Impaired Recognition and Regulation of Disgust Is Associated with Distinct but Partially Overlapping Patterns of Decreased Gray Matter Volume in the Ventroanterior Insula

Josh D. Woolley, Eric V. Strobl, Virginia E. Sturm, Tal Shany-Ur, Pardis Poorzand, Scott Grossman, Lauren Nguyen, Janet A. Eckart, Robert W. Levenson, William W. Seeley, Bruce L. Miller, and Katherine P. Rankin

ABSTRACT

BACKGROUND: The ventroanterior insula is implicated in the experience, expression, and recognition of disgust; however, whether this brain region is required for recognizing disgust or regulating disgusting behaviors remains unknown.

METHODS: We examined the brain correlates of the presence of disgusting behavior and impaired recognition of disgust using voxel-based morphometry in a sample of 305 patients with heterogeneous patterns of neurodegeneration. Permutation-based analyses were used to determine regions of decreased gray matter volume at a significance level $p <= .05$ corrected for family-wise error across the whole brain and within the insula.

RESULTS: Patients with behavioral variant frontotemporal dementia and semantic variant primary progressive aphasia were most likely to exhibit disgusting behaviors and were, on average, the most impaired at recognizing disgust in others. Imaging analysis revealed that patients who exhibited disgusting behaviors had significantly less gray matter volume bilaterally in the ventral anterior insula. A region of interest analysis restricted to behavioral variant frontotemporal dementia and semantic variant primary progressive aphasia patients alone confirmed this result. Moreover, impaired recognition of disgust was associated with decreased gray matter volume in the bilateral ventroanterior and ventral middle regions of the insula. There was an area of overlap in the bilateral anterior insula where decreased gray matter volume was associated with both the presence of disgusting behavior and impairments in recognizing disgust.

CONCLUSIONS: These findings suggest that regulating disgusting behaviors and recognizing disgust in others involve two partially overlapping neural systems within the insula. Moreover, the ventral anterior insula is required for both processes.

Keywords: Disgust, Emotion recognition, Frontotemporal dementia, Insula, Neurodegeneration, Voxel-based morphometry

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Disgust likely evolved from gustatory mechanisms that protect organisms from ingesting unsafe foods. Charles Darwin thought that disgust was elicited by "something revolting, primarily in relation to the sense of taste, as… perceived or imagined" (1). Disgust protects the body from infectious (e.g., fungi), inedible (e.g., rotten foods), unclean (e.g., feces), gory (e.g., body deformity), or morally offensive (e.g., incest) phenomena (2). Many sensory domains contribute to disgust, including gustation, olfaction, and interoception (3). The insula integrates information from these multiple sensory modalities and has been implicated in disgust processing (4). However, the functional and anatomical relationships between experiencing, expressing, and recognizing disgust remain unclear.

The anterior insula (AI) has been implicated in experiencing, expressing, and recognizing disgust. For example, the AI is activated in response to viewing disgusting scenes (e.g., cockroaches) (5,6) and smelling foul odorants (4). Furthermore, trait disgust sensitivity correlates with AI activation during viewing of disgusting images (6,7). Patients with obsessive-compulsive disorder who are preoccupied with contamination show abnormally increased AI activation when viewing disgusting scenes (8). When healthy subjects view disgusted faces, AI activity, as measured by functional magnetic resonance imaging and depth electrodes, increases significantly more than when viewing faces displaying other emotions (9–12). Additionally, a meta-analysis of 106 imaging studies found that the AI is significantly more activated in response to disgusting stimuli than to other emotional stimuli (13). Furthermore, direct electrical stimulation of the AI evokes unpleasant feelings in the throat (12), visceral changes associated with being sick (14), and vomiting (15). Yet, prior studies have been limited to interrogation of healthy systems or investigations with epileptic patients, who have substantial neural reorganization that makes brain-behavior mapping problematic. Lesion studies offer a unique opportunity to delineate the clinical correlates of individuals in whom loss of disgust appears to drive behavioral abnormalities and to facilitate understanding of brain regions necessary for disgust processing.

Few studies have investigated the effects of insular lesions on disgust. One patient with a left-hemisphere infarction involving the insula had selective deficits in recognizing disgust in scenes and faces and decreased subjective reports of disgust, even though he could accurately recognize other emotions and could discuss the logical aspects of disgust without difficulty (16). Another patient with bilateral insular (but also temporal and frontal) lesions showed a general deficit in recognizing emotional facial expressions from static pictures, but when dynamic facial signals were used, he had selectively impaired disgust recognition (17). Both patients' lesions were not restricted to the insula, let alone the AI, allowing for the possibility that insular lesions were not solely responsible for their disgust-processing deficits. Selective disruption in disgust recognition has also been reported in patients with Huntington's disease, a neurodegenerative disease that affects the insula and striatum (18–20), and a single, small study of Huntington's disease patients directly linked these recognition deficits to AI atrophy (21). Additionally, selective deficits in recognition of disgust have been found in patients with Parkinson's disease (22). One large study found that vascular damage to right somatosensory cortices, including the insula, was associated with impaired ability to recognize emotions, though it did not investigate disgust specifically (23). Finally, we found that behavioral, physiological, and subjective responses were all reduced in behavioral variant frontotemporal dementia (bvFTD) patients compared with control subjects while watching a disgust-eliciting film (24). Although the AI is a common early target of neurodegeneration in bvFTD, this study did not report the anatomy of these deficits. In sum, existing links between insular lesions and disgust recognition deficits are imprecise, and there has been limited investigation into the effects of insular lesions on the experience of disgust or on the regulation of disgusting behavior.

We investigated the neural correlates of patients' increased tendencies to engage in disgusting behaviors and disrupted recognition of disgust in a large sample of patients with heterogeneous patterns of brain damage. We aimed to determine whether neurodegeneration of the insula results in loss of the experience of disgust as indexed by the emergence of behaviors that are typically prevented by feelings of disgust. We hypothesized that neurodegeneration of the insula, a key hub in visceromotor disgust reactivity and subjective emotional experience, would be associated with the presence of disgusting behaviors. We further hypothesized that the tendency to engage in disgusting behaviors and the inability to recognize disgust would correspond to distinct, but partially overlapping, patterns of AI atrophy.

METHODS AND MATERIALS

Assessment

We analyzed the charts of 305 consecutive patients in our research project between 1999 and 2010 diagnosed with one of seven neurodegenerative diseases, as well as 25 asymptomatic first-degree relatives of bvFTD patients (FM). Patients were evaluated by a multidisciplinary team and had laboratory screening and brain magnetic resonance imaging. For neuropsychological analyses, data from a control group of 90 healthy older subjects (HS) (mean age: 69.4; SD: 7.0) were included for comparison. Neuropsychological testing was conducted on 287 of the 305 patients, all FM, and all HS and included the Clinical Dementia Rating Scale (CDR) and the Mini-Mental State Examination (MMSE), both measures of dementia severity (Table 1).

Disgusting Behaviors

Charts, including both patient and caregiver reports, as well as clinician observations, were reviewed by two raters for evidence of disgusting behaviors. Behaviors were recorded that fit into any of the categories of disgust derived from the Disgust Scale (25). Number or intensity of disgusting behaviors could not be accurately coded from retrospective chart review, so these variables were not quantified (i.e., a single episode of disgusting behavior was coded identically as multiple episodes). As not all patients with chart data had emotion recognition or neuroimaging data, subgroups with these data were analyzed to further explore the nature of these behavioral deficits. Studies of these rare neurodegenerative disorders are chronically underpowered. Therefore, we included all valid data to maximize power.

Emotion Recognition

One hundred forty-nine patients, 12 FM, and 90 HS were administered the Emotion Evaluation subtest of The Awareness of Social Inference Test (TASIT-EET) (26). Subjects watched 14 brief (20-second to 30-second) videos of actors displaying one of six emotions: disgust, happiness, sadness, fear, anger, surprise, or no emotion, using facial expressions, body language, and vocal tones. The perceived emotion was then selected from a list displayed on the screen without any time limit for responding. Importantly, patients with semantic variant primary progressive aphasia (svPPA) are not mute and are able to label basic emotions even late into the illness (27).

Behavioral Data Statistical Analysis

MMSE, CDR, and TASIT-EET score differences between patients with and without disgusting behaviors were analyzed using general linear models (Proc GLM) in SAS (SAS Institute Inc., Cary, North Carolina). To examine disgust-specific associations, we divided the TASIT-EET into two scores: the TASIT-EET disgust subscore and the sum of the subscores of the other emotions plus neutral.

Voxel-Based Morphometry

Magnetic resonance imaging scans of 231 of the 305 patients and all FM in the study were of sufficient quality for analysis within 6 months of disgust assessment. Voxel-based morphometry (VBM) is a technique for the detection of regional brain volume by voxel-wise comparison of combined gray and white matter volumes between groups of subjects. For the whole-brain analysis, the Anatomical Automatic Labeling atlas was used to name the regions with significantly less gray matter as