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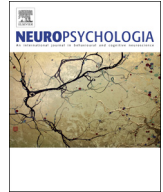
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Emotion regulation via visual avoidance: Insights from neurological patients^{☆, ☆☆}

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ABSTRACT

Visual avoidance of unpleasant stimuli (i.e., strategic positioning of eyes, head and torso away from an environmental stimulus) is a common attentional control behavior that may down-regulate emotion by reducing visual input. Despite its ubiquity, relatively little is known about how visual avoidance is affected by neurological diseases that impact neural circuits involved in emotional functioning. We examined visual avoidance in 56 behavioral variant frontotemporal dementia (bvFTD) patients, 43 Alzheimer's disease (AD) patients, and 34 healthy controls. Participants came to our laboratory and viewed an extremely disgusting film clip while visual avoidance was measured using behavioral coding of head, body, and eye position. Controlling for differences in cognitive functioning, bvFTD patients were less likely to engage in visual avoidance behaviors than both AD patients and healthy controls. Additional analyses revealed that diminished visual avoidance in this task was associated with lower levels of real-world emotion regulation but not with emotion reactivity as reported by the primary caregiver.

1. Introduction

The ability to regulate emotion is critical for adaptive emotional functioning. According to a prominent process model of emotion regulation (Gross, 1998, 2015), regulatory strategies can take effect at numerous places along the temporal sequence of emotion generation. Regulatory strategies that take place before an emotional response fully unfolds are known as *antecedent-focused* because they modify the situation, attentional processes, and appraisals that trigger emotion, rather than the emotional response itself. Four families of antecedent-focused emotion regulation have been identified, including *situation selection* (i.e., choosing to be in a situation that makes it more or less likely that you will experience a particular emotion), *situation modification* (i.e., altering aspects of a situation so that its emotional significance is changed), *attentional deployment* (i.e., mentally or visually attending toward or away from emotional aspects of a situation), and *cognitive change* (i.e., thinking about a situation in such a way that its emotional significance is altered) (Gross and Thompson, 2007).

To date, the most extensively studied antecedent-focused emotion regulation strategy has been cognitive reappraisal, a form of cognitive change that entails modifying one's appraisal of a situation in order to

change the resultant emotional experience. Although reappraisal is clearly an important form of emotion regulation, there is growing appreciation of the importance of regulatory activity that occurs even earlier in the emotion generation process particularly attention-mediated strategies (Bebko et al., 2011; Manera et al., 2014; van Reekum et al., 2007). Among attention-based emotion regulation strategies, distraction and rumination have been most extensively studied. Rumination (i.e., repeatedly thinking about an emotion eliciting event) is a prominent symptom of various psychopathologies, including anxiety and depression (Aldao et al., 2010), and has been found to impact mood, thinking, and behavior negatively (Lyubomirsky and Nolen-Hoeksema, 1993; Lyubomirsky and Nolen-Hoeksema, 1995; Lyubomirsky et al., 1998; McLaughlin et al., 2007; Mor and Winquist, 2002). Distraction involves mentally disengaging from negative stimuli, and has been associated with decreased self-report of emotion (Augustine and Hemenover, 2009).

Another potentially important yet understudied attention-based emotion regulation strategy is visual avoidance, a form of attentional control that directs attention away from a potential emotion elicitor (Field, 1981; Waters et al., 1975). Visual avoidance serves to gate emotionally powerful information, thus determining which aspects are

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available for additional processing. When visual sensory information is reduced in this way, it can short-circuit emotion generation, reducing or even eliminating downstream aspects of the emotional response.

1.1. Neurodegenerative disease as a model for studying visual avoidance

Prior research reports considerable disruptions in visual avoidance in various kinds of psychopathology (Bishop, 2009; Cisler et al., 2009; Derryberry and Reed, 2002; Eysenck et al., 2007; Joormann and Gotlib, 2007; Koster et al., 2005), yet little research has examined visual avoidance in neurodegenerative diseases (which can produce a number of psychiatric symptoms, Levenson et al., 2014). There are several reasons to believe that visual avoidance may be altered in neurodegenerative disease. First, attentional disturbances have been found in several neurodegenerative diseases, including subcortical vascular dementia and parkinsonian syndromes, such as dementia with Lewy bodies (Ballard et al., 2001; O'brain & Thomas, 2015). Second, disruption of visual processes is an early indicator of decline in several neurological diseases (Leigh and Kennard, 2004). For example, prominent abnormalities in visually guided saccades have been well-documented in neurodegenerative diseases with tau neuropathology, including progressive supranuclear palsy (PSP) and corticobasal syndrome (Garbutt et al., 2008; Vidailhet et al., 1994). Third, greater understanding of visual attention in neurological disease has clinical utility. Previous research finds that examining eye movement abnormalities is useful in diagnosing certain diseases (e.g., PSP) and helps differentiated them from other neurodegenerative diseases (Boxer et al., 2017; Rivaud-Péchoux et al., 2000). Moreover, attentional deficits have been linked with decreases in quality of life in patients with dementia, highlighting the real-world consequences of abnormal attentional processing (Lawson et al., 2016). Focusing on visual avoidance per se, prior research from our group has linked deficits in visual avoidance among patients with behavioral variant frontotemporal dementia (bvFTD) and Alzheimer's disease (AD) with greater psychological distress in spousal caregivers (Otero and Levenson, 2017), which is consistent with the important role that emotion regulation plays in interpersonal contexts.

Although most research on emotion regulation has studied patterns of activation using fMRI methods in neurologically healthy participants, patient models can also be extremely useful (e.g., allowing use of more intense emotion-eliciting stimuli than are feasible in the scanner environment). For both anatomical and clinical reasons, bvFTD provides a useful patient model for studying visual avoidance. bvFTD is characterized by atrophy of the frontal and temporal lobes (Rosen, 2005) and involves neural loss in areas thought to be important for emotion regulation (e.g., amygdala, anterior insula, prefrontal cortex; Seeley et al., 2009). Clinically, bvFTD patients present with profound behavioral changes, including diminished executive functioning (i.e., poor response inhibition, impulsivity), apathy, and blunted affect (Neary et al., 1998; Neary et al., 2005) and have deficits in several kinds of emotion regulation (Goodkind et al., 2010).

Disgust also plays a prominent role in the clinical presentation of bvFTD. For example, patients with bvFTD often presents with Diogenes syndrome, a clinical condition of extreme self-neglect and hoarding behavior characterized by home clutter and uncleanness (Finney and Mendez, 2017). Described as “senile squalor” (Macmillan and Shaw, 1966), this syndrome occurs in approximately 36% of individuals with bvFTD and may represent an underlying deficit in disgust-related processing (Lebert, 2005). In research from our laboratory, bvFTD patients have shown reduced physiological reactivity and expressive behavior to disgust-eliciting film stimuli compared to healthy controls (Eckart et al., 2012). Of direct relevance to visual avoidance, past work from our group has found disturbances in gaze behaviors in patients with bvFTD compared to other FTD subtypes and AD. Specifically, bvFTD patients spend less time looking at the faces of their caregivers compared to patients with AD and semantic dementia (Sturm et al., 2011). These

indications of diminished sensitivity to disgusting stimuli in the real world and in the laboratory and previously documented abnormalities in gaze behaviors, combined with the overlap between brain structures that degenerate in bvFTD and those likely involved in emotion regulation, support a hypothesis that bvFTD patients would show reduced levels of visual avoidance behaviors when encountering disgusting stimuli.

In the present study, we used data from a previous study (Otero and Levenson, 2017) to examine visual avoidance behavior to disgust eliciting stimuli in patients with bvFTD and patients with AD, a neurological condition that does not primarily affect emotion and emotion regulation centers of the brain. AD is characterized by progressive memory loss and atrophy of the hippocampus, medial temporal lobes, precuneus, entorhinal cortex, and posterior cingulate cortex (Braak and Braak, 1997; Greicius et al., 2004). Consistent with the relative sparing of emotional brain circuitry in the early stages of this disease (Braak and Braak, 1997; van Hoesen et al., 1991), abilities to generate and down-regulate emotion may be relatively preserved in AD patients (Goodkind et al., 2010; Mograbi et al., 2012). Thus, we expect AD patients to show relative preservation of visual avoidance behaviors when confronted with disgusting stimuli.

2. Methods

2.1. Participants

We recruited 56 patients with bvFTD, 43 patients with AD, and 34 healthy control participants through the Memory and Aging Center at the University of California, San Francisco. All participants underwent extensive examinations that included neurological testing, neuropsychological testing, and neuroimaging. Patient diagnoses were based on diagnostic criteria for bvFTD (Neary et al., 1998) and AD (McKhann et al., 1984) that were current at the time of their assessments. Control participants were screened to ensure that they had no history of neurologic, psychiatric, or cognitive disturbances. The current study included most of the bvFTD and AD patients that were included in an earlier study (Otero and Levenson, 2017), which reported on the adverse effects of diminished visual avoidance behavior in dementia patients on caregiver psychological distress. Patient overlap included 42 patients with bvFTD and 43 patients with AD. The current study included additional data from 49 participants (34 healthy controls and 14 new patients with bvFTD) that were not included in Otero and Levenson (2017).

Patient cognitive functioning was assessed using the Mini-Mental State Exam (MMSE), which was administered by a trained clinician. The MMSE covers several domains of cognitive functioning (i.e., orientation, memory, attention, naming and following verbal and written commands, writing a sentence, and drawing polygons) (Folstein et al., 1975). A summary score was computed for each participant by summing the total scores for each subtest, with higher scores indicating greater functional impairment.

2.2. Procedure

2.2.1. Laboratory assessment

Participants came to our laboratory at the University of California, Berkeley and participated in a day-long comprehensive assessment of emotional functioning (Levenson et al., 2008). Upon arrival at the lab, participants signed consent forms (approved by the Committee for the Protection of Human Subjects at the University of California, Berkeley) and were seated in a well lit, 3-m by 6-m room. A trained experimenter applied non-invasive physiological sensors that were used to monitor autonomic and somatic activity (see below).

The present study utilized data from a trial in which participants viewed a well-validated disgust-eliciting film clip (Shiota and Levenson, 2009) taken from the television show *Fear Factor*. The clip lasted 101 s

and shows a man sucking digestive fluids out of cow intestines, spitting them out into a cup, and gulping the fluids. Before viewing the film, participants were instructed to sit quietly for a 60-s baseline period. Participants then viewed the film clip and afterwards rated how much emotion they felt while viewing the film (see below). Participants were videotaped while watching the film for use in subsequent behavioral coding (see below). At the end of the day, participants provided written consent for the use of their video recordings and were paid \$30.

2.2.2. Audiovisual apparatus

All experimental stimuli were presented on a 21-inch LCD monitor positioned 1.75 m away from the participant. Task instructions and post-task questions were audio-recorded and played for the participant. A remotely controlled high-resolution color video camera placed behind darkened glass in a bookshelf recorded participants' facial behavior and body movement.

3. Measures

3.1. Visual avoidance behavior

Visual avoidance behavior was coded using the Attentional Control Coding System (ATCO; Otero and Levenson, 2017), which was developed by the authors. ATCO consists of 13 codes encompassing two forms of attentional control behaviors: (a) visual avoidance (i.e., head, body, and eye movements that serve to gate visual information) and (b) distancing (i.e., behaviors indicating mental or physical distancing from the stimuli).¹

Because of our interest in visual avoidance as a form of emotion regulation, the current study focuses on the 9 visual avoidance codes (head turn, head down, head up, head shake, gaze aversion, eyes closed, eyes covered, blink, squint) (see Fig. 1). Eight out of the nine visual avoidance codes (i.e., head turn, head up, head down, head shake, eye closed, eyes covered, gaze aversion, squint) were rated for intensity on a second by second basis, and one code (i.e., blinks) was rated for frequency across the task. Each code rated for intensity was coded by using one of three intensity scales: a) a 4-point scale assessing the intensity of head movements (i.e., head turn, head down, head up, head shakes) (0 = no head movement, 1 = slight head movement, 2 = moderate head movement, 3 = extreme head movement); b) a 3-point scale assessing the intensity of eye coverage (i.e., eyes closed, eyes covered) (0 = no eye coverage, 1 = partial eye coverage, 2 = complete eye coverage); c) a 2-point intensity scale assessing the presence or absence of gaze aversion and squints. Blinks were coded for frequency across the entire film clip (i.e., each blink counted as 1 and coders summed each discrete episode of a blink to create an overall blink score for each participant).

Three post-baccalaureate research assistants underwent six-weeks of training consisting of studying the ATCO manual, completing practice coding assignments, and participating in weekly one-hour meetings to discuss coding. Inter-rater reliability at the end of training was very high (intra-class correlation coefficient = 0.90). Once coders reached reliability standards, they began coding the video recordings of study participants. Coders were blind to the experimental stimulus and participant diagnosis. Inter-rater reliability for the present study was good (overall intra-class correlation coefficient = 0.82; reliabilities for individual codes ranged from 0.99 for blink to 0.65 for head turn).

¹ ATCO mental and physical distancing codes include: disapproving verbal utterances (e.g., "Oh Jeez"), explicit requests to have the film stopped, eye rolling, and pulling one's body backwards. Ad hoc exploratory analyses showed that distancing behavior occurred infrequently among participants (body backwards, eye roll, & stop requests: 0.8% of participants; disapproving speech: 1.5% of participants) thus, due to their low base rate, they were dropped from further analyses.

3.2. Emotional facial behavior

Emotional facial behavior was coded using the Expressive Emotional Behavior Coding System (Gross and Levenson, 1993). We have used this coding system previously to code disgust behavior of patients with neurodegenerative diseases and healthy adults (Eckart et al., 2012; Goodkind et al., 2010; Gross and Levenson, 1993). Ten emotions (i.e., contempt, anger, disgust, fear, sadness, surprise, embarrassment, happiness/amusement, confusion, interest) were coded on a 0–4 intensity scale (0 = no code; 1 = slight; 2 = moderate; 3 = strong) by a team of three undergraduate research assistants. Emotion behavior coders were different individuals than the visual avoidance coders. All coders underwent extensive training, including weekly meetings to discuss coding disagreements and practice assignments. Inter-coder reliability for emotion coding was high (intra-class correlation coefficient = 0.92). The present study focused on the facial display of disgust because that was the emotion targeted by the film stimulus.

3.3. Physiological activity

Autonomic and somatic nervous system activity was monitored continuously using BIOPAC modules and an online data acquisition software package written by one of the authors (R.W.L.). The software computed second-by-second averages of each of the following measures: (1) heart rate (Electrodes filled with conductive paste were placed on either sides of the participant's torso to record the electrocardiogram [EKG]). The inter-beat interval was measured by the time interval, in milliseconds, between successive R waves; (2) finger pulse amplitude (A UFI photoplethysmograph recorded the amplitude of blood volume in the finger using a photocell attached to the distal phalanx of the non-dominant hand's index finger); (3) finger pulse transmission time (The time interval, in milliseconds, was measured between the R wave of the EKG and the upstroke of the peripheral pulse recorded at the finger); (4) ear pulse transmission time (A UFI photoplethysmograph was attached to the participant's right earlobe and recorded the blood volume in the ear. The time interval, in milliseconds, was measured between the R wave of the EKG and the upstroke of the peripheral pulse at the ear); (5) finger temperature (A thermistor was attached to the distal phalanx of the non-dominant hand's little finger to record temperature in degrees Fahrenheit); (6) systolic and (7) diastolic blood pressure (A blood pressure cuff was positioned on the middle phalanx of the middle finger of the participant's non-dominant hand and continuously recorded blood pressure using an Ohmeda Finapres 2300); (8) skin conductance (A constant-voltage device passed a small voltage between electrodes attached to the middle phalanges of the ring and index fingers of the non-dominant hand); (9) general somatic activity (An electromechanical transducer attached to a platform under the participant's seat generated an electrical signal proportional to the amount of movement in any direction); (10) respiration period (A pneumatic bellows stretched around the thoracic region measured the inter-cycle interval, in milliseconds, between successive inspirations).

This set of measures comprises our standard laboratory assessment of peripheral physiological functioning (Eckart et al., 2012; Sturm et al., 2006, 2008; Verstaen et al., 2016). The measures were selected to provide a broad index of activity in autonomic and somatic systems, including cardiac, vascular, electrodermal, respiratory, and striate muscle activity, that have been found to change during emotion (Boiten et al., 1994; Bradley and Lang, 2010; Kreibig et al., 2011; Mauss and Robinson, 2009). Prior research characterizing the physiological changes that occur during disgust has found both activation and deactivation of cardiovascular measures (for a review see Kreibig, 2010), increased respiratory activation (Boiten, 1998; Collet et al., 1997; Gross and Levenson, 1993; Kreibig, 2010; Kunzmann et al., 2005; Levenson et al., 1992; Palomba et al., 2000), and increased skin conductance



Fig. 1. Images of a participant depicting visual avoidance behaviors (a) head turn and gaze aversion (b) head down and eyes closed. (Participant provided informed consent for publishing these images.)

levels (Christie and Friedman, 2004; Demaree et al., 2004; Gross and Levenson, 1993; Gross, 1998; Kunzmann et al., 2005; Rohrmann and Hopp, 2008) compared to baseline.

3.4. Self-reported emotion

Following the film, participants were asked to rate how intensely they experienced each of 11 emotions (affectionate, afraid, amused, angry, ashamed, calm, disgusted, embarrassed, enthusiastic, proud, sad) on a 0–2 scale (0 = not at all; 1 = a little; 2 = a lot). The present study focused on participants' subjective experience of disgust because that was the emotion targeted by the film stimulus. Group means and standard deviations for all self-report ratings are presented in Fig. 2.

3.5. Caregiver report of patient emotion regulation

Given that most studies of emotion regulation have not examined visual avoidance, we wanted to determine whether our laboratory-

based assessment of visual avoidance was related to a real-world measure of emotion regulation. To do this we used the 2-item emotion regulation subscale of the Caregiver Assessment of Socio-Emotional Functioning (CASEF; Ascher, 2012). On the CASEF, caregivers rate the patient's emotion regulation ability (without mention of any particular regulatory strategy) in the past month (i.e., "Patient expresses negative emotions appropriately for a given situation without letting them get out of hand" and "Patient expresses positive emotions appropriately for a given situation without letting them get out of hand") on a 5-point scale from 0 (not at all) to 4 (a lot). The emotion regulation score was computed by averaging the 2 items. Reliability for this score was high (Cronbach's α coefficient = 0.88).

In order to determine whether visual avoidance is uniquely associated to real-world emotional regulation and not emotional reactivity, we also examined the CASEF emotional reactivity subscale, which asks caregivers to rate the frequency of occurrence of 10 patient emotions (anger, fear, sadness, disgust, joy, amusement, embarrassment, shame, guilt, and pride) over the last month (e.g., "[Patient] Expresses anger")

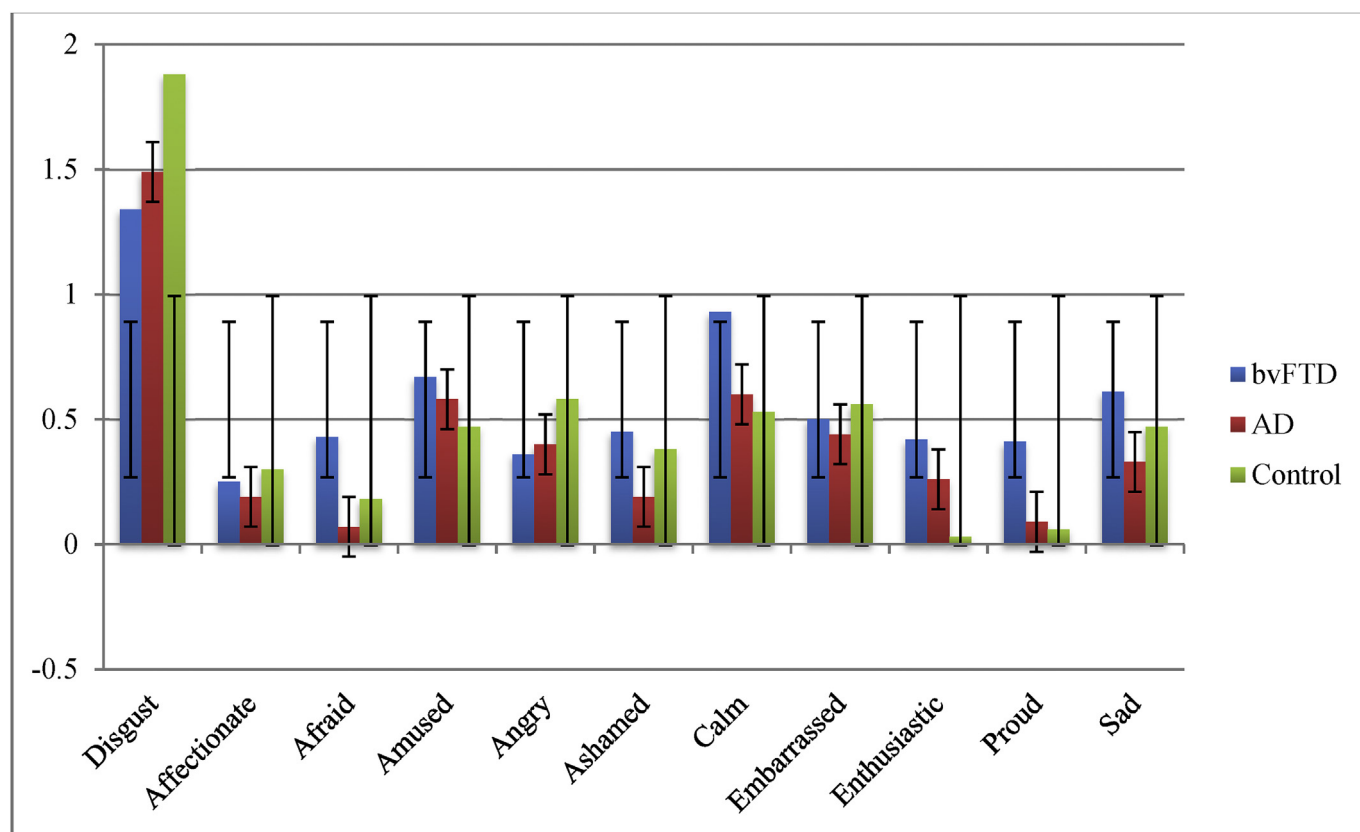


Fig. 2. Raw means of self-report emotional experience during the disgust reactivity task. Standard deviations are represented in the figure by error bars attached to each column.

on a 0–4 scale (0 = not at all; 4 = a lot). A total CASEF emotion reactivity score was computed by averaging the 10 items. Reliability for this score was moderately high (Cronbach's α coefficient = 0.68).

4. Data reduction

4.1. Visual avoidance behavior

Visual avoidance behavior was coded second by second for the entire duration of the disgust film stimulus (i.e., 101 s). We decided to code visual avoidance behaviors throughout the entire film rather than make a priori assumptions regarding when visual avoidance would be most likely to occur. Although it would be reasonable to expect visual avoidance to occur during the most emotionally intense moments of the film, it might also occur in anticipation of these moments or afterwards as part of the post-emotion recovery. Preliminary analyses showed that two of the nine visual avoidance codes (squint and eyes covered) occurred infrequently among participants (squint in 4.2% and eyes covered in 0.8% of participants). Due to their low base rates, squint and eyes covered were removed from further analyses, thus leaving 7 visual avoidance codes (head turn, head up, head down, gaze aversion, blink, eyes closed, and headshake).

Internal consistency of the 7 codes was low (Cronbach's α coefficient = 0.53). In an attempt to improve reliability, we removed items one at a time to determine their effect on overall reliability. Results showed that reliability among the visual avoidance codes (across the diagnostic groups) was greatest after removing headshake (Cronbach's α = .62), thus this code was removed from further analyses. Given that internal consistency of the resultant visual avoidance scale was good and to reduce the risk of Type I error, a single visual avoidance composite score was computed for each participant as follows: (a) for all codes scored for intensity on a second-by-second basis (i.e., head

turn, head down, head up, eyes closed, gaze aversion) we summed the second by second scores and divided this sum by 101 (total number of seconds coded). For blinks (the only code not coded for second by second), we divided the total number of blinks by 101 to create an average blink score; (b) we z-scored all average scores using the means and standard deviation from the entire sample to account for differences in intensity scaling; (c) we summed the z-scored scores to create a composite score representing overall visual avoidance throughout the entire task, with higher scores indicating greater visual avoidance.

4.2. Physiological activity

Data reduction for physiology measures followed our usual procedures (Eckart et al., 2012; Goodkind et al., 2010; Gyurak et al., 2012; Shiota and Levenson, 2009; Sturm et al., 2008; Verstaen et al., 2016). Second-by-second values for each physiological measure were averaged during the 60-s pre-film baseline period and during a 30-s "hot spot" within the film (i.e., the most emotionally intense 30 s of the film previously identified by a panel of raters). The baseline average was subtracted from the hot spot average to create a difference score. For eight of the 10 measures (all measures except for skin conductance and finger temperature) the entire 60 s of the baseline period were used. Because skin conductance and finger temperature values often show slow linear trends, we used the last ten seconds of the pre-film period to compute the baseline average to ensure that physiological reactivity elicited by the preceding task did not influence baseline calculations for the disgust reactivity task (e.g., Sturm et al., 2008). Each change score was normalized using means and standard deviations from the entire sample. Normalized scores for inter-beat interval, finger pulse amplitude, finger pulse transmission time, ear pulse transmission time, and respiration period were inverse scored by multiplying values by -1 so that for all measures larger Z-scores indicated greater activation. The

resultant Z-scores for all ten measures were averaged to compute a single composite score representing overall physiological activation. We have used previously used composite scores to provide an overall index of autonomic and somatic activity and to control for Type 1 error (e.g., Verstaen et al., 2016; Eckart et al., 2012; Sturm et al., 2008). However, given that the Cronbach's α coefficient for the 10 measures was low ($\alpha = 0.35$), we also conducted exploratory follow-up using the individual physiological measures.²

4.3. Facial behavior

Data analytic decisions for emotion behavior coding were made a priori, following procedures we have used in previous studies of healthy and patient populations (i.e., Eckart et al., 2012; Goodkind et al., 2010; Gyurak et al., 2012; Sturm et al., 2006; Sturm et al., 2008; Verstaen et al., 2016). An average score for disgust was computed by summing the coding scores during the film's hot spot and dividing this sum by the total number of seconds coded (i.e., 30). The 30-s segment used in the current study has been found to produce disgust reliably in healthy older adults (i.e., Shiota and Levenson, 2009).

5. Results

5.1. Demographic and clinical variables

The distribution of males and females among diagnostic groups was compared using a chi-square test. No significant sex difference among groups was found, $\chi^2(3, N = 134) = 2.52$, ns. Age differences between diagnostic groups were examined using analysis of variance (ANOVA). No significant age difference among the groups was found, $F(2, 130) = 1.89$, ns. ANOVA was also used to examine diagnostic group differences in cognitive functioning, as assessed by the MMSE. Results revealed significant group differences, $F(2, 130) = 29.50$, $p < .001$, with AD patients showing the greatest levels of cognitive impairment followed by bvFTD patients and healthy controls. Subsequently, we controlled for cognitive functioning in all analyses. Demographic and clinical data for all groups are presented in Table 1.

Given the association between Diogenes syndrome and bvFTD, we reviewed participant medical records for anecdotal accounts of Diogenes-like behavior. 18% of the study's participants with bvFTD demonstrated hoarding behavior (i.e., 10 out of the 56). 32.7% of bvFTD participants were rated as not following common norms for personal hygiene by their caregivers on the CASEF (i.e., "Follows common norms for personal hygiene", 0–4 point scale with 0 indicating "not at all" and 4 indicating "a lot"). CASEF personal hygiene score was used as a covariate in all subsequent analyses.

5.2. Task manipulation check

Table 2 shows participant's average subjective experience of disgust and average disgust facial display (Raw M and standard deviation). One-sample t -tests (test-value = 0; Bonferroni corrected for 2 comparisons) revealed that participants across diagnostic groups reported experiencing disgust at a level that significantly differed from zero, $t(132)$, $p < .001$. Participants' average disgust facial display also significantly differed from zero, $t(124)$, $p < .001$. These results indicated that our stimuli successfully elicited disgust.

² An exploratory principal component analysis (PCA) was run on the individual physiological measures. Derived composites from the PCA were examined. Results were highly similar to those found for the overall composite score as reported in the Results section.

5.3. Disgust reactivity

In examining group differences in any form of emotion regulation, it is important to consider possible group differences in the magnitude of the emotional response that needs to be regulated. Given that we had previously found bvFTD patients to be less reactive to disgusting stimuli than healthy controls (Eckart et al., 2012), we examined diagnostic group differences in three indicators of disgust reactivity: (a) disgust facial behavior, (b) physiological reactivity (the overall composite), and (c) self-reported disgust to the film using ANCOVAs with diagnosis as a fixed factor and MMSE score and CASEF personal hygiene score as covariates. No diagnostic group differences were found in disgust facial behavior, overall physiological activation or, self-reported disgust. Raw means and standard deviations for all emotion reactivity measures are presented in Table 2.

We also conducted similar analyses for the individual physiological measures, only finding a trending main effect for diagnosis for inter-cycle interval (ICI), $F(2, 86) = 3.088$, $p = .051$, $\eta^2 = 0.074$, with bvFTD patients showing less pronounced shortening of ICI from pre-film baseline compared to healthy controls patients ($M_{diff} = -0.701$, $SE = 0.28$, $p = .045$). This finding suggests that patients with bvFTD tended to show diminished respiratory activation to the disgusting film than did healthy controls; a finding consistent with prior work suggesting diminished disgust responding in this population (Eckart et al., 2012). No differences in ICI were found between bvFTD and AD patients ($M_{diff} = -0.074$, $SE = 0.26$, $p = 1.00$), or AD patients and healthy controls ($M_{diff} = -0.627$, $SE = 0.35$, $p = .242$). Raw group means and standard deviations for ICI are presented in Table 2.

5.4. Visual avoidance behavior

We first analyzed visual avoidance using an ANCOVA with diagnostic group as a fixed-factor and MMSE and CASEF personal hygiene score as covariates. The main effect for diagnosis was significant, $F(2, 129) = 5.197$, $p = .007$, $\eta^2 = 0.081$. Bonferroni-corrected pairwise comparisons revealed that bvFTD patients had lower levels of visual avoidance behaviors compared to AD patients ($M_{diff} = -1.919$, $SE = 0.76$, $p < .05$), and healthy controls ($M_{diff} = -2.286$, $SE = 0.87$, $p < .05$). No group differences were found between AD patients and controls (AD $M = .741$; control $M = 1.109$). Thus, our hypothesis that bvFTD patients would have diminished visual avoidance compared to AD patients and neurologically healthy controls was supported. Means and standard errors of visual avoidance behavior are presented in Table 2.

5.5. Visual avoidance and emotional reactivity

To examine how visual avoidance relates to measures of emotional responding, we computed bivariate correlations for participant visual avoidance scores and the three measures of disgust reactivity. Across the entire sample, greater visual avoidance was associated with greater disgust facial expressions ($r = 0.217$, $p < .05$), greater increases in ear pulse transmission time from pre-film baseline ($r = 0.284$, $p < .005$), and greater increases in skin conductance levels from pre-film baseline ($r = 0.178$, $p < .05$). No associations were found between visual avoidance and self-reported disgust or the composite physiology score. We followed this up with moderation analyses using the Hayes PROCESS macro (model 1, release 2.16.3; Hayes, 2013). Patient visual avoidance behavior across the entire task was the dependent variable. Predictor variables included 2 dummy coded variables (one for the bvFTD group and one for the AD group, with controls serving as the reference group), 2 interaction terms (created by multiplying the dummy variables by each index of emotional responding), and the index of emotional responding. No evidence of moderation by diagnosis was found.

Furthermore, to explore the influence that emotional reactivity

Table 1
Demographic and clinical variables.

	bvFTD (n = 56) M (SD)	AD (n = 43) M (SD)	Controls (n = 34) M (SD)	Statistical test value
Sex	21(F) 35(M)	18(F) 25(M)	19(F) 15(M)	$\chi^2 (3, N = 134) = 2.52, ns$
Age	61.64 (8.16)	61.81 (8.23)	64.94 (8.74)	$F (2, 130) = 1.89, ns$
MMSE	24.52 (5.11)	21.70 (5.27)	29.56 (0.61)	$F (2, 130) = 29.50, p < .001$

Note. MMSE = Mini-Mental State Exam. bvFTD = behavioral variant frontotemporal dementia. AD = Alzheimer's disease.

Table 2
Visual avoidance behavior composite score and disgust reactivity measures.

	bvFTD M (SD)	AD M (SD)	Controls M (SD)	Statistical test value
Self-reported disgust	1.34 (.88)	1.49 (.70)	1.88 (.33)	$F (2, 129) = .297, ns$
Physiological reactivity	-.10 (.39)	-.03 (.38)	.06 (.80)	$F (2, 125) = .37, ns$
Inter-cycle interval	-.21 (.74)	-.17 (.75)	.73 (1.45)	$F (2, 86) = 3.08, p = .051$
Disgust facial behavior	13.55 (17.98)	17.44 (17.27)	25.79 (20.39)	$F (2, 121) = 2.06, ns$
Visual avoidance behavior	-1.16 (1.68)	.64 (3.85)	1.06 (4.68)	$F (2, 129) = 5.20, p = .007$

Note. Raw means and standard deviations. Statistical test values for behavior, physiology, and self-report are from GLM analyses, with diagnosis as fixed factors and MMSE and CASEF personal hygiene score as covariates.

might have on visual avoidance behavior, linear regression analyses were run to examine whether disgust facial behavior (i.e., during the 30 most intense seconds of the film) predicted visual avoidance behavior in the next 14 s (i.e., from the end of the hot spot to the end of the stimulus clip). In the full sample, greater disgust expressivity during the emotional hotspot predicted greater subsequent visual avoidance ($\beta = 0.320, t (117) = 3.64, p < .001$). Follow up moderation analyses were conducted. Post hotspot visual avoidance behavior was the dependent variable. Predictor variables included 2 dummy coded variables (one for the bvFTD group and one for the AD group, with controls serving as the reference group), 2 interaction terms (created by multiplying the dummy variables by patient's disgust facial behavior during the hotspot), and the patient disgust facial behavior during the hotspot. No evidence of moderation by diagnosis was found.

5.6. Visual avoidance in the laboratory and emotion regulation and reactivity in the home

Using combined data from the AD and bvFTD participants, a partial correlation was computed to determine whether patient visual avoidance to the film was associated with CASEF ratings of emotion regulation in the home, controlling for a composite of disgust reactivity (average of facial behavior, physiology, and self-report) in response to the film. Results revealed that greater patient visual avoidance in response to the film was significantly associated with greater caregiver report of emotion regulation ($r = 0.227, p < .05$).

To examine if visual avoidance relates to other aspects of real-world emotional functioning, we computed a bivariate correlation to determine whether patient visual avoidance to the film was associated with CASEF ratings of emotional reactivity in the home. No association was found ($r = 0.008, ns$). These findings provide important validity data indicating that visual avoidance behavior measured in the laboratory is related to a measure of real-world emotion regulation but not to a measure of real-world emotional reactivity.

6. Discussion

Using a laboratory assessment of emotional responding, we found that patients with bvFTD were less likely to utilize visual avoidance behaviors than patients with AD and healthy controls when confronted with a disgusting film stimulus. Visual avoidance is a common form of avoidance that may function to regulate emotion, serving to limit sensory input early in the emotion elicitation sequence and thus

significantly down-regulating subsequent emotion response (i.e., “what you don't see can't affect you”). Assessing visual avoidance in neurodegenerative populations may be particularly informative because it is arguably a more “primitive” and less “deliberative” form of emotion regulation than more commonly studied emotional regulation strategies such as cognitive reappraisal (thinking about the eliciting stimuli in a different way) and suppression (attempting to reduce observable emotional responding while in the throes of emotion).

6.1. Implications for understanding behavioral deficits in bvFTD

Disgust plays a critical role in the clinical presentation of bvFTD, with powerful implications for both patients and caregivers. Avoidance behaviors associated disgust typically function to protect us from disease, decay, and contamination. Patients with bvFTD who have deficits in the activation of these withdrawal behaviors are prone to approach substances and situations that can be highly harmful. Viewed through a more interpersonal lens, patients with bvFTD often engage in behaviors that *others* find disgusting. Failure to avoid disgusting things can create embarrassing situations and significant social challenges for caregivers and family members. These concerns can foster increased social isolation, which reduces access to potentially helpful social resources. Visual avoidance may be an intermediary step between the experience of disgust and behavioral avoidance that works in the service of regulating emotion rather than protecting the body from physical harm. In this way, visual avoidance could be seen as protecting the mind against contamination rather than the body (Rozin et al., 2008). Results from the present study indicate that visual avoidance in response to disgusting stimuli is particularly diminished in bvFTD, but may be relatively preserved in AD (or at least in the early stages).

What causes the diminished visual avoidance in bvFTD found in the present study? In considering this question, several possible explanations emerge. First, it is possible that neurodegeneration of key attentional networks in bvFTD cause patients to no longer attend to disgusting stimuli. This could be driven by disease-related changes in either bottom-up (e.g., stimulus driven) and/or top-down (e.g., attentional control) neural circuits. However, in previous work we have found that patients with bvFTD evidenced no deficits in recalling the content of disgusting films (Eckart et al., 2012). Thus, they were clearly attending to the films and processing their content. Second, it is possible that bvFTD patients have deficits in the capacity to generate disgust. Consistent with this, in a prior study, bvFTD patients showed lower levels of subjective experience, expressive behavior, and

peripheral physiological response when exposed to a disgusting film compared to normal controls (Eckart et al., 2012). Additionally, bvFTD often presents with Diogenes syndrome, which is characterized by diminished avoidance of stimuli that would normally elicit disgust (e.g., domestic squalor and neglect of personal hygiene). If disgust generation is reduced, it is reasonable to expect that related avoidance behaviors would also be reduced and, thus, we expect that this is a contributing factor. However, it is important to note that in the present study (which used different patients and a different film stimulus), bvFTD patients did not differ from AD patients in disgust facial expression, subjective experience of disgust, or overall physiological activation but still showed less visual avoidance behavior. These findings suggest to us that another plausible explanation for our finding is that bvFTD patients have a deficit in the capacity of disgust to activate avoidance behaviors. The close links between particular emotions and particular patterns of motor behavior (e.g., disgust and avoidance) have been a central notion in many “functionalist/evolutionary” views of emotion (e.g., Frijda, 1986). Developmental research has found that visual avoidance appears in infancy (Fraiberg, 1982; Field, 1981; Waters et al., 1975) suggesting that looking away from noxious stimuli may be an innate motor response. Viewed through a contemporary dual-process framework of emotion regulation that distinguishes between effortful action aimed at altering an undesirable emotional state (i.e., deliberate emotion regulation) and unconscious processes initiated by the basic registration of sensory information (i.e., automatic emotion regulation) (Mauss et al., 2007; Gyurak et al., 2011; Koole et al., 2015), visual avoidance may be a more automatic form of emotion regulation, which occurs unconsciously and is largely initiated by the perception of sensory information. The disruption of visual avoidance in patients with bvFTD may indicate a breakdown in this automatic form of emotion regulation that results from the patterns of neurodegeneration that characterize the disease.

We expect that the generation of emotion and the activation of associated motor behaviors are subserved by overlapping, but somewhat dissociable neural circuitry. A functional analysis of visual avoidance suggests candidate neural circuitry in the attentional control network. The rapid detection of behaviorally relevant stimuli in the environment may entail bottom-up processing of sensory information, which relies on temporoparietal cortex and inferior frontal cortex (Corbetta and Shulman, 2002). Limbic structures such as the anterior insula and the amygdala that are involved in the detection of emotionally salient stimuli may assist other neural regions in generating behavioral responses to these stimuli (Wiech et al., 2010; Bush et al., 2000; Menon and Uddin, 2010; Amaral, 2003). At a perceptual level, visual avoidance requires processing of visual and auditory information from one's environment, thus brain regions involved in perceptual representations may be particularly important, such as the superior temporal cortex (Karnath, 2001). Visual avoidance may also require cognitive selection of sensory stimuli, and thus may involve top-down attentional control. Neuroimaging studies suggest that top-down attentional control is associated with intraparietal cortex and superior frontal regions (Ferri et al., 2013; Hopfinger et al., 2000). Finally, visual avoidance is carried out by controlling movements of the eyes, head, or body, thus likely involving frontal eye fields, superior colliculus, and motor cortices (Corbetta and Shulman, 2002; Mesulam, 1981). Future work will benefit from examining the links between visual avoidance deficits and specific areas of neural loss.

Laboratory tasks that assess aspects of emotional functioning can sometimes uncover deficits that do not translate well into real-world behaviors. In the case of our laboratory assessment of visual avoidance, this was not the case. Deficits in visual avoidance as measured in the laboratory were associated with deficits in emotion regulation in the home environment as viewed by the caregiver but were not associated with comparably measured deficits in emotional reactivity. This adds additional confidence to our view that our laboratory-based measure of visual avoidance in patients is sensitive to their ability to regulate

emotion in the real world.

6.2. Implications for normal emotional functioning

Although the primary focus of the present study was on understanding behavioral deficits in bvFTD, the work also has implications for our understanding of normal emotional functioning. Many laboratory studies of emotional reactivity and emotion regulation use visual stimuli that elicit disgust (e.g., images of decay and disease, surgical procedures, bodily waste). Such images are often highly effective in eliciting quite strong emotions in neurologically intact populations. With potent disgust eliciting visual stimuli, visual avoidance (looking away) may be an extremely common response which can be viewed as a precursor to the “action tendency” of behavioral withdrawal associated with disgust (Frijda, 1986). Viewed in this way, visual avoidance serves as an emotion regulation strategy and intermediary step between the experience of emotion and full-formed behavioral avoidance. Although the current study does not allow for precise examination of the temporal dynamics of emotional responding and visual avoidance, our finding of a relationship between emotional responding at the peak emotional moment of the film and subsequent visual avoidance lends some support to this temporal sequence. In this case, visual avoidance may be an effective strategy for down-regulating emotion (i.e., if sensory input is reduced, then the subsequent emotional experience, behavior, and physiology should also be reduced). Visual avoidance may be most effective and functional in low-urgency situations when individuals can afford to be less vigilant of their surroundings. Prior work lends support to this assumption. For example, visual avoidance has been found in specific phobias (i.e., blood-injection-injury phobia), but not in posttraumatic stress disorder, which is characterized by hypervigilance to threatening stimuli in the environment (Armstrong et al., 2013a, 2013b; Armstrong and Olatunji, 2012; Dalgleish et al., 2001). Alternatively, visual avoidance may be particularly effective in short-lived, high intensity emotional states. The process-specific timing hypothesis provides a theoretical framework for this assumption (Sheppes and Gross, 2011). According to this view, different emotion regulation strategies may be more or less sensitive to emotional intensity depending on the cognitive processes they target. Strategies that rely on early-stage cognitive processes, such as attention, are less sensitive to emotional intensity because they filter out emotional information before emotion is allowed to develop completely, and thus require less effort to enact. Strategies that rely on later-stage cognitive processes, such as semantic processing, would be more sensitive to emotional intensity because emotional information has not been filtered out and accordingly would require greater effort to halt the unfolding emotion (Sheppes and Gross, 2011, 2012). Importantly, prior empirical work suggests that early-stage cognitive processes may be effectively enacted at later time points and, thus, may not be temporally limited to occurring at the start of the emotion generative process (Gross, 2015; Sheppes and Meiran, 2007). Moreover, visually mediated emotion regulation may account for some of the effectiveness of late-stage regulation (van Reekum et al., 2007; Manera et al., 2014).

Ironically, despite the ubiquity of visual avoidance in real life and its clear theoretical importance, most laboratory research on emotion regulation has focused on more cognitive (e.g., re-appraising the meaning of the emotional stimulus) and motor (e.g., suppressing expressive behavior) strategies, both of which arguably occur later in the emotion elicitation sequence and require more elaborate neural and psychological processing than visual avoidance. Obviously, appraisal and suppression are extremely important ways that emotions are regulated, but the relative paucity of research on visual avoidance strategies is unfortunate. Moreover, prior research on emotion regulation suggests that strategies targeting attention may in fact have powerful effects on emotional responding. For example, the greater use of rumination has been associated with reduced willingness to take part in pleasurable activities, increased pessimism, and greater recall of

negative autobiographical information (Lyubomirsky and Nolen-Hoeksema, 1993; Lyubomirsky and Nolen-Hoeksema, 1995; Lyubomirsky et al., 1998; McLaughlin et al., 2007; Mor and Winquist, 2002). Physiologically, negative rumination is associated with increased cardiovascular activation including elevated heart rate (McClelland et al., 2009). Interestingly, the current study found significant associations between increased EPT and SCL (i.e., greater disgust reactivity in response to the disgust-eliciting film) and visual avoidance. The findings that greater visual avoidance is associated with greater EPT and SCL change from baseline may suggest that more intense emotion generation can trigger greater efforts to down-regulate via visual avoidance behavior. However, causality cannot be inferred in the current study. An alternative explanation could be that the greater use of visual avoidance promotes increased emotional reactivity, similar to prior work on the physiological effects of behavioral suppression (e.g., Gross and Levenson, 1993). Future empirical work should examine the temporal relationship between visual avoidance and autonomic nervous system reactivity (particularly in measures such as EPT and SCL, which reflect sympathetic nervous system activity) to clarify the regulatory effects of visual avoidance. Moreover, in laboratory studies where individuals are explicitly instructed to use regulation strategies such as suppression and/or reappraisal, it will be important to determine the extent that they instead utilize the more readily available visual avoidance strategies. One motivation for our developing the methods for studying and objectively coding visual avoidance behaviors used in the present study is the hope that these will prove useful for others who wish to study this important form of emotion regulation in both healthy populations and in those with neurodegenerative and psychiatric disorders.³

6.3. Strengths and limitations

To our knowledge this study provides the first systematic examination of visual avoidance behaviors in individuals with neurodegenerative disease. Strengths of the study include having relatively large patient samples, including individuals with two different diseases (bvFTD and AD) and a group of healthy controls; controlling for differences in cognitive functioning; and developing and applying an objective observational coding system for quantifying visual avoidance and other attentional control behaviors. Limitations of the study include the use of a single emotion (disgust), the use of a single disgust-eliciting film, and the inability to characterize individual patients in terms of their particular patterns of neural degeneration. We should also note that in this initial study, we did not instruct subjects to down-regulate emotion or to do so by using a particular emotion regulation strategy (e.g., instructing subjects to increase or decrease visible emotional behaviors; Gyurak et al., 2011). Thus, this study is sensitive to deficits in spontaneous visual avoidance; we cannot know whether similar deficits would occur if participants were explicitly instructed to use visual avoidance. Additionally, future studies of visual avoidance may benefit from using eye-tracking methodology to capture gaze patterns and fixation times during visual avoidance behavior. This will allow for a more nuanced understanding of the attentional processes underlying visual avoidance behavior. Lastly, the emotion-elicitation method (i.e., watching a particular disgusting film) used in the current study did not produce sufficient amounts of potentially important non-visual distancing behaviors (e.g., moving the body away from the film stimulus and eye rolling) to allow analyses of diagnostic group differences. Future work would benefit from using other elicitation methods that would enable determining whether deficits in avoidance behavior in bvFTD are limited to the visual domain.

³ To request a copy of the Attentional Control Coding System (ATCO) manual, please contact the authors via email at marcela.otero@berkeley.edu. or boblew@socrates.berkeley.edu

7. Conclusion

The present study utilized laboratory techniques derived from basic affective science to assess disgust responding and associated visual avoidance behaviors in individuals with bvFTD and AD and in healthy controls. The finding that visual avoidance behaviors are diminished in bvFTD patients relative to AD patients and neurologically intact controls provides important clues as to the neural circuitry likely to be necessary for this important form of emotion regulation. Comparisons between our laboratory-based assessments of visual avoidance and caregiver ratings of patients' emotional functioning in the home suggest that visual avoidance is related to emotion regulation in the real world but is not related to emotional reactivity. The findings may have applied utility as well. Declines in visual avoidance behaviors may provide a useful window into the kinds of emotional deficits in patients with bvFTD that have real-world consequences for caregivers and family members. Longitudinal research can help determine whether declines in visual avoidance behaviors are early indicators of the broader declines in emotional functioning that occur as the disease progresses.

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References

- Aldao, A., Nolen-Hoeksema, S., Schweizer, S., 2010. Emotion-regulation strategies across psychopathology: A meta-analytic review. *Clin. Psychol. Rev.* 30 (2), 217–237. <https://doi.org/10.1016/j.cpr.2009.11.004>.
- Amaral, D.G., 2003. The amygdala, social behavior, and danger detection. *Ann. N. Y. Acad. Sci.* 1000 (1), 337–347. <https://doi.org/10.1196/annals.1280.015>.
- Armstrong, T., Bilsky, S.A., Zhao, M., Olatunji, B.O., 2013a. Dwelling on potential threat cues: an eye movement marker for combat-related PTSD. *Depress. Anxiety* 30 (5), 497–502. <https://doi.org/10.1002/da.22115>.
- Armstrong, T., Hemminger, A., Olatunji, B.O., 2013b. Attentional bias in injection phobia: overt components, time course, and relation to behavior. *Behav. Res. Ther.* 51 (6), 266–273. <https://doi.org/10.1016/j.brat.2013.02.008>.
- Armstrong, T., Olatunji, B.O., 2012. Eye tracking of attention in the affective disorders: a meta-analytic review and synthesis. *Clin. Psychol. Rev.* 32 (8), 704–723. <https://doi.org/10.1016/j.cpr.2012.09.004>.
- Ascher, E.A., 2012. From Lab to Life: Concordance between Laboratory and Caregiver Assessment of Emotion in Dementia. Retrieved from. <https://escholarship.org/uc/item/8201h65p.pdf>.
- Augustine, A.A., Hemenover, S.H., 2009. On the relative effectiveness of affect regulation strategies: A meta-analysis. *Cognit. Emot.* 23 (6), 1181–1220.
- Ballard, C., O'Brien, J., Gray, A., Cormack, F., Ayre, G., Rowan, E., et al., 2001. Attention and fluctuating attention in patients with dementia with Lewy bodies and Alzheimer disease. *Arch. Neurol.* 58, 977–982.
- Bebko, G.M., Franconeri, S.L., Ochsner, K.N., Chiao, J.Y., 2011. Look before you regulate: differential perceptual strategies underlying expressive suppression and cognitive reappraisal.
- Bishop, S.J., 2009. Trait anxiety and impoverished prefrontal control of attention. *Nat. Neurosci.* 12 (1), 92–98. <https://doi.org/10.1038/nn.2242>.
- Boiten, F.A., 1998. The effects of emotional behaviour on components of the respiratory cycle. *Biol. Psychol.* 49 (1), 29–51. [https://doi.org/10.1016/S0301-0511\(98\)00025-8](https://doi.org/10.1016/S0301-0511(98)00025-8).
- Boiten, F.A., Frijda, N.H., Wientjes, C.J., 1994. Emotions and respiratory patterns: review and critical analysis. *Int. J. Psychophysiol.* 17 (2), 103–128.
- Boxer, A.L., Yu, J.T., Golbe, L.I., Litvan, I., Lang, A.E., Höglinger, G.U., 2017. Advances in progressive supranuclear palsy: new diagnostic criteria, biomarkers, and therapeutic approaches. *Lancet Neurol.* 16 (7), 552–563.
- Braak, H., Braak, E., 1997. Frequency of stages of Alzheimer-related lesions in different age categories. *Neurobiol. Aging* 18 (4), 351–357.
- Bradley, M.M., Lang, P.J., 2010. Measuring emotion: behavior, feeling, and physiology. *J. Cognit. Neurosci. Emot.* 25, 49–59.
- Bush, G., Luu, P., Posner, M.I., 2000. Cognitive and emotional influences in anterior cingulate cortex. *Trends Cognit. Sci.* 4 (6), 215–222.

- Christie, I.C., Friedman, B.H., 2004. Autonomic specificity of discrete emotion and dimensions of affective space: a multivariate approach. *Int. J. Psychophysiol.* 51 (2), 143–153. <https://doi.org/10.1016/j.ijpsycho.2003.08.002>.
- Cisler, J.M., Olatunji, B.O., Lohr, J.M., 2009. Disgust, fear, and the anxiety disorders: A critical review. *Clin. Psychol. Rev.* 29 (1), 34–46. <https://doi.org/10.1016/j.cpr.2008.09.007>.
- Collet, C., Vernet-Maury, E., Delhomme, G., Dittmar, A., 1997. Autonomic nervous system response patterns specificity to basic emotions. *J. Auton. Nerv. Syst.* 62 (1), 45–57. [https://doi.org/10.1016/S0165-1838\(96\)00108-7](https://doi.org/10.1016/S0165-1838(96)00108-7).
- Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. *Nat. Rev. Neurosci.* 3 (3), 215–229. <https://doi.org/10.1038/nrn755>.
- Dalgleish, T., Moradi, A.R., Taghavi, M.R., Neshat-Doost, H.T., Yule, W., 2001. An experimental investigation of hypervigilance for threat in children and adolescents with post-traumatic stress disorder. *Psychol. Med.* 31 (3), 541–547. <https://doi.org/10.1017/S0033291701003567>.
- Demaree, H., Schmeichel, B., Robinson, J., Everhart, D.E., 2004. Behavioural, affective, and physiological effects of negative and positive emotional exaggeration. *Cognit. Emot.* 18 (8), 1079–1097. <https://doi.org/10.1080/02699930441000085>.
- Derryberry, D., Reed, M.A., 2002. Anxiety-related attentional biases and their regulation by attentional control. *J. Abnorm. Psychol.* 111 (2), 225.
- Eysenck, M.W., Derakshan, N., Santos, R., Calvo, M.G., 2007. Anxiety and cognitive performance: Attentional control theory. *Emotion* 7 (2), 336–353. <https://doi.org/10.1037/1528-3542.7.2.336>.
- Eckart, J.A., Sturm, V.E., Miller, B.L., Levenson, R.W., 2012. Diminished disgust reactivity in behavioral variant frontotemporal dementia. *Neuropsychologia* 50 (5), 786–790. <https://doi.org/10.1016/j.neuropsychologia.2012.01.012>.
- Ferri, J., Schmidt, J., Hajcak, G., Canli, T., 2013. Neural correlates of attentional deployment within unpleasant pictures. *NeuroImage* 70, 268–277. <https://doi.org/10.1016/j.neuroimage.2012.12.030>.
- Field, T.M., 1981. Infant gaze aversion and heart rate during face-to-face interactions. *Infant Behav. Dev.* 4, 307–315. [https://doi.org/10.1016/0163-6383\(81\)80032-X](https://doi.org/10.1016/0163-6383(81)80032-X).
- Finney, C.M., Mendez, M.F., 2017. Diogenes syndrome in frontotemporal dementia. *Am. J. Alzheimer's Dis. Other Dementias*, 1533317517717012. <https://doi.org/10.1177/1533317517717012>.
- 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. *J. Psychiatr. Res.* 12 (3), 189–198.
- Fraiberg, S., 1982. Pathological defenses in infancy. *Psychoanal. Q.* 51 (4), 612–635.
- Frijda, N.H., 1986. *The Emotions*. Cambridge University Press.
- Garbutt, S., Matlin, A., Hellmuth, J., et al., 2008. Oculomotor function in frontotemporal lobar degeneration, related disorders and Alzheimer's disease. *Brain* 131 (pt 5) 1268–1281. <https://doi.org/10.1093/brain/131.5.1268>.
- Goodkind, M.S., Gyurak, A., McCarthy, M., Miller, B.L., Levenson, R.W., 2010. Emotion regulation deficits in frontotemporal lobar degeneration and Alzheimer's disease. *Psychol. Aging* 25 (1), 30.
- Greicius, M.D., Srivastava, G., Reiss, A.L., Menon, V., 2004. Default-mode network activity distinguishes Alzheimer's disease from healthy aging: evidence from functional MRI. *Proc. Natl. Acad. Sci. U. S. A.* 101 (13), 4637–4642.
- Gross, J.J., 1998. Antecedent and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. *J. Personal. Soc. Psychol.* 74 (1), 224.
- Gross, J.J., Levenson, R.W., 1993. Emotional suppression: physiology, self-report, and expressive behavior. *J. Personal. Soc. Psychol.* 64 (6), 970–986. <https://doi.org/10.1037/0022-3514.64.6.970>.
- Gross, J.J., Thompson, R.A., 2007. Emotion regulation: conceptual foundations. *Handb. Emot. Regul.* 3, 24.
- Gross, J.J., 2015. Emotion regulation: current status and future prospects. *Psychol. Inq.* 26 (1), 1–26. <https://doi.org/10.1080/1047840X.2014.940781>.
- Gyurak, A., Goodkind, M.S., Kramer, J.H., Miller, B.L., Levenson, R.W., 2012. Executive functions and the down-regulation and up-regulation of emotion. *Cognit. Emot.* 26 (1), 103–118. <https://doi.org/10.1080/02699931.2011.557291>.
- Gyurak, A., Gross, J.J., Etkin, A., 2011. Explicit and implicit emotion regulation: A dual-process framework. *Cognit. Emot.* 25 (3), 400–412. <https://doi.org/10.1080/02699931.2010.544160>.
- Hayes, A.F., 2013. *Introduction to Mediation, Moderation, and Conditional Process Analysis: a Regression-Based Approach*. Guilford Press, New York.
- Hopfinger, J.B., Buonocore, M.H., Mangun, G.R., 2000. The neural mechanisms of top-down attentional control. *Nat. Neurosci.* 3 (3), 284–291.
- Joormann, J., Gotlib, I.H., 2007. Selective attention to emotional faces following recovery from depression. *J. Abnorm. Psychol.* 116 (1), 80–85. <https://doi.org/10.1037/0021-843X.116.1.80>.
- Karnath, H.-O., 2001. New insights into the functions of the superior temporal cortex. *Nat. Rev. Neurosci.* 2 (8), 568–576. <https://doi.org/10.1038/35086057>.
- Koster, E.H.W., De Raedt, R., Goeleven, E., Franck, E., Crombez, G., 2005. Mood-congruent attentional bias in dysphoria: maintained attention to and impaired disengagement from negative information. *Emotion* 5 (4), 446–455. <https://doi.org/10.1037/1528-3542.5.4.446>.
- Koole, S.L., Webb, T.L., Sheeran, P.L., 2015. Implicit emotion regulation: feeling better without knowing why. *Emot. Regul.* 3, 6–10. <https://doi.org/10.1016/j.copsyc.2014.12.027>.
- Kreibitz, S.D., 2010. Autonomic nervous system activity in emotion: a review. *Biopsychology Emot. Curr. Theor. Empir. Perspect.* 84 (3), 394–421. <https://doi.org/10.1016/j.biopsycho.2010.03.010>.
- Kreibitz, S.D., Wilhelm, F.H., Roth, W.T., Gross, J.J., 2011. Affective modulation of the acoustic startle: does sadness engage the defensive system? *Biol. Psychol.* 87 (1), 161–163.
- Kunzmann, U., Kupperbusch, C.S., Levenson, R.W., 2005. Behavioral inhibition and amplification during emotional arousal: a comparison of two age groups. *Psychol. Aging* 20 (1), 144–158. <https://doi.org/10.1037/0882-7974.20.1.144>.
- Lawson, R.A., Yarnall, A.J., Duncan, G.W., Breen, D.P., Khoo, T.K., Williams-Gray, C.H., ICICLE-PD study group, 2016. Cognitive decline and quality of life in incident Parkinson's disease: the role of attention. *Park. Relat. Disord.* 27, 47–53.
- Lebert, F., 2005. Diogenes syndrome, a clinical presentation of fronto-temporal dementia or not? *Int. J. Geriatr. Psychiatry* 20 (12), 1203–1204. <https://doi.org/10.1002/gps.1430>.
- Leigh, R.J., Kennard, C., 2004. Using saccades as a research tool in the clinical neurosciences. *Brain* 127 (3), 460–477.
- Levenson, R.W., Ascher, E., Goodkind, M., McCarthy, M., Sturm, V., Werner, K., 2008. Laboratory testing of emotion and frontal cortex. *Handb. Clin. Neurol.* 88, 489–498.
- Levenson, R.W., Ekman, P., Heider, K., Friesen, W.V., 1992. Emotion and autonomic nervous system activity in the Minangkabau of West Sumatra. *J. Personal. Soc. Psychol.* 62 (6), 972–988. <https://doi.org/10.1037/0022-3514.62.6.972>.
- Levenson, R.W., Sturm, V.E., Haase, C.M., 2014. Emotional and behavioral symptoms in neurodegenerative disease: a model for studying the neural bases of psychopathology. *Annu. Rev. Clin. Psychol.* 10 (1), 581–606.
- Lyubomirsky, S., Nolen-Hoeksema, S., 1993. Self-perpetuating properties of dysphoric rumination. *J. Personal. Soc. Psychol.* 65 (2), 339.
- Lyubomirsky, S., Nolen-Hoeksema, S., 1995. Effects of self-focused rumination on negative thinking and interpersonal problem solving. *J. Personal. Soc. Psychol.* 69 (1), 176.
- Lyubomirsky, S., Caldwell, N.D., Nolen-Hoeksema, S., 1998. Effects of ruminative and distracting responses to depressed mood on retrieval of autobiographical memories. *J. Personal. Soc. Psychol.* 75 (1), 166.
- Macmillan, D., Shaw, P., 1966. Senile breakdown in standards of personal and environmental cleanliness. *Br. Med. J.* 2 (5521), 1032.
- Manera, V., Samson, A.C., Pehrs, C., Lee, I.A., Gross, J.J., 2014. The eyes have it: the role of attention in cognitive reappraisal of social stimuli. *Emotion* 14 (5), 833–839. <https://doi.org/10.1037/a0037350>.
- Maus, I.B., Robinson, M.D., 2009. Measures of emotion: a review. *Cognit. Emot.* 23 (2), 209–237. <https://doi.org/10.1080/02699930802204677>.
- Maus, I.B., Bunge, S.A., Gross, J.J., 2007. Automatic emotion regulation. *Soc. Personal. Psychol. Compass* 1 (1), 146–167. <https://doi.org/10.1111/j.1751-9004.2007.00005.x>.
- McClelland, A.B., Jones, K.V., Gregg, M.E.D., 2009. Psychological and cumulative cardiovascular effects of repeated angry rumination and visuospatial suppression. *Int. J. Psychophysiol.* 74 (2), 166–173.
- McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., Stadlan, E.M., 1984. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group* under the auspices of department of Health and human services task force on Alzheimer's disease. *Neurology* 34 (7) 939–939. <https://doi.org/10.1212/WNL.34.7.939>.
- McLaughlin, K.A., Borkovec, T.D., Sibrava, N.J., 2007. The effects of worry and rumination on affect states and cognitive activity. *Behav. Ther.* 38 (1), 23–38.
- Menon, V., Uddin, L.Q., 2010. Saliency, switching, attention and control: a network model of insula function. *Brain Struct. Funct.* 214 (5–6), 655–667. <https://doi.org/10.1007/s00429-010-0262-0>.
- Mesulam, M., et al., 1981. A cortical network for directed attention and unilateral neglect. *Ann. Neurol.* 10 (4), 309–332.
- Mograb, D.C., Brown, R.G., Morris, R.G., 2012. Emotional reactivity to film material in Alzheimer's disease. *Dement. Geriatr. Cognit. Disord.* 34 (5–6), 351–359.
- Mor, N., Winquist, J., 2002. Self-focused attention and negative affect: a meta-analysis. *Psychol. Bull.* 128 (4), 638.
- Neary, D., Snowden, J., Mann, D., 2005. Frontotemporal dementia. *Lancet Neurol.* 4 (11), 771–780.
- Neary, D., Snowden, J.S., Gustafson, L., Passant, U., Stuss, D., Black, S., 1998. Frontotemporal lobar degeneration: A consensus on clinical diagnostic criteria. *Neurology* 51 (6), 1546–1554.
- O'Brien, J., Thomas, A., 2015. Vascular dementia. *The Lancet* 386 (10004), 1698–1706.
- Otero, M.C., Levenson, R.W., 2017. Lower visual avoidance in dementia patients is associated with greater psychological distress in caregivers. *Dement. Geriatr. Cognit. Disord.* 43 (5–6), 247–258.
- Palomba, D., Sarlo, M., Angrilli, A., Mini, A., Stegagno, L., 2000. Cardiac responses associated with affective processing of unpleasant film stimuli. *Int. J. Psychophysiol.* 36 (1), 45–57. [https://doi.org/10.1016/S0167-8760\(99\)00099-9](https://doi.org/10.1016/S0167-8760(99)00099-9).
- Rivaud-Péchéux, S., Vidailhet, M., Galloudec, G., Litvan, I., Gaymard, B., Pierrot-Deseilligny, C., 2000. Longitudinal ocular motor study in corticobasal degeneration and progressive supranuclear palsy. *Neurology* 54 (5), 1029–1032. <https://doi.org/10.1093/brain/123.5.1029>.
- Rohrmann, S., Hopp, H., 2008. Cardiovascular indicators of disgust. *Int. J. Psychophysiol.* 68 (3), 201–208. <https://doi.org/10.1016/j.ijpsycho.2008.01.011>.
- Rosen, H.J., 2005. Neuroanatomical correlates of behavioural disorders in dementia. *Brain* 128 (11), 2612–2625. <https://doi.org/10.1093/brain/awh628>.
- Rozin, P., Haidt, J., McCauley, C.R., 2008. *Disgust*. In: Lewis, M., Haviland-Jones, J.M., Barrett, L.F. (Eds.), *Handbook of Emotions*, third ed. Guilford Press, New York, NY, US, pp. 757–776.
- Seeley, W.W., Crawford, R.K., Zhou, J., Miller, B.L., Greicius, M.D., 2009. Neurodegenerative diseases target large-scale human brain networks. *Neuron* 62 (1), 42–52. <https://doi.org/10.1016/j.neuron.2009.03.024>.
- Sheppes, G., Gross, J.J., 2011. Is timing everything? Temporal considerations in emotion regulation. *Pers. Soc. Psychol. Rev.* 15 (4), 319–331. <https://doi.org/10.1177/1088868310395778>.
- Sheppes, G., Gross, J.J., 2012. Emotion regulation effectiveness: what works when. *Handb. Psychol.* 391–406.

- Shiota, M.N., Levenson, R.W., 2009. Effects of aging on experimentally instructed detached reappraisal, positive reappraisal, and emotional behavior suppression. *Psychol. Aging* 24 (4), 890.
- Sturm, V.E., McCarthy, M.E., Yun, I., Madan, A., Yuan, J.W., Holley, S.R., ... Levenson, R.W., 2011. Mutual gaze in Alzheimer's disease, frontotemporal and semantic dementia couples. *Soc. Cognit. Affect Neurosci.* 6 (3), 359–367. <https://doi.org/10.1093/scan/nsq055>.
- 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. <https://doi.org/10.1037/a0013765>.
- Sturm, V.E., Rosen, H.J., Allison, S., Miller, B.L., Levenson, R.W., 2006. Self-conscious emotion deficits in frontotemporal lobar degeneration. *Brain* 129 (9), 2508–2516.
- van Hoesen, G.W., Hyman, B.T., Damasio, A.R., 1991. Entorhinal cortex pathology in Alzheimer's disease. *Hippocampus* 1 (1), 1–8.
- van Reekum, C.M., Johnstone, T., Urry, H.L., Thurow, M.E., Schaefer, H.S., Alexander, A.L., Davidson, R.J., 2007. Gaze fixations predict brain activation during the voluntary regulation of picture-induced negative affect. *Neuroimage* 36, 1041–1055. <https://doi.org/10.1016/j.neuroimage.2007.03.052>.
- Verstaen, A., Eckart, J.A., Muhtadie, L., Otero, M.C., Sturm, V.E., Haase, C.M., Levenson, R.W., 2016. Insular atrophy and diminished disgust reactivity. *Emotion* 16 (6), 903–912. <https://doi.org/10.1037/emo0000195>.
- Vidailhet, M., Rivaud, S., Gouider-Khouja, N., Pillon, B., Bonnet, A.M., Gaymard, B., Pierrot-Deseilligny, C., 1994. Eye movements in parkinsonian syndromes. *Ann. Neurol.* 35 (4), 420–426.
- Waters, E., Matas, L., Sroufe, L.A., 1975. Infants' reactions to an approaching stranger: description, validation, and functional significance of wariness. *Child Dev.* 46 (2), 348–356. <https://doi.org/10.2307/1128127>.
- Wiech, K., Lin, C. -s., Brodersen, K.H., Bingel, U., Ploner, M., Tracey, I., 2010. Anterior insula integrates information about salience into perceptual decisions about pain. *J. Neurosci.* 30 (48), 16324–16331. <https://doi.org/10.1523/JNEUROSCI.2087-10.2010>.