutter, acquisition, difficulty discarding, distress, and impairment, each on a 0- to 8-point scale. Other psychiatric diagnoses were ascertained using the Anxiety Disorders Interview Schedule for *DSM-IV*.[27] Severity of HD was assessed using the Saving Inventory–Revised,[30] a 23-item questionnaire. Nonhoarding OCD severity was assessed using the Obsessive Compulsive Inventory–Revised (OCI-R),[31] an 18-item self-report measure. For use in analysis of covariance, a total OCI-R score was calculated that omitted the 3 hoarding items. Depression severity was assessed using the Hamilton Rating Scale for Depression (HRSD),[32] a 17-item semistructured interview. The Structured Interview Guide for the HRSD[33] was used for administration. Global impressions of illness severity were recorded using the Clinician's Global Impression[28] scale. A series of visual analog scales (VASs) were constructed for the present study. For each VAS, an emotion label and numeric scale (0-100) were presented on the computer screen. The emotions to be rated included anxiety, indecisiveness, sadness, and "not just right" feelings.

STUDY MATERIALS

For the decision-making task, we selected 2 different sets of stimuli. The first set was paper items (eg, junk mail and newspapers) that belonged to the participants. Participants were instructed to bring to the scanner session paper items from their homes without sorting them first. We refer to these items as participant's possessions (PPs). The second set of stimuli was comparable paper items that did not belong to the participant. For each participant, we selected items that were roughly the same amount, size, and type as the participant's items. We refer to these items as experimenter's possessions (EPs).

STUDY APPARATUS

Imaging data were acquired using a scanner (Siemens 3T Allegra scanner). Head motion was restricted using a custom-built apparatus that interfaced with the head coil. Functional image volumes were collected with an EPI gradient-echo pulse sequence (repetition time/echo time, 1500/28 milliseconds; flip angle, 65°; field of view, 24 × 24 cm; 64 × 64 matrix; 3.4 × 3.4-mm plane resolution; 5-mm section thickness; 29 sections; 4 + 1-mm gap) that effectively covers the entire brain in 1.5 seconds. Visual stimuli were presented using a projection system (5000 ANSI lumens) and displayed on a high-resolution screen located just behind the individual's head. Participants viewed this screen using a mirror attached to the head coil. A magnetic resonance–compatible fiberoptic response device (Photon Control) acquired participant responses for offline assessment.

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STUDY PROCEDURES

All the study procedures were approved by the institutional review board at Hartford Hospital. Participants signed written informed consent forms before the study. Study procedures were conducted from November 9, 2006, to August 13, 2010.

Before the fMRI appointment, participants completed all self-report measures and were interviewed by a doctoral-level assessor or an advanced research assistant. Each PP and EP was scanned into the computer. Participants engaged in a practice trial in the assessor's office in which they sat in front of a computer screen, with instructions as follows: "You will be shown a paper item and you will have to decide whether to discard it or not. If you choose to discard the item, we will put it through the shredder. If you choose to keep the item, we will not shred this item and will give it to you. During this task, you will see both your mail and our mail. Before you see your item, you will see the word 'yours.' You will then be shown a picture of your item surrounded by a red border. Before you see each piece of our paper items, you will see the word 'ours' followed by a picture of the item with a black border." Participants were then shown several PPs and EPs. After each, they indicated whether they chose to keep or discard the item. At the end of the practice trial, the items to be discarded were placed in a paper shredder while the participant watched. Items to be kept were given to the participant.

After watching the possessions being placed in the scanner and being given sufficient time to habituate to the environment, participants were presented with pictures of the PPs or EPs and asked to make the decision of whether to keep or discard the items, with the order of item presentation counterbalanced across fMRI sessions and across participants. Participants were given 6 seconds to indicate their decision (keep vs discard) via a button press. If no response was made, the next stimulus was presented. Participants completed 2 sessions, each containing 25 EP and 25 PP images.

After each fMRI session, participants were presented with the VASs, preceded by the following written and spoken instructions: "Think back to when you were deciding whether or not to shred your mail during these past few minutes. We want to know about a variety of emotions you might have been feeling during the task. For each emotion tell us how you were feeling on a scale from 0 to 100 where 0 equals none/not at all and 100 equals extremely/the most you have felt in your life." Participants responded verbally to each VAS. After the end of both fMRI sessions, the items to be discarded were destroyed in the shredder while participants watched and items to be kept were given to the participant.

IMAGE PROCESSING

Functional images were reconstructed offline and reoriented to approximately the anterior commissure–posterior commissure plane. The 2 functional image runs were realigned using INRIAlign, spatially normalized using custom linear and nonlinear algorithms,[34] smoothed, and analyzed in standard Montreal Neurological Institute space using Statistical Parametric Mapping. Event-related responses were modeled using a synthetic hemodynamic response function and a second temporal derivative term. The modeled hemodynamic response for each run was derived by constructing a sequence of appropriately located synthetic responses for each EP and PP class of stimuli. Any time point for which estimates of head motion exceeded 1 voxel length in any x, y, z dimension were censored from the model by inclusion of a separate regressor that accounted for variance related to that image only. A 128-second, high-pass filter was incorporated into the model to remove noise associated with low-frequency confounders (eg, respiratory artifact).

For both groups, contrasts were specified on an individual basis that evaluated the effects of deciding to discard PPs or EPs relative to unmodeled fixation time, using estimates of blood oxygenation level–dependent signal change from the 6-second decision-making periods. The images that contained these amplitudes were then entered into the second-level analyses (ie, random-effects analyses).

STATISTICAL ANALYSIS

Self-report measures and behavioral data were analyzed using 1-way analyses of variance with Tukey follow-up tests. Categorical data were compared using χ^2 analyses. Imaging results were analyzed using a 3 (group: HD, OCD, HC) × 2 (item type: PP, EP) mixed-factor generalized linear model with appropriate pairwise comparisons. To control for the possible effects of OCD symptoms and depression, these analyses were repeated using HRSD and OCI-R total score (without hoarding items) as covariates. Because this is a novel task, no previous studies exist to precisely select a priori ROIs. Therefore, the overall analytic strategy was to identify brain regions with a main effect of item type (ie, PP vs EP) in all participants, then to query these regions for significant item type × diagnostic group differences. Main effects of diagnostic group also were evaluated. In this way, we were able to focus our inquiry on those brain regions most relevant to decision making related to the subjective context of ownership. Once these ROIs were identified, we used a small volume correction assessment within 8-mm-radius spheres centered on the coordinates of peak item type effects in each region. Small volume correction analyses used a familywise error rate ($P < .05$) to control for searching multiple voxels within each ROI. Finally, we conducted several post hoc analyses of the HD group to determine whether brain activation to PPs was associated with Saving Inventory–Revised and HRSD scores, as well as VAS ratings of anxiety, indecisiveness, sadness, or feeling just not right during scanning. After determining these significant correlations, the group × item type interactions were conducted again using each of the 4 VAS ratings as covariates.

RESULTS

SAMPLE DESCRIPTION

The HD and HC groups were well matched for age and sex (**Table 1**); however, the OCD group was significantly younger and contained more male participants than did the other 2 groups. Analyses of covariance, controlling for age and sex, did not alter the obtained results and are, therefore, not reported in detail. As expected, the HD group exhibited significantly greater hoarding severity than did the other 2 groups, and the OCD group exhibited significantly greater OCD severity than did the other 2 groups (although some minor but significant elevation was seen in HD participants as well). The HD and OCD participants exhibited higher levels of depression than did the HC group and did not differ from each other, although the HD group was more likely than the OCD group to be diagnosed as having a comorbid depressive disorder. The OCD group was more likely to be taking psychiatric medications (primarily selective serotonin reuptake inhibitor antidepressants) than was the HD group.

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Table 1. Characteristics of the Study Participants[a]

Characteristic	Mean (SD)				
	Patients With HD (n = 43)	Patients With OCD (n = 31)	Healthy Control Subjects (n = 33)	*F*	χ^2
Age, y	49.81 (8.72) A	32.16 (11.97) B	46.61 (12.68) A	24.73[b]	
Female, No. (%)	32 (74.4) A	10 (32.3) B	25 (75.8) A		17.20[b]
White, No. (%)	39 (90.7)	29 (93.5)	30 (90.9)		0.90
SI-R clutter	27.28 (5.82) A	4.57 (5.89) B	1.67 (2.65) B	293.38[b]	
SI-R difficulty discarding	19.86 (4.02) A	5.13 (5.02) B	1.39 (1.97) C	246.50[b]	
SI-R acquiring	16.21 (5.32) A	3.87 (3.30) A	2.03 (2.07) A	143.41[b]	
HRSD	7.14 (4.72) A	5.46 (5.46) A	1.12 (1.75) B	18.76[b]	
OCI-R hoarding	9.84 (2.37) A	1.61 (1.99) B	0.79 (1.11) B	254.93[b]	
OCI-R checking	1.88 (1.90) A	3.52 (3.77) B	0.18 (0.39) C	15.87[b]	
OCI-R neutralizing	1.26 (1.80) A	2.84 (3.13) B	0.12 (0.42) C	14.18[b]	
OCI-R obsessions	1.67 (2.49) A	6.81 (3.75) B	0.12 (0.48) C	59.35[b]	
OCI-R ordering	3.70 (2.86) A	2.90 (2.94) A	1.06 (1.17) B	10.67[b]	
OCI-R washing	1.21 (1.77) A	3.16 (3.41) B	0.06 (0.24) A	16.88[b]	
Comorbid anxiety disorder, No. (%)	23 (53.5)	11 (35.5)			2.35
Comorbid depressive disorder, No. (%)	22 (51.2) A	8 (25.8) B			4.80[c]
Taking psychiatric medications, No. (%)	24 (55.8)	24 (82.8)			5.66[c]

Abbreviations: HD, hoarding disorder; HRSD, Hamilton Rating Scale for Depression; OCD, obsessive-compulsive disorder; OCI-R, Obsessive Compulsive Inventory–Revised; SI-R, Saving Inventory–Revised.

[a] Data are presented as mean (SD) unless otherwise indicated. Within each row, groups with different small capital letters are significantly different ($P < .05$).

[b] $P < .01$.

[c] $P < .05$.

BEHAVIORAL DATA

The HD group chose to discard significantly fewer PPs than did the OCD and HC groups (**Table 2**). No group differences were found for the number of EPs discarded. The VAS ratings revealed that HD participants reported greater anxiety, indecisiveness, and sadness than did the other 2 groups. The HD and OCD participants both reported greater not just right feelings during the task than did HCs. Anxiety, indecisiveness, sadness, and not just rightVAS ratings correlated significantly ($P < .05$) with the number of PPs discarded ($r = -0.40$, -0.54, -0.35, and -0.39, respectively) and the number of EPs discarded ($r = -0.22$, -0.39, -0.20, and -0.32, respectively). Thus, the experimental manipulation successfully distinguished HD patients from the other groups for the number of items discarded and aversive emotions during the task.

IDENTIFYING ROIs ASSOCIATED WITH OWNERSHIP

The PP vs EP decisions were associated with significantly ($P < .05$) greater activity across a range of regions (**Table 3**), including the middle and inferior frontal gyrus, ACC, insular cortex, midcingulate gyrus, inferior parietal lobule, precuneus, amygdala, parahippocampal gyrus, hippocampus, fusiform gyrus, uncus, superior temporal gyrus, caudate, globus pallidus, thalamus, cerebellum, midbrain, and pons (no regions were associated with significantly greater activity for EP decisions than for PP decisions). These ROIs were then examined further for group differences and group × item interactions.

DIFFERENCES IN HEMODYNAMIC ACTIVITY AMONG PATIENTS WITH HD, PATIENTS WITH OCD, AND HCs

Group × item interactions (**Table 4** and **Figure**) were detected in the ACC, inferior frontal gyrus, insula, precuneus, hippocampus, globus pallidus, and cerebellum. Post hoc pairwise comparisons of PP vs EP decisions revealed that patients with HD differed significantly from HCs and patients with OCD in the ACC ($P < .01$) and left and right insular cortex ($P < .05$). In the ACC and left insular cortex, patients with HD had a relative lack of fMRI signal during EP decisions and greater activity during PP decisions. In the right insular cortex, patients with HD experienced a greater proportional increase in fMRI signal during PP decisions. The other interaction effects were all driven by the OCD group failing to show a differential reaction to PPs vs EPs compared with the HD and HC groups, which did not differ from each other.

In addition to these interaction effects, main group effects were detected in the middle and inferior frontal gyrus, midcingulate gyrus, inferior parietal lobule, precuneus, amygdala, parahippocampal gyrus, fusiform gyrus, uncus, superior temporal gyrus, caudate, and thalamus. Pairwise comparisons revealed that in each of these regions, patients with OCD had a significantly lower fMRI signal than did the other 2 groups. The HD group had a lower fMRI signal than did the HC group in the left fusiform gyrus, left thalamus, and right thalamus.

When controlling for depression (HRSD), the interaction and group main effects were identical, suggesting that depression did not contribute significantly to the observed patterns. When controlling for OCD (OCI-R total without hoarding items), the item type × group

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Table 2. Behavioral Data of the Study Participants[a]

Variable	Patients With HD (n = 43)	Patients With OCD (n = 31)	Healthy Control Subjects (n = 33)	*F*
No. of PPs discarded	29.42 (11.04) A	36.77 (11.09) B	40.36 (10.60) B	9.99[b]
No. of EPs discarded	40.60 (10.55)	43.07 (9.66)	45.48 (10.40)	2.12
Response time for PP decisions, milliseconds	2803.76 (615.18) A	2410.62 (575.38) B	2285.70 (738.14) B	6.58[c]
Response time for EP decisions, milliseconds	2295.58 (847.28) A	2038.34 (700.93)	1746.22 (746.04) B	4.60[c]
Anxiety ratings during task	34.65 (23.39) A	20.48 (16.61) B	10.00 (13.34) B	16.34[b]
Indecisiveness ratings during task	31.63 (24.63) A	16.53 (19.09) B	5.68 (8.86) B	17.22[b]
Sadness ratings during task	11.86 (16.45) A	2.82 (5.11) B	0.00 (0.00) B	12.67[b]
"Not just right" ratings during task	25.41 (21.65) A	18.15 (21.23) A	4.92 (8.48) B	11.56[b]

Abbreviations: EPs, experimenter's possessions; HD, hoarding disorder; OCD, obsessive-compulsive disorder; PPs, participant's possessions.
[a]Within each row, groups with different small capital letters are significantly different ($P < .05$). Data are presented as mean (SD) unless otherwise indicated.
[b] $P < .01$.
[c] $P < .05$.

Table 3. Significant Main Effects of Item Type (Personal Possessions vs Experimenter Possessions) in Hemodynamic Activity During Decision Making

Region	MNI	*F*
Left middle frontal gyrus (BA 6)	−21, 15, 60	59.21
Right middle frontal gyrus (BA 6)	30, 18, 57	57.88
Midline superior frontal gyri (BA 6/32)	−3, 24, 42	99.43
Left middle frontal gyrus (BA 9/46)	−39, 21, 30	42.56
Right middle frontal gyrus (BA 9)	36, 36, 42	29.51
Anterior cingulate cortex	0, 33, 21	59.73
Left inferior frontal gyrus (BA 46)	−42, 39, 15	35.55
Right inferior frontal gyrus (BA 46/10)	48, 45, 15	45.20
Midline medial frontal gyrus (ventromedial cortex)	0, 48, −9	51.57
Left inferior frontal gyrus (BA 47/11)	−27, 27, −21	99.52
Left inferior frontal gyrus	−39, 33, 0	27.67
Right inferior frontal gyrus (BA 47/11)	27, 33, −18	82.82
Left insular cortex	−36, 15, −3	53.15
Right insular cortex	33, 15, −3	48.44
Middle cingulate gyrus	−3, −33, 39	146.15
Left inferior parietal lobule	−45, −39, 42	28.68
Right inferior parietal lobule	51, −33, 45	34.78
Left precuneus and superior parietal lobule (BA 19/7)	−33, −72, 42	66.68
Left precuneus and superior parietal lobule and angular gyrus (BA 19/7/39)	33, −72, 45	62.57
Left posterior cingulate and precuneus	−9, −57, 15	165.90
Right posterior cingulate and precuneus	9, −48, 12	74.61
Left amygdala	33, −3, −21	32.25
Right amygdala	24, 0, −18	26.32
Left parahippocampal gyrus	−30, −24, −21	73.34
Right parahippocampal gyrus	30, −21, −24	65.49
Left hippocampus	−24, −15, −21	23.08
Right hippocampus	15, −3, −15	25.14
Left fusiform gyrus	−21, −45, −12	46.97
Right fusiform gyrus	24, −42, −12	76.01
Right uncus	30, −3, −39	34.49
Left superior temporal gyrus (temporal pole)	−42, 15, −21	37.56
Bilateral cuneus and inguinal (BA 18/17/19)	6, −93, 15	283.72
Left caudate	−18, 18, −3	27.08
Left globus pallidus and putamen	−9, 0, −6	76.68
Right globus pallidus and putamen	18, −9, 3	32.64
Left thalamus	−6, −12, 0	48.60
Right thalamus	12, −9, 0	49.87
Anterior cerebellum (vermis)	0, −63, −30	34.02
Left posterior cerebellum (declive)	−36, −69, −27	27.95
Right posterior cerebellum (declive)	36, −69, −30	33.52
Midbrain	−6, −30, −21	56.34
Brainstem (pons)	0, −36, −39	38.56

Abbreviations: BA, Brodmann area; MNI, Montreal Neurological Institute.

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Table 4. Significant Group and Item Type × Group Interaction Effects in Hemodynamic Activity During Decision Making for Regions Identified as Relevant to Ownership

	Main Effect of Group			Item Type × Group Interaction		
Region	MNI	*F*	*d*	MNI	*F*	*d*
Right middle frontal gyrus (BA 9)	36, 33, 42	7.76[a]	0.39	36, 36, 45	4.11	
Anterior cingulate cortex	0, 30, 21	0.35		0, 30, 21	5.61[b]	0.33
Left inferior frontal gyrus (BA 46)	−42, 39, 12	5.66[b]	0.33	−42, 39, 15	5.28[b]	0.32
Right inferior frontal gyrus (BA 46/10)	45, 45, 15	5.09[b]	0.31	45, 45, 15	2.57	
Left inferior frontal gyrus	−42, 33, 0	6.53[b]	0.35	−36, 33, 0	1.25	
Left insular cortex	−36, 12, −3	3.83		−36, 12, −3	4.76[b]	0.30
Right insular cortex	30, 15, −3	2.55		33, 15, 0	6.94[a]	0.37
Middle cingulate gyrus	−3, −33, 42	9.73[a]	0.43	−6, −33, 39	1.06	
Right inferior parietal lobule	51, −33, 42	7.15[a]	0.37	48, −33, 45	1.68	
Left precuneus and superior parietal lobule	−33, −69, 42	4.81[b]	0.30	−33, −69, 42	1.63	
Right posterior cingulate and precuneus	9, −48, 9	4.39		9, −45, 12	7.11[a]	0.37
Left amygdala	33, −6, −21	5.59[b]	0.33	33, −3, −24	1.49	
Right amygdala	27, 0, −18	6.20[b]	0.35	24, −3, −18	3.12	
Left parahippocampal gyrus	−27, −24, −21	7.53[a]	0.38	−30, −21, −21	3.21	
Right parahippocampal gyrus	27, −21, −24	6.13[b]	0.34	30, −21, −21	2.51	
Left hippocampus	−21, −15, −21	6.42[b]	0.35	−24, −15, −18	7.05[a]	0.37
Right hippocampus	18, −3, −15	3.11		15, −6, −15	6.23[b]	0.35
Left fusiform gyrus	−21, −42, −12	11.64	0.47	−21, −45, −15	1.41	
Right uncus	30, −3, −36	6.52[b]	0.35	30, 0, −39	0.49	
Left superior temporal gyrus (temporal pole)	−45, 15, −21	5.75[b]	0.33	−39, 15, −21	2.37	
Left caudate	−18, 21, −3	5.01[b]	0.31	−18, 18, −6	2.49	
Left globus pallidus and putamen	−12, 0, −6	4.70[b]	0.30	−9, 0, −3	4.86[b]	0.31
Right globus pallidus and putamen	21, −9, 3	8.44[a]	0.40	21, −9, 3	6.80[a]	0.36
Left thalamus	−9, −12, 0	5.60[b]	0.33	−6, −9, 0	2.66	
Right thalamus	12, −12, 0	8.31[a]	0.40	15, −9, 0	4.55	
Anterior cerebellum (vermis)	0, −66, −30	6.94[a]	0.37	0, −60, −30	5.56[b]	0.33
Left posterior cerebellum (declive)	−36, −66, −27	3.75		−33, −69, −27	4.24[b]	0.29
Right posterior cerebellum (declive)	36, −69, −30	6.43[a]	0.35	36, −69, −30	5.41[b]	0.32

Abbreviations: BA, Brodmann area; MNI, Montreal Neurological Institute.
[a] $P < .01$.
[b] $P < .05$.

interactions remained significant in the ACC, inferior frontal gyrus, insula, precuneus, hippocampus, globus pallidus, and cerebellum but not the inferior frontal gyrus. Thus, nonhoarding OCD does not seem to have contributed to the hoarding-related significant interactions. Most of the group main effects (within which the OCD group had been the outlier) became nonsignificant, with the exception of the midcingulate gyrus, right inferior parietal lobule, left parahippocampal gyrus, left fusiform gyrus, and right uncus.

RELATIONSHIPS BETWEEN HEMODYNAMIC ACTIVITY DURING PP DECISIONS AND INDICES OF SYMPTOM SEVERITY FOR PATIENTS WITH HD

Anxiety ratings during PP decisions correlated positively with activity in the inferior and middle frontal gyrus (**Table 5**). Indecisiveness ratings also correlated positively with activity in the inferior frontal gyrus but also with activity in the insula and uncus. Sadness ratings correlated positively with activity in the inferior frontal gyrus, superior temporal gyrus, and ventral striatum. Not just right feelings correlated positively with activity in the inferior frontal gyrus, ACC, insula, superior temporal gyrus, precuneus, ventral striatum, and hippocampus. Each of these 4 VAS ratings were then entered as covariates into the group × item type interactions; results were unchanged (data not shown), suggesting that the obtained interactions cannot be explained solely on the basis of acute emotional reaction.

Total scores on the Saving Inventory–Revised were positively correlated ($P < .01$) with activity in the right insula and right superior parietal lobule and negatively correlated with activity in the right precentral gyrus and cuneus. The ratio of saved to discarded items was positively correlated with activity in the right fusiform gyrus and pons. The HRSD scores were positively correlated ($P < .01$) with activity in the right middle frontal gyrus and right caudate (head and tail) and negatively correlated with activity in the left middle and inferior frontal gyrus, midcingulate gyrus, right inferior frontal and superior temporal gyrus, midline precuneus, and left middle and superior temporal gyrus.

COMMENT

The present findings of ACC and insula abnormality comport with emerging models of HD that emphasize problems in decision-making processes[3,35] that contribute to patients' difficulty discarding items. The region of ACC in the present findings is commonly associated with error monitoring under conditions of uncertainty,[16,17] and

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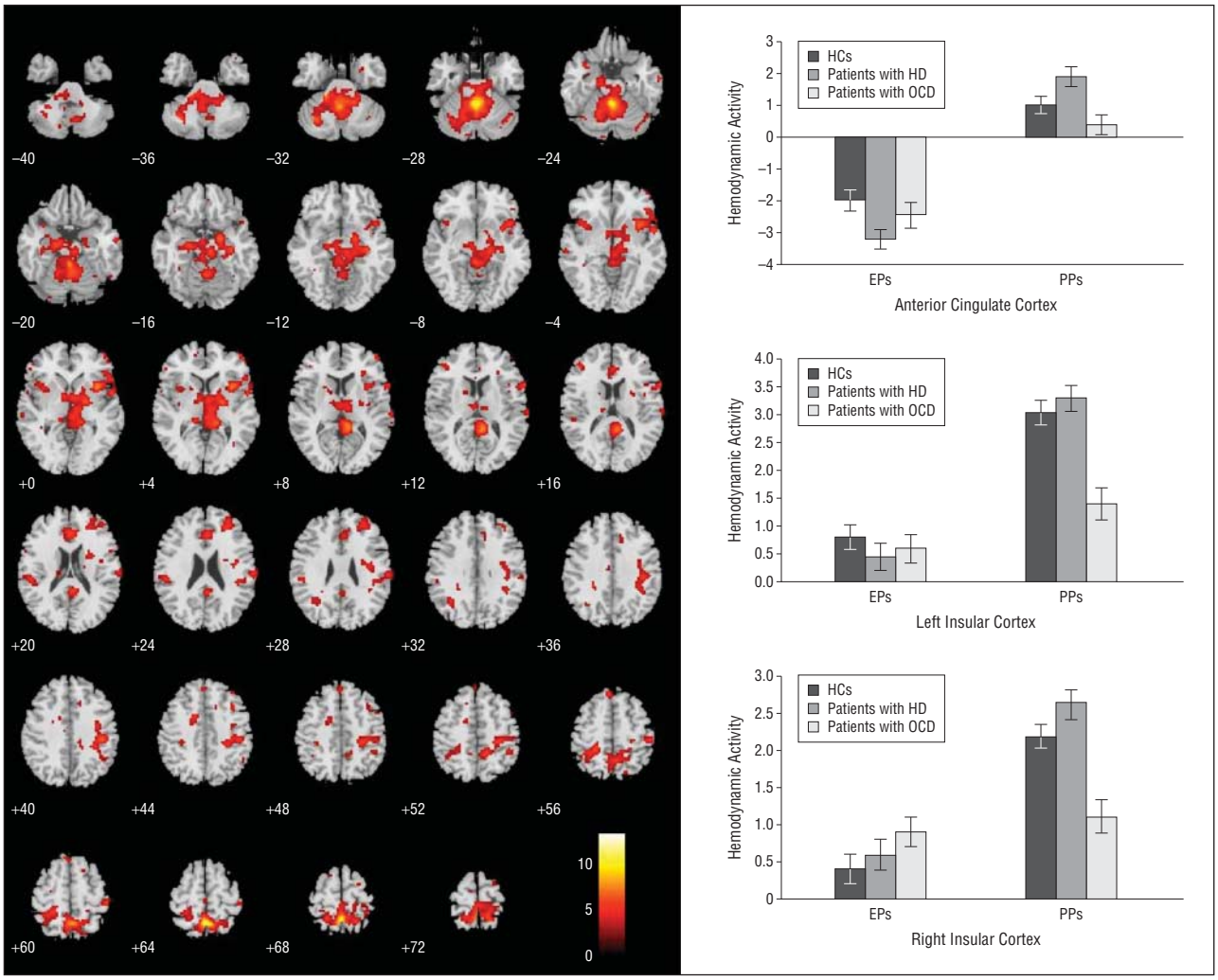

Figure. Increased hemodynamic activity for patients with hoarding disorder (HD), patients with obsessive-compulsive disorder (OCD), and healthy control subjects (HCs) while deciding about experimenter's possessions (EPs) vs personal possessions (PPs). Error bars indicate mean (SD).

the mid-to-anterior insula regions in the present findings are thought to be associated with interoception, perception of unpleasant feeling states, and the salience of stimuli,[36,37] error monitoring,[18] risk assessment,[38] and emotion-driven decisions.[39] Together, these regions are thought to be part of a functionally connected network of structures used to identify the emotional significance of a stimulus, generate an emotional response, and regulate affective state.[36,37,40-42]

The apparent biphasic pattern (ie, hypofunction to EPs but hyperfunction to PPs) of ACC and insula activity in patients with HD merits further study. These regions, considered to be at the core of a "salience network,"[42(p656)] were hypoactive in patients with HD when not making decisions about their own possessions, a finding that is consistent with the baseline positron emission tomography results of Saxena et al.[21] Low activity in this network, a pattern reminiscent of that seen in patients with autism spectrum disorders,[43] may result in attenuated response to salient stimuli (including disgust-eliciting stimuli[44,45]) and may contribute to the diminished motivation and poor insight frequently observed in patients with HD.[14,15] When deciding about personal possessions, however, a shift is seen in which these same regions become hyperactive, a pattern seen among patients with anxiety disorders.[46,47] Hyperactivity in these regions may hamper the decision-making process by leading to a greater sense of outcome uncertainty,[47] which would be consistent with the present correlations of subjective indecisiveness and not just right feelings, contributing to a subjective sense that the wrong decision is being made,[48] increasing response conflict, and leading to exaggerated risk judgments.[49] The fact that the obtained interaction effect remained significant when controlling for VAS ratings, however, suggests that the emotional responses alone cannot account for the findings. Rather, it appears that hyperactivity in the ACC-insula network during decision making is characteristic of HD and may contribute to subjective indecisiveness and decisions to save.

Notably, among patients with HD, anxiety, indecisiveness, sadness, and not just right feelings were associated with inferior frontal gyrus activation, possibly indicating an inhibitory signal to accept a risky option.[50,51] Findings from behavioral economics, such as the endowment effect[52] in which ownership of an item can increase its per-

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ceived worth, may be informative for the study of hoarding. The endowment effect has been demonstrated to be associated with inflated estimates of the desirability of objects[53,54] and may be mediated by activity in the inferior frontal gyrus and insula,[55] regions implicated in the present study, and the ventral striatum and nucleus accumbens,[56] which could be reflected in the obtained striatal activity. Contrary to previous research,[22-24] we did not find evidence that PP decisions were associated with excessive activity in the ventromedial prefrontal cortex or OFC, perhaps reflecting the fact that PP and EP decisions taxed these decision-making regions equally.

Perhaps the most striking finding for the patients with OCD is the apparent absence of differential responding to PP vs EP items. The patients with OCD experienced less change in hemodynamic activity between these 2 item types than did HCs or patients with HD (for regions other than ACC and insula, the attenuated differentiation for patients with OCD drove the significant interaction effects). A possible explanation for this lack of differentiation is that the patients with OCD simply might have been less engaged with the task, perhaps due to ongoing obsessive ruminations or anxiety, although the higher rate of selective serotonin reuptake inhibitor use in that group may have a role. In addition, the present results for patients with HD differ from those seen in patients with OCD under symptom provocation conditions, in which greater activity is noted in OFC and prefrontal regions[22,57-60] and the amygdala[57,61] and caudate.[62] Furthermore, the HD-specific findings remained significant even while controlling for nonhoarding OCD symptoms (as well as depression).

Several study limitations should be noted. The first of these concerns the sampling procedures. Because an aim of the present study was to compare patients with primary HD to patients with primary OCD, potential participants with comorbid HD and OCD were excluded from the study. Although only one participant was excluded for this reason, previous research suggests that 18% of patients with HD meet diagnostic criteria for nonhoarding OCD.[63] The self-report measures suggest some degree of subclinical hoarding (difficulty discarding) in patients with OCD and some degree of subclinical OCD symptoms (checking, neutralizing, obsessions, and/or ordering) in patients with HD. The equivalent not just right experiences during the fMRI task also may be indicative of an OCD-like process in patients with HD. The HD sample was predominantly female and white and thus may not represent the larger population of individuals with HD. Previous research has suggested that HD may be more common in men.[64] The ethnic/racial composition of the HD population is not known. The present sample also likely did not include the least insightful (and perhaps most severely impaired) patients with HD who would not identify themselves as such and thus would not volunteer for the present study. Because of the younger age of the OCD group, an age effect cannot be definitively ruled out (although there was no age difference between the HD and HC groups and covarying for age did not alter the findings).

The second limitation involves the examination of the decision-making process. Decision making is a complex process that includes assessing available options, selecting the appropriate action, and evaluating outcomes associated with the action. The longer response time for patients with HD vs other participants introduces the possibility that the activation in the insula and ACC derives

Table 5. Significant ($P < .01$) Correlations Between Neural Activity (at Least 10 Contiguous Voxels) During Decisions About Personal Possessions and Visual Analog Scale Ratings in Patients With Hoarding Disorder

Correlation	MNI
Anxiety	
Positive correlation	
Left precentral gyrus	–57, 6, 30
Right middle and inferior frontal gyri (BA 45/46)	54, 30, 21
Negative correlation	
Right inferior frontal gyrus	39, 33, 0
Left postcentral and supramarginal gyri	–51, –33, 57
Left superior temporal gyrus	–63, –12, 6
Right hippocampus (posterior)	24, –24, –18
Left brainstem	–15, –21, –30
Left cerebellum (declive)	–27, –72, –27
Right cerebellum (crus 1)	30, –69, –27
Indecisiveness	
Positive correlation	
Right middle frontal gyrus	27, 3, 60
Left middle frontal gyrus (BA 9)	–39, 12, 33
Midline rostral cingulate and medial frontal gyrus	6, 48, 9
Left inferior and middle frontal gyri	–45, 39, 6
Right middle frontal gyrus	39, 51, –3
Left inferior frontal gyrus (BA 47/11)	–21, 27, –12
Right inferior frontal gyrus (BA 47/11)	24, 24, –9
Right insular (BA 13)	27, 15, 12
Left middle and inferior temporal gyri	–45, –33, –18
Left uncus and amygdala	–15, –3, –24
Sadness	
Positive correlation	
Left precentral/middle frontal gyri (BA 6/9)	–51, 0, 48
Right middle and precentral gyri (BA 6)	39, 6, 48
Right inferior frontal gyrus (BA 45/44/46)	60, 24, 24
Left inferior frontal gyrus (BA 47)	27, 21, –9
Right superior parietal lobule/precuneus	24, –51, 57
Left superior temporal gyrus (BA 38)	–36, 12, –30
Right cuneus/precuneus (BA 19/18/31)	30, –75, 18
Left ventral striatum	–12, 6, –12
Right ventral striatum	15, 12, –6
Negative correlation	
Left precuneus and posterior hippocampus	–12, –42, 9
"Not just right"	
Positive correlation	
Left superior and middle frontal gyrus (BA 6)	–24, 6, 54
Left inferior frontal gyrus (BA 46)	–45, 36, 9
Medial frontal gyrus and anterior cingulate cortex	3, 39, 12
Right middle frontal gyrus (BA 10)	42, 57, 12
Right medial frontal gyrus	18, 54, 0
Right inferior frontal gyrus and insula (BA 47)	27, 15, –21
Left superior parietal lobule and precuneus (BA 7/5)	–18, –45, 54
Left superior parietal lobule/precuneus (BA 7/5)	–9, –63, 51
Right superior parietal lobule/precuneus (BA 7/5)	12, –60, 51
Right middle and superior temporal gyri	63, –24, –12
Left ventral striatum	–12, 6, –12
Left hippocampus	–12, –9, –24
Left cerebellum posterior lobe tonsil	–15, –51, –42
Right cerebellum posterior lobe tonsil	21, –48, –42
Negative correlation	
Left postcentral and inferior parietal lobule	–60, –24, 45

Abbreviations: BA, Brodmann area; MNI, Montreal Neurological Institute.

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from greater time on task in regions associated with attentional control.[64-66] Indeed, activity in the inferior frontal gyrus and insula was correlated with self-reported indecisiveness; however, results remained significant even after controlling for indecisiveness, suggesting that HD processing may be both longer than and qualitatively different from that in participants without HD. We considered controlling for response time; however, we ultimately decided not to because slowed decision making may be a central feature of impaired decision making in hoarding. Future studies might investigate the temporal dynamics of decision making to examine changes in neural activity from earlier to later stages, using behavioral tasks that are well suited for that purpose.[67]

The third limitation involves the task structure itself. The stimuli in the present study were limited to paper items. Although paper items are among the most commonly hoarded possessions in HD,[1] other items, such as clothing, craft supplies, sentimental items, and food, are also commonly hoarded. It is possible that a different set of stimuli would have elicited a different neural response, and future research is needed to explore this possibility. Furthermore, it cannot be conclusively determined that the words "yours" and "ours," which preceded the stimuli, or the red and black margins surrounding the stimuli affected neural response. An examination of neural response to these words and colors alone would have facilitated interpretation of the results. In addition, because the VASs were administered after each run (which contained both PP and EP decisions), the specific emotional reaction to decisions about PPs cannot be pinpointed. The addition of a true neutral baseline condition (rather than a comparison of 2 kinds of decision making) would also help clarify the full range of neural processes involved in the decision-making process.

Finally, although α levels were corrected for searching within an ROI (ie, the number of voxels) using small volume correction, the large number of ROIs searched underscores the need for replication in future studies. We considered whole-brain analyses as an alternative to ROI analysis; however, given the amount of statistical correction that would be needed for such analysis, the sample would have lacked sufficient statistical power to detect differences at the whole-brain level with the appropriate corrections.

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