Neuropsychologia 50 (2012) 786–790

Contents lists available at SciVerse ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

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.

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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0028-3932/$ – see front matter
doi:10.1016/j.neuropsychologia.2012.01.012

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. Intercoder 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 Finapress 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