Brain Activation by Disgust-Inducing Pictures in Obsessive-Compulsive Disorder

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Background: *There is growing interest in the role of disgust in the pathogenesis of obsessive-compulsive disorder (OCD).*

Methods: *Eight OCD subjects with contamination preoccupations and eight gender- and age-matched healthy volunteers viewed pictures from the International Affective Picture System during functional magnetic resonance imaging scans.*

Results: *A different distribution of brain activations was found during disgust-inducing visual stimulation in several areas, most notably the insula, compared with neutral stimulation in both OCD subjects and healthy volunteers. Furthermore, whereas activation during the threat-inducing task in OCD subjects showed a pattern similar to that in healthy volunteers, the pattern of activation during the disgust-inducing task was significantly different, including greater increases in the right insula, parahippocampal region, and inferior frontal sites.*

Conclusions: *This pilot study supports the relevance of disgust in the neurocircuitry of OCD with contamination-preoccupation symptoms; future studies looking at non-OCD individuals with high disgust ratings, non–contamination-preoccupied OCD individuals, and individuals with other anxiety disorders are needed.* Biol Psychiatry 2003;54:751–756 © *2003 Society of Biological Psychiatry*

Key Words: Disgust, obsessive-compulsive disorder, functional magnetic resonance imaging, contamination, insula

Introduction

The emotion of disgust may have an important role in the psychobiology of obsessive-compulsive disorder (OCD) (for a review, see Stein et al 2001). Recent studies have identified several regions of the brain that are involved in the facial recognition of "disgust" (e.g., the insula and putamen) (Sprengelmeyer et al 1997, 1998). Sprengelmeyer et al (1997) have noted that OCD patients have deficits when asked to identify facial representations of disgust, in comparison with other anxiety disorders. Furthermore, Phillips et al (2000) have shown that OCD individuals respond to "disgusting" stimuli differently from healthy volunteers—with functional magnetic resonance imaging (fMRI) activity in the insula. In this study, we used disgust-inducing pictures from the International Affective Picture System (IAPS)[1] (Center for the Study of Emotion and Attention 2001; Lang et al 2001) to evaluate insula activation in OCD subjects compared with healthy volunteers. Activation patterns to disgust-inducing stimuli were compared, with activations prompted both by neutral pictures and by other arousing pictures (i.e., scenes of physical threat). As whole-brain data were collected, differences in all functionally active areas were similarly tested.

Methods and Materials

Subjects

Eight right-handed OCD subjects (five female/three male, age range 24–55, mean 41.8 years) with obsessions and compulsions predominantly focused on contamination (mean Yale-Brown Obsessive-Compulsive Scale [Y-BOCS] score of 25.13 ± 5.69) and eight right-handed healthy volunteers, gender- and age-matched (five female/three male, age range 34–44, mean 38 years), from a pool of 12 volunteers, participated. All participants signed written, informed consent as approved by the Health Science Center Institutional Review Board of the University of Florida and were medication free (≥5 half-lives). All healthy volunteers underwent a medical examination and psychiatric review and denied any past psychiatric pathology. Psychometric evaluations for the OCD subjects included the MINI Neuropsychiatric Interview (version 5.0; Sheehan et al 2000), Y-BOCS

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[1] Picture numbers for the IAPS pictures used in this study were as follows: Disgust: 2703, 2730, 2769, 7359, 7380, 9301, 9374, 9375, 9923, 9925; Threat: 1050, 1120, 1300, 1525, 1932, 6230, 6242, 6250, 6510, 6560; Neutral: 2190, 2222, 2383, 2393, 5001, 5201, 5390, 5594, 5661, 7550.

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(Goodman et al 1989), and the 32-item Disgust Scale (Haidt et al 1994). One of the OCD subjects required vision correction during the procedure.

Tasks

Pictures from the IAPS were presented on a screen with a visual angle of approximately 11° by back-projection using a liquid crystal display projector. Three primary categories of pictures were used: disgust-inducing (D), threat-inducing (T), and neutral (N) with slightly positive valence (Lang et al 1998). Each category contained 10 pictures and was divided into two subcategories (five pictures each) according to picture content. Disgust-inducing subcategories were food contamination (D1) and body product (D2); threat-inducing subcategories were human attack (T1) and animal attack (T2); neutral subcategories (control condition) were landscapes (N1) and people unfamiliar to the subjects (N2). A fixation condition (X) consisting of a black screen with a central white "X" was also used as a control condition. Pictures were presented in 30-sec blocks (five different pictures, each one for 6 sec), with eight blocks (e.g., X-D1-N1-T1-X-N2-T2-D2) repeated in a second run. The order of the picture contents was counter-balanced across participants and runs. The participants were instructed to passively view the pictures without overt response. Compliance with these instructions was confirmed in debriefing of all participants immediately after the experimental session.

fMRI Image Acquisition and Data Analysis

The experiment was performed on a GE 3.0 Signa scanner (General Electric Medical Systems, Milwaukee, WI). Using echo planar imaging–blood oxygen level dependent (EPI-BOLD) sequence for the whole brain (imaging 22–24 axial slices, 6-mm thickness, no gap, field of view = 240 mm, matrix size 64×64, repetition time = 2.5 sec/echo time = 25 msec/flip angle = 90°). Data analysis was focused on comparisons between the patterns of brain activation by disgust-inducing and threat-inducing in general and on the difference between the two groups of participants. The comparison between the primary categories was conducted by averaging the fMRI BOLD response over both fMRI runs.

The fMRI images were first co-registered and aligned using a motion correction program in MEDx (Sensor Systems, Sterling, VA) and in-house programs coded in MATLAB (The Mathworks, Natick, MA) for linear de-trending (Liu et al 1999). The fMRI response was then determined individually by voxel-wise *t* tests comparing images acquired during different conditions using a spatial clustering technique (Xiong et al 1995). First, comparisons were made between viewing disgust-inducing or threat-inducing conditions and neutral conditions for an emotion-specific effect. Second, comparisons were made between viewing disgust-inducing, threat-inducing, neutral, and fixation conditions for the control of visual arousal effect. The resulting statistical parametric maps or *t*-score maps were further standardized into Talairach space (Talairach and Tournoux 1988) using a spatial normalization program (Lancaster et al 1998) and averaged over participants in each group and over the two fMRI runs. The averaged *t* scores were then transformed to *z* scores, and the activation maps were generated by applying both the clustering threshold (the minimal clustering size was 27, based on three-dimensional searching) and the *z* threshold corresponding to a statistical level of $p < .01$.

Functional clusters defined on the averaged functional maps were further quantified for the between-group comparison. The statistical significance of the difference in the activation magnitudes in these clusters between the healthy volunteers and OCD subjects was determined based on individual data (not shown) thresholded at the same *p* level ($p < .01$).

Results

Psychological and Behavioral Measures

On Haidt's 32-item Disgust Scale (Haidt et al 1994), OCD subjects showed higher mean values than the healthy volunteers (73.5 ± 19.2 vs. 59.4 ± 13.6), with a near significant Mann–Whitney *U* test: [$Z(7) = -1.84$, $p = .065$]. The correlation between the level of disgust measured by the Haidt disgust scale and the level of OCD subject's impairment measured by the Y-BOCS was positive ($R = .55$), but not significant for this small population.

Activation in Healthy Volunteers

Different patterns of brain activation were found during viewing of the disgust-inducing and threat-inducing pictures as compared with viewing neutral pictures (Tables 1 and 2 and Figure 1). The functional maps of two representative brain slices demonstrated differences in the activation in the insula and parahippocampal region (PHc) between viewing in the disgust-inducing and threat-inducing conditions (Figure 1), as well as overlapping activation mostly located in the visual cortex and posterior cingulate cortex.

Although the threat-inducing condition, as compared with the neutral condition, was mostly associated with activation in the PHc, the premotor area (Brodmann's area [BA] 6), the putamen in the basal ganglia, and dorsolateral prefrontal cortex (BA 9/46), the disgust-inducing condition was strongly associated with activation in the insula, the PHc, the inferior frontal gyrus (BA 47), the caudate nucleus in the basal ganglia, and the primary sensory cortex (see Tables 1 and 2).

To determine whether activation during emotionally arousing pictures (including disgust-inducing pictures) prompted increased processing in the visual cortex (Lang et al 1998), we compared the activations in the visual cortex during the disgust-inducing, threat-inducing, and neutral conditions with those during fixation conditions (Figure 2). Although any picture-viewing task induces activation in the primary visual cortex, when assessed at

Table 1. Disgust-Induced Activation in Healthy Volunteers ($n = 8$)

Region (Brodmann's Area)	Side	Talairach Coordinates (mm)			Activated Cluster Volume (mm^3)
Cerebellum	L	−34	−69	−17	2764
	R	23	−65	−16	448
Parahippocampus Region	L	−25	8	−15	592
	R	21	14	−15	216
Inferior Frontal Gyrus (47)	L	−41	25	−12	344
	R	40	22	−10	992
Posterior Cingulate Gyrus (24/25/32)	L	−4	15	−9	2520
Lingual Gyrus (18/19)	L	−26	−68	−7	720
	R	26	−67	−6	416
Inferior Occipital Gyrus (18)	L	−40	−75	−2	936
Caudate Nucleus/Putamen	L	−19	13	1	224
	R	18	11	−1	688
Inferior Temporal Gyrus (19)	L	−46	−68	−1	864
Medial Temporal Gyrus (21/37)	L	−54	−42	1	440
	R	−49	−44	2	1960
Cuneus (17/18)	L	−19	−75	3	824
Insula	L	−36	11	6	264
	R	33	12	6	888
Anterior Cingulate Gyrus (24/32)	L	−6	42	9	680
Superior Temporal Gyrus (22)	L	−53	−32	16	1056
	R	57	−33	17	608
Medial Frontal Gyrus (9/46)	L	−41	39	28	280
	R	39	37	30	832
Postcentral Gyrus (1/2/3)	R	52	−23	34	632
Inferior Parietal Lobule (40)	R	41	−42	40	448

The output of brain activation during the visual stimulation (viewing disgust-inducing pictures vs. viewing neutral pictures) was spatially normalized into a standard Talairach space. The activated brain regions were determined by group *t* tests with a threshold corresponding to a statistical significance level of $p < .01$. The Talairach coordinates *(x, y, z)* represent the *t* score–weighted centroid of the image voxels within each cluster. The data were rounded to integers.

L, left; R, right

Table 2. Threat-Induced Activation in Healthy Volunteers ($n = 8$)

Region (Brodmann's Area)	Side	Talairach Coordinates (mm)			Cluster Volume (mm^3)
Cerebellum	L	−32	−75	−18	1976
	R	23	−69	−17	520
Parahippocampus Region	L	−26	2	−16	1032
	R	22	6	−16	216
Fusiform Gyrus (18)	L	−35	−60	−10	904
Posterior Cingulate Gyrus (24/25/32)	L	−8	20	−8	2632
Lingual Gyrus (18/19)	L	−24	−67	−6	976
	R	27	−65	−4	464
Inferior Occipital Gyrus (18)	L	−38	−77	−2	528
	R	36	−76	−2	232
Putamen	L	−22	2	−2	224
	R	21	1	−2	1304
Inferior Temporal Gyrus (19)	L	−48	−66	−2	280
Medial Occipital Gyrus (19)	L	−32	−70	−1	328
	R	38	−68	−1	224
Medial Temporal Gyrus (21/37)	L	−50	−44	1	304
	R	−47	−50	2	440
Cuneus (17/18)	L	−18	−77	4	248
Anterior Cingulate Gyrus (24/32)	L	−4	41	8	1248
Superior Temporal Gyrus (22)	L	−54	−32	18	256
	R	58	−31	18	1088
Medial Frontal Gyrus (9/46)	L	−39	36	29	448
	R	38	35	28	1232
Inferior Parietal Lobule (40)	R	40	−41	44	240
Precuneus (7)	L	−25	−56	45	232
Precentral Gyrus (6)	L	−38	−2	52	1024

The output of brain activation during the visual stimulation (viewing threat-inducing pictures vs. viewing neutral pictures) was spatially normalized into a standard Talairach space. See the footnotes to Table 1.

L, left; R, right

the threshold used in this analysis ($p < .01$), both the disgust-inducing and threat-inducing stimuli prompted more widespread and more intense activation than neutral stimuli.

Comparing Activation in Healthy Volunteers and OCD Subjects

Activation during the threat-inducing condition in the OCD subjects showed a similar pattern as that found in healthy volunteers (no significant differences at any site for $p < .01$). In contrast, the level of activation during the disgust-inducing condition was significantly greater for OCD subjects than for volunteers at several sites, especially in the region of the insula, as predicted, but also in the PHc and BA 47 (see Table 3, Figure 3). Group differences at the putamen and BA 9/46 also approached significance, suggesting that, with a larger sample, greater activation in OCD might also be confirmed in these structures.

Interestingly, instead of an increase of arousal effect in the visual cortex, as expected with an increase of activity in the insular and primary sensory cortex, the overall activity in the visual cortex was decreased during the disgust-inducing task in the OCD subjects (Figure 4) but not in the healthy volunteers (Figure 2).

Discussion

In this preliminary work, we aimed to identify the neural substrates recruited in the brains of individuals with OCD (concerned with cleaning and germs) and a matched group of healthy volunteers, when presented with pictures that are considered disgusting or that depict physical threat. The brain activation found for disgust included, most notably, the insula, part of the gustatory cortex that processes unpleasant tastes and smells, and a region reported to mediate the disgust response by different researchers, using varying paradigms (Phillips et al 1997, 1998; Sprengelmeyer et al 1996, 1997). The patterns

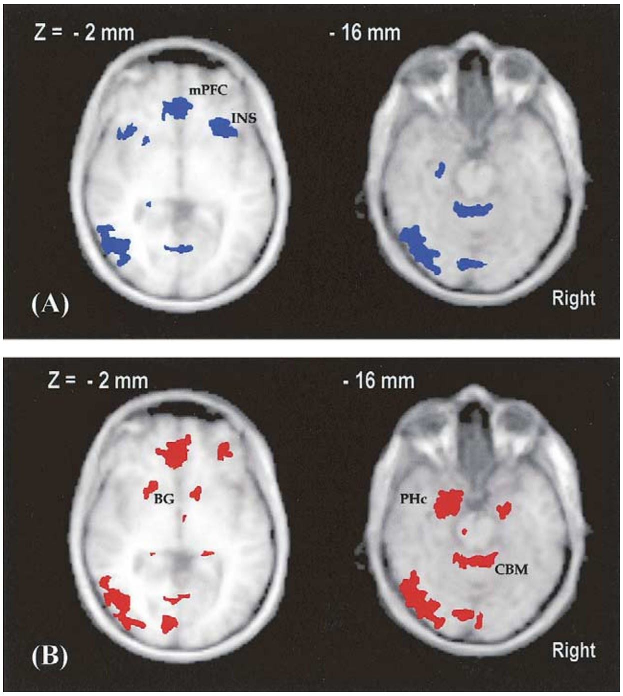

Figure 1. Differential brain activation by disgust and threat in healthy volunteers (n = 8). **(A)** Viewing disgust-inducing pictures versus neutral pictures. **(B)** Viewing threat-inducing pictures versus neutral pictures. The colored functional maps (blue: disgust; red: threat) were overlaid on anatomical magnetic resonance imaging (MRI; gray) of two representative axial brain sections (Talairach coordinates $z = -2$ mm and $z = -16$ mm). The functional MRI (fMRI) response was first determined individually by voxel-wise t tests, comparing images acquired during different conditions (disgust or threat vs. neutral) using a spatial clustering technique. The resulting statistical parametric maps were then standardized into Talairach space using a spatial normalization program and averaged over participants in each group and over the two fMRI runs. The clustering threshold (the minimal clustering size was 27 based on three-dimensional searching) and the z threshold were set to reflect a statistical significance level of $p < .01$ for the detected changes. INS, insula; BG, basal ganglia; mPFC, medial prefrontal cortex; CBM, cerebellum; PHc, parahippocampal region.

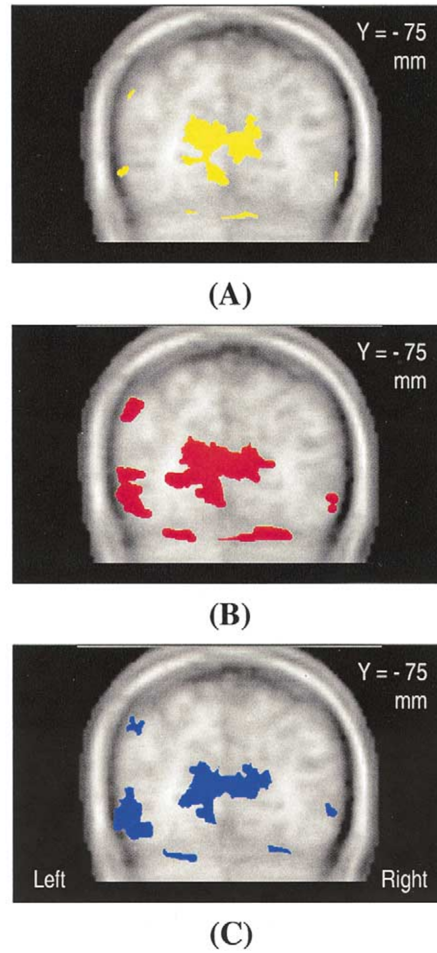

Figure 2. Activation in the visual cortex in the healthy volunteers (n = 8). **(A)** Viewing neutral pictures versus fixation. **(B)** Viewing threat-inducing pictures versus fixation. **(C)** Viewing disgust-inducing pictures versus fixation. The colored functional maps (yellow: neutral; red: threat; blue: disgust) were overlaid on anatomical magnetic resonance imaging (MRI; gray) of a representative coronal brain section through the primary visual cortex (Talairach coordinates $y = -75$ mm). The functional MRI response was first determined individually by voxel-wise t tests, comparing images acquired during different conditions (neutral or threat or disgust vs. threat) using a spatial clustering technique. See Figure 1 legend.

associated with threat pictures were clearly different from those found for disgust and did not show significant insula activation. Although the sample size of this study is small, differences between groups were clear. Thus, OCD subjects and healthy volunteers showed markedly dissimilar activation patterns in response to disgust pictures, differing significantly at six separate neural sites, most notably at the right insula. In contrast, the two groups were similar in their response to threat-inducing pictures, with no significant group differences at any site ($p < .01$). This research supports the hypothesis that the disgust reaction is a distinct emotional response, involving a pattern of brain activation that differs from fear (Miller 1997; Stein et al 2001).

As anticipated, we found a general activation increase in disgust-related brain regions for OCD subjects, relative to healthy volunteers. An exception to this latter finding concerns the BOLD response in visual cortex, which suggests less activity for OCD subjects than for healthy volunteers. It is possible that some OCD subjects sometimes responded to disgust pictures by closing their eyes, automatically blocking primary visual processing. If so, it

Table 3. Disgust-Induced Activation in Subjects with OCD (n = 8) and Comparisons with Healthy Volunteers in Table 1

Region (Brodmann's Area)	Side	Talairach Coordinates (mm)			Cluster Volume (mm^3)	p[a]
Parahippocampus Region	L	−24	9	−16	1240	I (<.01)
Inferior Frontal Gyrus	L	−43	24	−11	1680	I (<.01)
(47)	R	42	21	−11	2492	I (<.01)
Posterior Cingulate Gyrus (24/25/32)	L	−3	16	−8	224	D (<.01)
Inferior Occipital Gyrus (18)	L	−41	−76	−3	224	D (<.01)
Insula	R	32	11	7	4880	I (<.01)

L, left; R, right; I, increase; D, decrease.
[a] Significance level of the difference in the activation magnitudes (i.e., the volume of these clusters) between the healthy volunteers and subjects with OCD was determined by unpaired, one-tailed t test based on the individual data (corrected for multiple comparisons; see Methods and Materials).

is clear that this did not prevent OCD subjects from showing greater-than-normal processing of disgust stimuli elsewhere in the cortex. Codispoti et al (2001) have shown that even when affective pictures are presented for only a half second, emotional reflexes are nevertheless activated (startle potentiation and augmented skin conductance), similar amplitude to those found for picture-viewing times of several seconds. Furthermore, Junghöfer et al (2001)

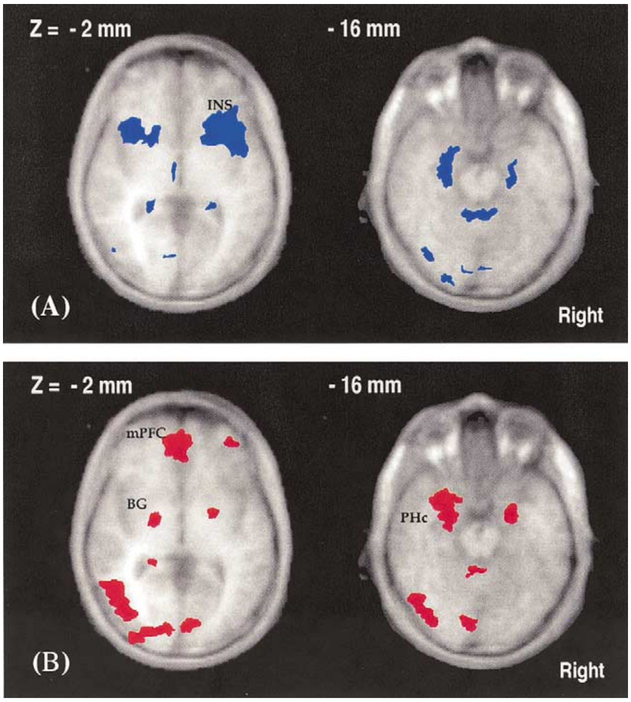

Figure 3. Differential brain activation by disgust and threat in subjects with OCD (n = 8). **(A)** Viewing disgust-inducing versus neutral pictures. **(B)** Viewing threat-inducing versus neutral pictures. See Figure 1 legend.

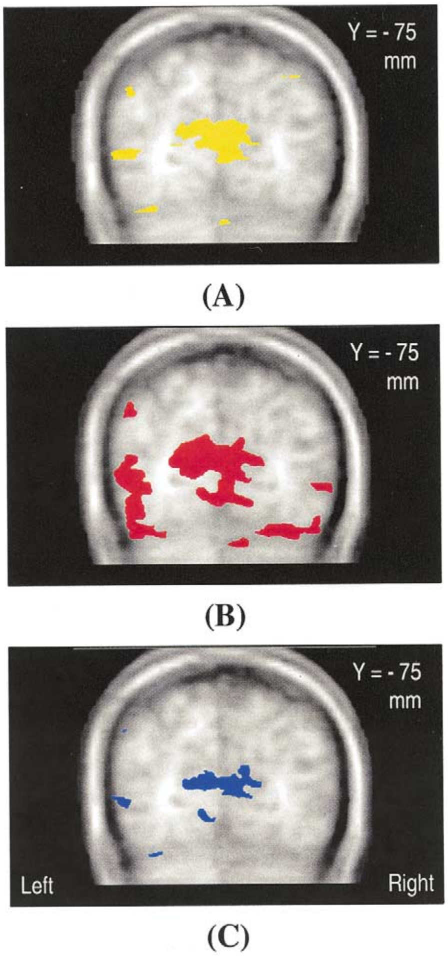

Figure 4. Activation in the visual cortex during viewing of International Affective Picture System pictures (vs. fixation) in the subjects with OCD (n = 8). **(A)** Viewing neutral pictures versus fixation. **(B)** Viewing threat-inducing pictures versus fixation. **(C)** Viewing disgust-inducing pictures versus fixation. See Figure 2 legend.

found arousal-specific electroencephalogram responses to emotional pictures presented as briefly as 0.2 sec. Thus, we may conclude that even brief exposure to a disgusting picture is sufficient to evoke sustained emotional processing. Indeed, subjects so distressed that they defy instruction and close their eyes after glimpsing the disgust content may well be the most distressed subjects, showing the strongest disgust activation pattern at anterior sites. These eye movement patterns will be monitored more closely in our program's next experiment.

In summary, this research provides clear evidence of a difference in brain activation patterns between disgust and threat stimuli. Furthermore, the findings are consistent with other recent research, using different paradigms and procedures, in highlighting the insula's role in disgust. The current research method will be expanded (using more participants) and the analyses refined in future studies, including comparisons between subjects with contamination- and non–contamination-preoccupied OCD and between volunteers high and low on disgust rating measures. Using a larger sample of healthy volunteers, we can determine whether subscales of the 32-item Disgust Scale better predict brain activation than does the full scale. We will also explore the impact of threat stimuli that are not inherently disgusting but that may be more pertinent to obsessive concerns (e.g., pictures related to microbial contagion or various toxins) in subjects with OCD. This current research represents an advance in the study of brain circuits in disgust and provides a powerful paradigm for development in functional imagery studies of OCD.

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