



Diminished disgust reactivity in behavioral variant frontotemporal dementia

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ARTICLE INFO

Article history:

Received 1 June 2011

Received in revised form

28 November 2011

Accepted 11 January 2012

Available online 20 January 2012

Keywords:

Frontotemporal dementia

Emotion

Disgust

Autonomic nervous system

Behavior

ABSTRACT

Frontotemporal dementia is a neurodegenerative disease that impacts emotion and social behavior. Using laboratory measures of emotional reactivity, our past work has found that reactivity to loud noises and to thematically simple happy and sad emotional films are preserved in the early stages of the disease while other emotional responses (e.g., embarrassment) are severely compromised. In the present study we examined disgust, an emotion whose function is to distance us from offending objects and situations. We measured disgust reactivity in 21 patients with behavioral variant frontotemporal dementia (bvFTD, a subtype of frontotemporal dementia characterized by emotional blunting) and 25 neurologically healthy controls. Disgust is an emotion of particular interest in bvFTD, due to caregiver and clinician reports that patients engage in acts that suggest this emotion may be compromised; in addition, the pattern of neurodegeneration in bvFTD includes atrophy of key frontotemporal structures (e.g., anterior insula) with known roles in visceral emotions such as disgust. In the present study, participants had their emotional facial behavior, physiology, and self-reported emotional experience measured while watching a disgust-eliciting film. We found that behavioral, physiological, and self-reported experiential responses were all reduced in bvFTD patients compared to controls (with behavioral and physiological differences still found after controlling for patients' cognitive deficits). We discuss the implications of these findings for bvFTD patients' problems in social functioning and their typical patterns of neurodegeneration.

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1. Introduction

Frontotemporal dementia is a neurodegenerative disease that selectively affects the frontal and anterior temporal lobes of the brain, regions that are crucial for proper social and emotional functioning (Rosen et al., 2005; Werner et al., 2007). Dramatic social and emotional changes (e.g., emotional blunting, lack of empathy, disinhibition, and poor insight) are early and striking manifestations of this disease (Boxer & Miller, 2005; Neary, Snowden, & Mann, 2005). Frontotemporal dementia includes three clinical subtypes: behavioral variant frontotemporal dementia (bvFTD), semantic dementia, and progressive non-fluent aphasia. In bvFTD, the subtype that primarily affects the frontal lobes and is the focus of the present study, early and profound emotional and social deficits (e.g., impulsive and inappropriate behavior and a lack of insight into deficits) are common (Boxer & Miller, 2005; Kipps, Mioshi, & Hodges, 2009).

The anterior cingulate cortex and anterior insula are among the earliest brain regions affected in bvFTD (Rosen et al., 2002; Seeley, 2010; Seeley et al., 2008). The anterior cingulate cortex,

which is important for the generation of visceromotor emotional responding, is reciprocally connected with the anterior insula (Bush, Luu, & Posner, 2000; Devinsky, Morrell, & Vogt, 1995). The anterior insula, located deep between the frontal and temporal lobes within the lateral fissure, integrates afferent visceral information with higher-order subjective emotional processing (Craig, 2002; Critchley, 2005). Activation of the insula is commonly found in neuroimaging studies while participants are exposed to disgust-eliciting stimuli (Wicker et al., 2003; Wright, He, Shapira, Goodman, & Liu, 2004). Together, the anterior cingulate cortex and anterior insula play key roles in the generation of emotional responses and interoceptive processing of feeling states. Thus, loss in these structures in the context of neurodegenerative disease may result in social and emotional impairment as patients fail to generate emotional reactions and/or lose access to internal physiological cues that typically guide behavior (Damasio, Tranel, & Damasio, 1990).

In our own work, we have used methods derived from affective science (Levenson et al., 2008) to provide a detailed assessment of emotional functioning in bvFTD. These laboratory-based methods enable us to examine preservation and loss of emotional functioning objectively and directly, using measures that are not as subject to biases that can occur with caregiver retrospective reports or clinician observations. Taking this approach, we have found evidence that suggests that while many aspects of emotional reactivity are clearly disrupted in bvFTD, other aspects remain intact in the early

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stages of the disease. For example, we have found that patients with bvFTD have intact emotional responses to unexpected loud noises (i.e., a 115 db acoustic startle stimulus; Sturm, Rosen, Allison, Miller, & Levenson, 2006) and to thematically simple film clips that elicit happiness and sadness (Werner et al., 2007) but have deficits in self-conscious emotions (Sturm, Ascher, Miller, & Levenson, 2008; Sturm et al., 2006). In terms of the emotion of disgust, a previous study of reaction times in lexical and numerical judgment tasks did not find deficits when patients with bvFTD processed disgusting stimuli (Bedoin, Thomas-Antérion, Dorey, & Lebert, 2009). However, we are aware of no previous studies that measured the physiological and facial reactions of patients with bvFTD while they viewed disgusting stimuli.

In the present study we addressed the need to examine disgust reactivity in bvFTD. Disgust is an emotion with a characteristic facial expression (wrinkled nose, raised upper lip, and tongue moving forward in the mouth), action tendency (distancing of the self from the offensive object), and physiological profile (nausea, gagging) that directs us away from unpleasant objects in the environment (Ekman, Friesen, & Ancoli, 1980; Rozin & Fallon, 1987; Rozin, Lowery, & Ebert, 1994). Behaviorally, disgust is thought to have evolved with an oral/nasal focus; the origins of the facial muscle movements that occur during a disgust display may have served to reject offensive foods, smells, and other contaminated materials (Rozin, Haidt, & McCauley, 2008). Physiologically, disgust is a highly visceral emotion (i.e., it is often accompanied by the experience of nausea). Sensations associated with these visceral changes play an important role in disgust, providing a signal that helps us to avoid potentially harmful food and other contaminated substances (Rozin & Fallon, 1987). In humans, disgust has generalized into a “moral” emotion, helping guide us away from a wide range of ethically undesirable objects, situations, acts, and people (Rozin, Haidt, & Fincher, 2009). For example, a person may feel disgusted by someone who has performed a morally reprehensible act.

In the present study, we examined disgust reactivity (i.e., facial behavior, physiological activation, and subjective experience) in patients with bvFTD and neurologically healthy controls while they watched a disgust-eliciting film. Anecdotal evidence and early neurodegeneration of the insula (Seeley, 2010) suggest that disgust may be particularly vulnerable in bvFTD. Consistent with this, caregivers have reported that some patients with bvFTD pick up garbage, drink beverages found on the street, eat out of trashcans, and sample food from strangers' plates in restaurants. Thus, we hypothesized that patients with bvFTD would show deficits in disgust reactivity compared to controls.

2. Methods

2.1. Participants

Patients with bvFTD ($n=21$) were recruited through the Memory and Aging Center at the University of California, San Francisco (UCSF). Patients were diagnosed using consensus research criteria (Neary et al., 1998) by a multidisciplinary team that included neurologists, neuropsychologists, and nurses. Patients underwent extensive neurological, neuropsychological, and neuroimaging examinations. Neurologically healthy control participants ($n=25$) were also recruited at UCSF using newspaper ads and underwent the same diagnostic assessment as the patients. All participants were given the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) to assess their cognitive status.

2.2. Procedure

A 6-h laboratory session (with a 1-h break midway) designed to provide a comprehensive assessment of emotional functioning (Levenson et al., 2008) was conducted at our laboratory at the University of California, Berkeley. The present study focuses on one trial in which participants viewed a disgust-eliciting film clip.

After arriving at the laboratory, participants or their caregivers signed an informed consent form. Participants were seated in a chair in a 3 m × 6 m room, 1.75 m away from a 21-in. television screen. Participants viewed a 69-s-long disgusting film clip, preceded by a 60-s baseline. The film clip, from the movie

“Trainspotting,” depicts a man defecating in a filthy toilet and then reaching his hand into the toilet to look for a package of drugs, sifting through his own feces. While watching the film, participants' facial behavior was videotaped and their physiological activity was recorded.

At the end of their participation in the laboratory session, participants were paid \$30 and consent was obtained for subsequent use of the video recordings.

2.3. Measures

2.3.1. Emotional reactivity

Three aspects of emotional reactivity were measured while participants watched the film: facial behavior, physiological reactivity, and self-reported emotional experience.

2.3.1.1. Facial behavior. Each participant was videotaped using a partially concealed video camera that was embedded in a bookshelf and placed behind darkened glass. Facial behavior was later coded using the Emotional Expressive Behavior Coding System (Gross & Levenson, 1993) by trained coders blind to group membership. Ten emotions were coded on a 0 to 3 intensity scale: anger, contempt, confusion, disgust, fear, happiness/amusement, embarrassment, interest, sadness, and surprise. Inter-coder reliability was high (intra-class correlation coefficient = .76). Disgust codes were averaged across the 30 most intense seconds of the film clip (previously determined by a panel of raters) to obtain a single disgust expression score for each participant.

2.3.1.2. Physiological reactivity. Physiological reactivity was recorded continuously using a system consisting of a Grass Model 7 polygraph and a computer. Ten physiological measures were obtained: (1) Inter-beat interval: electrodes with conductive paste were placed on opposite sides of the participant's chest to assess heart rate. Inter-beat interval was calculated as the interval between successive R waves. (2) Finger pulse amplitude: a photoplethysmograph recorded the amplitude of blood volume in the finger, using a photocell taped to the third finger of the participant's nondominant hand. (3) Ear pulse transmission time: a photoplethysmograph attached to the participant's right earlobe recorded the volume of blood in the ear. Transmission time was measured between the R wave of the EKG and the upstroke of pulse at the ear. (4) Skin conductance level: a constant-voltage device was used to pass a small voltage between electrodes attached to the first and third fingers of the participant's nondominant hand. (5) Finger temperature: a thermistor attached to the fourth finger of the participant's nondominant hand recorded temperature in degrees Fahrenheit. (6) Respiration period: a pneumatic bellows was stretched around the thoracic region, and the intercycle interval was measured between breaths. (7) Respiration depth: the point of maximum inspiration minus the point of maximum expiration was determined from the respiratory signal. (8) General bodily activity: an electromechanical transducer attached to a platform under the participant's chair generated an electrical signal proportional to the amount of movement in any direction. (9) Systolic blood pressure and (10) diastolic blood pressure: a blood pressure cuff placed on the second finger of the participant's nondominant hand continuously recorded blood pressure using an Ohmeda Finapres 2300.

Change scores were computed for each measure, subtracting the average of the pre-film baseline from the average level during the 30 most intense seconds of the film. For eight of the physiological channels (every channel except skin conductance level and finger temperature), the entire 60 s of the pre-film baseline were used when calculating the baseline average. For skin conductance level and finger temperature, which are relatively slow-changing measures, we averaged only the last 10 s of the pre-film baseline (this was to ensure that participants' physiological responses to the previous task in our day-long battery did not affect the calculations of baseline response). All change scores were normalized (using the mean and standard deviation from the entire sample) to obtain Z-scores, and four measures (inter-beat interval, finger pulse amplitude, ear pulse transmission time, respiration period) were multiplied by -1 so that larger Z-scores always indicated greater activation. Finally, the average Z-score of all 10 measures was computed to provide a single composite score representing overall physiological activity. We have used these kinds of composite measures of physiological reactivity previously as a way of controlling for Type 1 error associated with having multiple dependent measures (e.g., Sturm et al., 2008, 2006). Follow-up analyses of individual measures were conducted to ensure that the findings with the composite measure did not obscure important differences at the level of particular measures.

2.3.1.3. Self-reported emotional experience. After the film, participants were asked to rate how intensely they experienced each of eight emotions while watching the film (anger, disgust, fear, happiness, embarrassment, sadness, sexual arousal, and surprise). Each emotion term was presented on an 8½ × 11 page and read aloud by the experimenter. Participants were asked, “Did you feel ... while watching the film?” and were given the response choices of “No,” “A Little,” or “A Lot.” These answers were given a numerical score of 0, 1, or 2, respectively.

2.3.2. Control tasks

2.3.2.1. Film comprehension. In studies of patients with dementia it is important to ensure that any group differences in emotional reactivity that are found are not

Table 1
Demographic and clinical variables of the participants.

	bvFTD (n = 21)	Controls (n = 25)	Statistical test values
Age M (SD)	58.8 (5.6)	67.1 (8.3)	$F(1,44) = 15.08, p = .000^{**}$
Sex M/F	17/4	13/12	$\text{Chi-Square}(1) = 4.22, p = .040^*$
MMSE M (SD)	25.5 (5.5)	29.7 (.46)	$F(1,44) = 14.68, p = .000^{**}$

Note: Statistical test values for age and MMSE are from a one-way ANOVA comparing the two groups. The Statistical test values for sex are from a crosstabulation using a Pearson Chi-Square test. bvFTD = behavioral variant frontotemporal dementia; MMSE = Mini-Mental State Examination.

* $p < .05$.

** $p < .01$.

secondary to cognitive deficits or behavioral problems. To assess whether participants attended to, comprehended, and remembered the film content appropriately, they were asked two “memory” questions a few minutes after the film had ended. The questions were presented on an $8\frac{1}{2} \times 11$ page and read aloud by an experimenter. Question 1: “What happened in this film? (A) A man sticks his hand into a dirty toilet, (B) A man eats a bug, or (C) A man smells rotten food.” (A is the correct answer.) Question 2: “What happened in this film? (A) The man is alone, (B) A bug is on the stove, or (C) A janitor is mopping the floor.” (A is the correct answer.) Answers were coded as correct, incorrect, or no answer given.

2.3.2.2. Emotional word knowledge. Self-report data obtained from dementia patients is also vulnerable to language deficits. In order to evaluate whether patients with bvFTD could comprehend the emotion words used in the experimental tasks and ratings, we assessed their knowledge of the following emotion terms: anger, disgust, fear, happiness, embarrassment, sadness, sexual arousal, and surprise. Using a multiple choice format, participants were asked to pick the two emotion words they would feel most strongly in response to eight different emotion-eliciting scenarios. The scenarios were designed to elicit an emotion corresponding to one of the eight emotion words (e.g., “You smell dog poo” for disgust). Answers were coded as correct if the target emotion word was provided as either the first or second response.

3. Results

3.1. Demographic and clinical variables

Age differences between the bvFTD and control groups were compared using analysis of variance (ANOVA). The age difference between groups was significant, $F(1,44) = 15.08, p < .05$, with controls being older than bvFTD patients (see Table 1 for a summary of the demographic data). Consequently, age was included as a covariate in all analyses. The distribution of males and females in the diagnostic groups was examined using a Chi-Square test. The sex differences between groups were also significant ($\text{Chi-Square}(1) = 4.22, p < .05$, see Table 1 for group differences); therefore, sex was used as a fixed factor in all analyses. On the MMSE, used as a measure of overall cognitive functioning, scores were lower for patients with bvFTD than for controls, $F(1,44) = 14.68, p < .05$ (means are shown in Table 1). Thus, we

conducted our major analyses with and without MMSE scores as covariates.

3.2. Emotional reactivity

The three dependent variables, facial behavior, physiological reactivity, and self-reported emotional experience, were examined separately using univariate general linear model procedures. We conducted 2×2 analyses of covariance (ANCOVAs) for each dependent variable, with diagnosis and sex as between-subject factors and age as a covariate.

3.2.1. Facial behavior

Analyses revealed a main effect for diagnostic group, $F(1,41) = 6.88, p < .05$, partial eta squared = .14, with the bvFTD group showing less disgust behavior than controls (means are shown in Table 2). There was no main effect for sex, and the interaction between diagnostic group and sex was not significant. Thus, our hypothesis that patients with bvFTD would show less disgust behavior than controls was supported.

3.2.2. Physiological reactivity

Analyses with the composite measure revealed a main effect for diagnostic group, $F(1,41) = 5.26, p < .05$, partial eta squared = .11, with patients with bvFTD demonstrating less physiological reactivity than controls (means are shown in Table 2). There was no main effect for sex, and the interaction between diagnosis and sex was not significant. Thus, our hypothesis that patients with bvFTD would be less physiologically reactive than controls was supported. Follow-up analysis of individual physiological measures revealed diminished blood pressure reactivity in bvFTD (systolic blood pressure, $F(1,29) = 5.00, p < .05$; diastolic blood pressure, $F(1,29) = 5.48, p < .05$). See Table 2 for group means. Although only these two blood pressure variables were statistically significant in this follow-up analysis, examination of the pattern of findings in individual measures reveals that all of the other cardiovascular measures (as well as skin conductance) showed similar patterns of smaller responding for bvFTD patients than controls.

3.2.3. Self-reported emotional experience

We first examined the total level of subjective emotional experience (summing across all emotions) that was endorsed by the participants. We found that patients with bvFTD reported significantly more emotion overall than controls, $F(1,40) = 4.81, p < .05$. Thus, we controlled for total endorsed emotion (not including disgust) and found that patients with bvFTD reported less subjective experience of disgust than controls, $F(1,39) = 4.58, p < .05$, partial eta squared = .11. See Table 2 for group means. There was no main effect of sex, and the interaction between sex and diagnosis was not

Table 2
Facial behavior, physiological reactivity, self-reported emotional experience, and performance on memory questions.

	bvFTD (n = 21)	Controls (n = 25)	Statistical test values
Disgust facial behavior	.190	.577	$F(1,41) = 6.88, p = .012^*$
Physiological reactivity (composite)	-.138	.117	$F(1,41) = 5.26, p = .027^*$
Systolic blood pressure Change score (mmHg)	2.46	6.29	$F(1,29) = 5.00, p = .033^*$
Diastolic blood pressure Change score (mmHg)	1.11	3.35	$F(1,29) = 5.48, p = .026^*$
Self-reported disgust	1.40	1.72	$F(1,39) = 4.58, p = .039^*$ (if total emotion other than disgust is a covariate)
Total self-reported emotion	4.25	3.28	$F(1,40) = 4.81, p = .034^*$
Percent correct on post-film memory question #1	85.7	100	$\text{Chi-Square}(2) = 3.82, p = .148$
Percent correct on post-film memory question #2	81.0	96.0	$\text{Chi-Square}(2) = 3.88, p = .148$

Note: Statistical test values for behavior, physiology, and self-report are from GLM analyses, with sex and diagnosis as fixed factors and age as a covariate. One bvFTD patient did not provide self-reported emotion responses. Six patients with bvFTD and six controls did not have blood pressure data. Statistical test values for memory question performance are from a crosstabulation (using a Pearson Chi-Square test) with three possible responses: correct, incorrect, or no answer given. (Only three percent of the memory questions were not answered.) bvFTD = behavioral variant frontotemporal dementia.

* $p < .05$.

significant. Thus, our hypothesis that patients with bvFTD would report less disgust than controls was supported.

3.3. Control analyses

3.3.1. Film comprehension

To account for the possibility that patients may not have understood the film clip because of cognitive or behavioral factors, we examined the results for the two film comprehension questions. There were no differences between patients with bvFTD and controls on these questions (the percentages of patients and controls who answered each question correctly are shown in Table 2). Thus, the patients with bvFTD understood the content and storyline of the film clip.

3.3.2. Emotional word knowledge

Examining overall performance on the eight emotional scenarios using an ANOVA, we found that patients scored significantly lower than controls, $F(1,43) = 13.58$, $p < .05$. When we added this overall score as a covariate in our analysis of self-reported emotional experience, our finding of lower self-reported disgust was no longer statistically significant. Because we were most interested in disgust, we ran a follow-up analysis using just those patients who responded correctly on the disgust item in the emotional word knowledge test ($N = 14$), comparing them with the controls ($N = 25$, all controls responded correctly on the disgust item). In this analysis, the difference between bvFTD and control groups in self-reported disgust was again not significant, $F(1,33) = .22$, $p = .64$; however, the pattern of means was in the hypothesized direction with bvFTD patients (mean = 1.57, $SD = .65$) reporting less disgust than controls (mean = 1.72, $SD = .54$).

3.3.3. Cognitive status

To determine whether our findings were attributable to general cognitive impairment, we repeated our primary analyses with MMSE as a covariate. The general pattern of findings still held. Patients with bvFTD continued to exhibit significantly less disgust reactivity on our measures of facial behavior, $F(1,40) = 5.45$, $p < .05$, and physiological reactivity, $F(1,40) = 5.53$, $p < .05$. However, our finding that patients with bvFTD reported less disgust than controls (controlling for total emotion other than disgust) was now only significant at the trend level, $F(1,38) = 2.74$, $p = .106$.

4. Discussion

Disgust is an emotion that plays an integral role in helping us to avoid contaminated objects in the environment. The visceral qualities of disgust (e.g., queasiness, gagging, nausea) are thought to provide signals that help mobilize and guide avoidance behaviors. In the present study, we assessed disgust reactivity in patients with bvFTD and healthy control participants while they watched a disgusting film clip. Given the clinical observations that suggest a loss of disgust in bvFTD and the early neural loss in the anterior insula in bvFTD (Seeley, 2010), we hypothesized that patients with bvFTD would show diminished disgust reactions. In line with our expectations, patients with bvFTD exhibited less disgust facial behavior and less reactivity in our composite physiological measure in response to the film than controls. Follow-up analyses of individual physiological measures revealed that the reduced physiological reactivity in bvFTD was found most clearly in two cardiovascular measures, diastolic and systolic blood pressure, which reflect both cardiac (e.g., cardiac contractility) and vascular (e.g., peripheral vascular resistance) influences that are largely controlled by the sympathetic branch of the autonomic nervous

system. Importantly, these findings could not be explained by differences between the patients and controls in their comprehension of the film or in general cognitive status using the MMSE.

We also found that bvFTD patients reported less subjective experience of disgust than controls, but this finding was less robust than the behavioral and physiological findings, emerging only when we controlled for differences in overall emotional experience between the groups and no longer reaching statistical significance when controlling for emotional word knowledge or general cognitive status. In our experience, assessing self-reported emotional experience reliably in patients with bvFTD is difficult. In the present study, this was exemplified by changes in the significance of findings when controlling for covariates.

Our findings of diminished disgust reactivity in the laboratory are consistent with anecdotal reports that patients with bvFTD engage in activities that usually produce strong disgust reactions in neurologically healthy individuals (e.g., consuming discarded food and beverages). Given that disgust is an emotion that protects us from engaging in potentially harmful activities in part by producing strong internal signals of avoidance (Rozin et al., 2008), the present study suggests that these signals may be missing or diminished in bvFTD.

Although we did not directly measure and quantify regional brain volumes in this study, the pattern of neurodegeneration typically seen in bvFTD supports some speculation as to the likely anatomical basis of our findings. One possibility is that loss in the anterior insula (Rosen et al., 2002; Seeley, 2010), a region that is important for processing visceral cues (Craig, 2002, 2009; Mutschler et al., 2009) and is often implicated in disgust responding (Adolphs, Tranel, & Damasio, 2003; Wright et al., 2004), renders patients with bvFTD unable to access internal sensations that provide “gut level” disgust cues. A second possibility is that loss in the anterior cingulate cortex, a region important for initiating an autonomic and behavioral emotional response, disrupts the mobilization of an emotional reaction in the patients with bvFTD in emotional contexts that normally trigger disgust. Thus, disruptions in either the efferent visceromotor pathways or afferent viscerosensation pathways may underlie the disruptions in disgust that we found in bvFTD.

Our prior research and that of others is providing a more differentiated picture of domains of emotional sparing and loss in bvFTD. The present study increases our understanding of the specific types of emotions that are impacted as this disease progresses, extending the emotional deficits to include disgust—an emotion that is important for basic survival and that also has important social and moral implications. While our previous research had found that other basic emotions (e.g., happiness and sadness) may be preserved in bvFTD (Werner et al., 2007), we had not previously directly assessed disgust reactivity using this approach. The one previous study of disgust processing in bvFTD that we are aware of (Bedoin et al., 2009) evaluated the impact of disgusting lexical and visual stimuli on reaction times, finding that bvFTD patients and normal controls were both slower to respond on trials that included disgusting images. The authors interpreted this finding as indicating that disgust reactivity was intact in bvFTD. These different conclusions might reflect the marked methodological differences between the Bedoin et al. study and ours (e.g., implicit versus explicit directions to attend to the emotional stimuli, inferring disgust reactivity from response time modulation versus direct measurement of multiple aspects of the disgust response to an emotion-eliciting film). Clearly this is an area that would benefit from additional research; however, we note that our findings of reduced disgust reactivity in bvFTD are quite consistent with clinical descriptions of the syndrome and neuroanatomical correlates of the disease.

4.1. Limitations

There are several limitations to the present study that should be considered. First, we did not include measures of regional brain volumes and thus cannot correlate deficits in disgust with loss in specific brain regions of interest (e.g., the anterior cingulate and insula). Second, we only assessed patients with bvFTD and did not examine those with other frontotemporal dementia subtypes (e.g., semantic dementia and progressive non-fluent aphasia) or with other neurodegenerative diseases. Thus, we do not know whether findings of diminished disgust reactivity are specific to bvFTD or whether they extend to other forms of neurodegenerative disease. Third, we did not assess emotional responding on repeated occasions within individuals as the disease progressed, thus we cannot know exactly when in the course of the disease deficits in disgust reactivity first appear.

4.2. Future directions

In future work, we plan to measure regional brain volumes in order to examine the relationship between specific areas of loss and compromised disgust reactivity. We are particularly interested in the insula. Recent models suggest the posterior insula is important for the objective mapping of internal sensations while the anterior insula is integral for the subjective experience of those sensations (Craig, 2002). Thus, anterior and posterior insula volumes may have different relationships with various components of disgust reactivity. For example, the posterior insula may be associated with physiological reactions to disgusting stimuli and the anterior insula may be more related to levels and qualities of subjective emotional experience.

Another important avenue to explore is the role that diminished disgust reactivity plays in patients' real-world behavior. Deficits in disgust reactivity may shed light on the unusual and socially inappropriate behaviors engaged in by bvFTD patients outside of the laboratory. Loss of disgust may not only be related to patients' lack of aversion to physically contaminated objects, but could also play a role in the changes that occur in their moral decision-making and behavior (Mendez, Chen, Shapira, & Miller, 2005).

5. Conclusions

The present study underscores the usefulness of applying techniques derived from basic affective science to the study of emotional functioning in patients with neurodegenerative disease (Levenson et al., 2008). Using our laboratory methods, we were able to document robust deficits in behavioral and physiological aspects of disgust reactivity and also found some evidence for reduced subjective experience of disgust reactivity in response to a disgust-eliciting film in patients with bvFTD. These findings build on our previous work and provide additional information about areas of preserved and compromised emotional functioning in this disease.

Role of the funding source

This work was supported by Grants from the National Institute on Aging AG017766, AG019724; National Institute of Mental Health MH020006; the State of California Alzheimer's Disease Research Center of California 03-75271; and the Hellman Family Center. These sponsors had no involvement in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Conflict of interest statement

The authors report no conflict of interest.

References

- Adolphs, R., Tranel, D., & Damasio, A. R. (2003). Dissociable neural systems for recognizing emotions. *Brain and Cognition*, 52(1), 61–69.
- Bedoin, N., Thomas-Antérion, C., Dorey, J.-M., & Lebert, F. (2009). Implicit sensitivity to disgust-inducing stimuli in self-neglect FTD patients. *Cognitive and Behavioral Neurology: Official Journal of the Society for Behavioral and Cognitive Neurology*, 22(4), 236–241.
- Boxer, A. L., & Miller, B. L. (2005). Clinical features of frontotemporal dementia. *Alzheimer Disease and Associated Disorders*, 19(Suppl. 1), S3–S6.
- Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences*, 4(6), 215–222.
- Craig, A. D. (2002). How do you feel? Interoception: The sense of the physiological condition of the body. *Nature Reviews Neuroscience*, 3(8), 655–666.
- Craig, A. D. (2009). How do you feel – now? The anterior insula and human awareness. *Nature Reviews Neuroscience*, 10(1), 59–70.
- Critchley, H. D. (2005). Neural mechanisms of autonomic, affective, and cognitive integration. *Journal of Comparative Neurology*, 493(1), 154–166.
- Damasio, A. R., Tranel, D., & Damasio, H. (1990). Individuals with sociopathic behavior caused by frontal damage fail to respond autonomically to social stimuli. *Behavioural Brain Research*, 41(2), 81–94.
- Devinsky, O., Morrell, M. J., & Vogt, B. A. (1995). Contributions of anterior cingulate cortex to behaviour. *Brain*, 118(Pt 1), 279–306.
- Ekman, P., Friesen, W. V., & Ancoli, S. (1980). Facial signs of emotional experience. *Journal of Personality and Social Psychology*, 39(6), 1125–1134.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12(3), 189–198.
- Gross, J. J., & Levenson, R. W. (1993). Emotional suppression: Physiology, self-report, and expressive behavior. *Journal of Personality and Social Psychology*, 64(6), 970–986.
- Kipps, C. M., Mioshi, E., & Hodges, J. R. (2009). Emotion, social functioning and activities of daily living in frontotemporal dementia. *Neurocase*, 15(3), 182–189.
- Levenson, R. W., Ascher, E., Goodkind, M., McCarthy, M., Sturm, V., & Werner, K. (2008). Laboratory testing of emotion and frontal cortex. In G. Goldenberg & B. L. Miller (Eds.), *Handbook of clinical neurology*. Vol. 88: *Neuropsychology and behavioral neurology* (pp. 489–498). Edinburgh, Scotland: Elsevier.
- Mendez, M. F., Chen, A. K., Shapira, J. S., & Miller, B. L. (2005). Acquired sociopathy and frontotemporal dementia. *Dementia and Geriatric Cognitive Disorders*, 20(2–3), 99–104.
- Mutschler, I., Wieckhorst, B., Kowalewski, S., Derix, J., Wentlandt, J., Schulze-Bonhage, A., et al. (2009). Functional organization of the human anterior insular cortex. *Neuroscience Letters*, 457(2), 66–70.
- Neary, D., Snowden, J. S., Gustafson, L., Passant, U., Stuss, D., Black, S., et al. (1998). Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria. *Neurology*, 51(6), 1546–1554.
- Neary, D., Snowden, J. S., & Mann, D. M. A. (2005). Frontotemporal dementia. *Lancet Neurology*, 4(11), 771–780.
- Rosen, H. J., Allison, S. C., Schauer, G. F., Gorno-Tempini, M. L., Weiner, M., & Miller, B. L. (2005). Neuroanatomical correlates of behavioural disorders in dementia. *Brain*, 128(Pt 11), 2612–2625.
- Rosen, H. J., Gorno-Tempini, M. L., Goldman, W. P., Perry, R. J., Schuff, N., Weiner, M., et al. (2002). Patterns of brain atrophy in frontotemporal dementia and semantic dementia. *Neurology*, 58(2), 198–208.
- Rozin, P., & Fallon, A. E. (1987). A perspective on disgust. *Psychological Review*, 94(1), 23–41.
- Rozin, P., Haidt, J., & Fincher, K. (2009). From oral to moral. *Science*, 323(5918), 1179–1180.
- Rozin, P., Haidt, J., & McCauley, C. R. (2008). Disgust. In M. Lewis, J. M. Haviland-Jones, & L. F. Barrett (Eds.), *Handbook of emotions* (3rd ed., pp. 757–776). New York, NY: Guilford Press.
- Rozin, P., Lowery, L., & Ebert, R. (1994). Varieties of disgust faces and the structure of disgust. *Journal of Personality and Social Psychology*, 66(5), 870–881.
- Seeley, W. W. (2010). Anterior insula degeneration in frontotemporal dementia. *Brain Structure & Function*, 214(5–6), 465–475.
- Seeley, W. W., Crawford, R., Rascovsky, K., Kramer, J. H., Weiner, M., Miller, B. L., et al. (2008). Frontal paralimbic network atrophy in very mild behavioral variant frontotemporal dementia. *Archives of Neurology*, 65(2), 249–255.
- Sturm, V. E., Ascher, E. A., Miller, B. L., & Levenson, R. W. (2008). Diminished self-conscious emotional responding in frontotemporal lobar degeneration patients. *Emotion*, 8(6), 861–869.
- Sturm, V. E., Rosen, H. J., Allison, S. C., Miller, B. L., & Levenson, R. W. (2006). Self-conscious emotion deficits in frontotemporal lobar degeneration. *Brain*, 129(Pt 9), 2508–2516.
- Werner, K. H., Roberts, N. A., Rosen, H. J., Dean, D. L., Kramer, J. H., Weiner, M. W., et al. (2007). Emotional reactivity and emotion recognition in frontotemporal lobar degeneration. *Neurology*, 69(2), 148–155.
- Wicker, B., Keysers, C., Plailly, J., Royet, J.-P., Gallese, V., & Rizzolatti, G. (2003). Both of us disgusted in my insula: The common neural basis of seeing and feeling disgust. *Neuron*, 40(3), 655–664.
- Wright, P., He, G., Shapira, N. A., Goodman, W. K., & Liu, Y. (2004). Disgust and the insula: fMRI responses to pictures of mutilation and contamination. *Neuroreport*, 15(15), 2347–2351.