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An Examination of Visual Avoidance as an Emotion Regulation Strategy in Neurodegenerative Disease

By

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requirements for the degree of

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Abstract

An Examination of Visual Avoidance as an Emotion Regulation Strategy
in Neurodegenerative Disease

by

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Visual avoidance (VA) is the strategic positioning of the head and body to limit exposure to aversive stimuli in the environment. Despite VA being a basic behavioral response to aversive emotional stimuli and ubiquitous in everyday life, little is known about how it may function as a strategy for regulating emotion. Prior research finds VA deficits in behavioral variant frontotemporal dementia (bvFTD), a neurodegenerative disease characterized by progressive and marked changes in behavior and emotional responses. Clinically, deficits in VA among patients with bvFTD and Alzheimer's disease (AD) have been tied to worse mental health in familial caregivers. Understanding VA in the context of neurodegenerative disease may help elucidate how VA relates to emotional responding, cognitive functioning, and how VA might uniquely contribute to caregiver wellbeing.

The current study aimed to examine VA in neurologically intact individuals and patients with neurodegenerative disease. Specifically, objective behavioral coding of VA was used to examine how participant VA while watching a disgusting film clip (i.e., disgust reactivity task) related to indices of emotional responding (i.e., peripheral physiology and emotional facial behavior) during the task, emotion regulation on laboratory-based measures and in the home, and measures of neuropsychological functioning given VA's possible reliance on cognitive processes to monitor and attend to emotional stimuli and re-orient visual attention. Given that deficits in emotional functioning have been tied with lower levels of caregiver mental health, the present study also examined whether patient VA impacted caregiver mental health (overall psychological distress, anxiety, and depression) independently from another domain of emotional functioning affected in neurodegenerative disease- the ability to recognize other's emotion accurately (i.e., emotion recognition). This comparison provided a more nuanced understanding of how particular patient emotional deficits contribute to caregiver mental health outcomes.

The sample consisted of 67 patients with bvFTD, 67 patients with AD, 35 neurologically healthy control participants, and their spousal caregivers. 7 VA behaviors were coded for intensity and frequency while participants viewed a disgusting film clip, including head movements up, down, and to the side, gaze aversion, headshakes, blinks, and eye closures. Laboratory-based measures of emotion regulation included instructed and spontaneous suppression of emotional behavior following an acoustic startle, and instructed suppression of disgust behavior while watching a disgusting film clip. Domains of neuropsychological functioning assessed included cognitive flexibility, working memory, set-shifting, and response inhibition. Results indicated that greater increases in skin conductance prior to the onset of VA predicted greater overall VA across the disgust reactivity task. Additionally, greater cognitive flexibility predicted greater overall VA behavior. Both findings were moderated by diagnosis, such that greater increase in skin conductance prior to the onset of VA and greater cognitive flexibility predicted greater VA in controls, but not in either patient group. Lastly, patient deficits in VA significantly predicted greater caregiver depression independently from patient deficits in emotion recognition.

Current findings extend our basic knowledge of VA by providing evidence for the context in which VA occurs (i.e., increasing sympathetic nervous system activation), suggesting that VA may represent the intent to down-regulate negative emotion via behavioral responding. Furthermore, cognitive flexibility may support VA by enabling the monitoring and updating of ongoing behavioral responses and flexible implementation of new regulatory strategies. Importantly, the current findings have clinical implications for dementia caregivers and patients. Examining VA deficits in patients with bvFTD and AD may help identify caregivers who are at-risk for depression, allowing for earlier psychosocial intervention and prevention of mental illness in dementia caregivers.

Dedication

Para mi familia quienes siempre me apoyaron con amor. Gracias por el cariño y la fortaleza que me dieron todos estos años.

To my academic mentors, particularly my graduate school advisor Dr. Robert Levenson, who taught me how to observe and explore human behavior as a scientist and gave me an education that will last a lifetime.

To my closest friends, from grade school to graduate school, who share with me the ups and downs of life and remind me how laughter heals and strengthens the soul. Thank you for being a part of this journey.

To my dearest Reinhard for a love that makes anything seem possible and a relationship that helps me grow. Meeting you was the best thing to happen to me while writing this, and I am grateful for it every day.

An Examination of Visual Avoidance as an Emotion Regulation Strategy
In Neurodegenerative Disease

Visual avoidance (VA) is movement of the eyes, head, and torso that limits the type of visual information taken in from the immediate environment. VA characterizes the behavioral response tendencies of several emotion states (i.e., to avoid or limit exposure to a noxious stimulus), with the most prominent being disgust (Frijda, 1988; Frijda, 1987; Frijda, Kuipers, & Ter Schure, 1989). Though scientifically underexplored, there are several reasons to assume that VA may be a basic strategy for regulating emotion. In the following sections, I will review these reasons starting with an overview of the function of VA in regulatory processes. Specifically, the associations between VA use and increased self-regulation in both children and adults will be reviewed (Ayduk et al., 2000; Rodriguez, Mischel, & Shoda, 1989). Following this, I will discuss VA as a visually mediated form of attentional deployment. The potential importance of attentional deployment as a form of emotion regulation will be discussed, including its impact on measures of emotional responding in the central nervous system, and past work suggesting that visual gaze may actually mediate the regulatory success of other more commonly studied emotion regulation strategies (Dunning & Hajcak, 2009; Manera, Samson, Pehrs, Lee, & Gross, 2014; Strauss, Ossenfort, & Whearty, 2016; van Reekum et al., 2007).

Next, I will make an argument for studying VA in neurodegenerative diseases. Specifically, I will discuss how neurodegenerative diseases are characterized by neural loss in distributed brain regions (Rabinovici et al., 2008; Seeley, Crawford, Zhou, Miller, & Greicius, 2009), which impact emotion differentially (Bathgate, Snowden, Varma, Blackshaw, & Neary, 2001; Lavenu & Pasquier, 2004; Zhou & Seeley, 2014), enabling the study of how VA impacts emotional responding across a broad spectrum of emotional ability. Prior work related to VA and dementia will also be reviewed, including work showing that that patients with known deficits in emotional functioning, behavioral variant frontotemporal dementia (bvFTD), show diminished VA to disgust-eliciting stimuli compared to healthy controls and patients with Alzheimer's disease (AD), a neurodegenerative disease characterized by primary cognitive deficits (Otero & Levenson, 2019). Moreover, I will highlight the clinical utility of examining whether VA in patients with dementia impacts caregivers independently from other emotional deficits, including patient's ability to recognize others' emotions accurately (i.e., emotion recognition), Third, I will discuss the possible cognitive mechanisms that underlie VA deficits with a focus on higher-level processes (i.e., executive functioning) that may support VA by facilitating the monitoring of the environment, selection and execution of VA, and updating of regulatory behavior based on goal-congruent outcomes, such as down-regulation of negative emotion. Lastly, I will present an outline of the current dissertation, including gaps in the literature it aims to address.

Visual Avoidance in Regulatory Processes

The use of avoidance behaviors is found in various vertebrate species and consists of the physical positioning of the head and body away from a noxious stimulus (Hart, 1988; Loehle, 1995). These behaviors are thought to be innate coping strategies that evolved to reduce exposure to pathogens and protect the body from illness (Hart, 1988). In humans, VA is theorized to constitute the action tendency of several negative emotion states, including fear, anxiety, and disgust (Frijda, 1986; Frijda, 1987; Frijda et al., 1989). Clinical research has found that greater use of VA (e.g., gaze aversion) among individuals with specific phobias, such as blood-injection-injury phobia, in response to phobia-related images (Armstrong & Olatunji, 2012; Borkovec, Alcaine, & Behar, 2004). In the context of fear and anxiety, VA may be a conditioned response aimed to protect the individual from anticipated harm. Though maladaptive when generalized to non-threatening stimuli, such as health promoting vaccinations or routine blood-drawing, the tendency to avoid disgusting objects in the environment by physically withdrawing is adaptive in disgust because it serves to limit exposure to a contaminant and protect the individual against possible harm (Rozin & Fallon, 1987). Research suggests that VA not only functions to protect against physical harm, but also functions to protect against psychological harm by playing a role in the regulatory processes that underlie short and long-term goal attainment. The following sections will examine research on VA as it pertains to self-regulation and the down-regulation of emotion.

Self-regulation. Broadly, self-regulation has been defined as the ability to modify behavior according to the cognitive, emotional, and social demands of a given situation (Ruff & Rothbart, 2001; Vohs & Baumeister, 2013). It is a core aspect of adaptive human behavior and has been theorized to rely on attentional control processes heavily (Baumeister & Heatherton, 1996; Carver & Scheier, 2012). Developmental studies on delay-of-gratification provide empirical support for the association between VA and self-regulatory ability. In the classic paradigm, preschoolers are asked to postpone immediate gratification in order to obtain a larger reward at a later time (Mischel, 1974; Mischel & Baker, 1975; Mischel & Moore, 1980). Greater ability to delay gratification has been related to numerous positive outcomes including greater academic success and intellectual aptitude, higher social competency, and greater ability to cope with stress and frustration (Mischel, Shoda, & Peake, 1988; Shoda, Mischel, & Peake, 1990). Research using this paradigm suggests that strategically employing VA during the task significantly impacts regulatory ability. Specifically, greater use of visually-based attentional deployment, such as looking away from a reward or covering it from view, predicted greater self-regulation while waiting for a more valued prize (Rodriguez et al., 1989). Visually attending to a reward, on the other hand, predicted worse regulatory ability as evidenced by shorter delay times (Peake, Hebl, & Mischel, 2002). Importantly, the relationship between visually-based attentional deployment and self-regulatory ability has been shown to remain stable over time. For example, the greater use of gaze aversion at 12-24 months of age is associated with more effective use of attentional control and subsequent self-regulation in later childhood, suggesting that the strategic use of attentional deployment is an enduring regulatory skill (Sethi, Mischel, Aber, Shoda, & Rodriguez, 2000). Moreover, longitudinal work found that greater visually-based attentional deployment at age 5 predicted greater cognitive control on a go/no-go task in adolescence and young adulthood (Eigsti et al., 2006), indicating that that the ability to look away from visually compelling stimuli may share common mechanisms with the ability to inhibit behavioral and attentional responses.

Emotion regulation. One of the most important forms of self-regulation is an individual's ability to modify his or her emotional experience. Emotion regulation refers to the processes by which individuals alter the intensity and valence of their emotions, and change how they experience and express them (Gross & Thompson, 2007). In the adult literature, the predominant framework of emotion regulation is Gross's process model of emotion regulation (1998). The process model is built on the modal model of emotion, which suggests that an emotionally relevant situation is attended to and appraised on a number of different dimensions, including affective valence and relevance to an individual's current goals (Barrett, Ochsner, & Gross, 2007; Gross & Thompson, 2007). The resultant appraisal gives rise to emotional responding, which manifests as behavioral, experiential, and physiological changes that prepare an individual to meet situational demands (Levenson, 1994). According to the process model, regulatory strategies occur along the temporal sequence of emotion generation (Gross, 2015). 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. Gross identifies 4 families of antecedent-focused emotion regulation, 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 & Thompson, 2006). While VA can be used across families (e.g., looking away from an emotional trigger as one physically modifies the environment, or re-appraises a situation), it may be conceptualized best as a form of attentional deployment given that it is characterized by visually engaging/disengaging with emotional stimuli in the environment.

To date, the most extensively studied antecedent-focused emotion regulation strategy is cognitive reappraisal. Although research on cognitive reappraisal has been invaluable in furthering our understanding of emotion regulation, there is reason to believe that other antecedent-focused strategies, particularly attentional deployment, may also be important subjects of investigation. First, developmental research has found that regulation of affective states using attention-based strategies begins in early infancy. Infants between the ages of 3 and 18 months use spontaneous gaze aversion during states of extreme stress, such as parental neglect (Fraiberg, 1982). In 4 to 7 month olds, greater gaze aversion is found during stressful face-to-face interactions, where it is associated with heart rate deceleration, suggesting that looking away from arousing stimuli may down-regulate sympathetic responding in early childhood (Field, 1981; Waters, Matas, & Sroufe, 1975). Second, attentional deployment is theorized to occur at the very start of the emotion-generative process, and as such it is the first form of regulation enacted in the presence of an emotion elicitor (Gross & Thompson, 2007). Given its strategic position, attentional deployment may target emotion early on, reducing or even short-circuiting the emotional response before it is allowed to gain full force. Fully formed emotion may become increasingly difficult to regulate as the three response systems of emotion become more fully engaged and require more effort to stop or modify them. These systems include an individual's (1) subjective of experience of emotion, (2) behavioral responding, including facial expression, verbal utterances, and body gesturing, and (3) physiological activation/deactivation (Levenson, 1994). Third, given that attentional deployment may occur at the early perceptual stage of emotion generation, it may rely on more automatic regulatory processes (Mauss, Bunge, & Gross, 2007). Under a contemporary dual-process framework of emotion regulation, regulation can occur at both effortful and spontaneous levels (Gyurak, Gross, & Etkin, 2011; Koole, Webb, & Sheeran, 2015; Mauss et al., 2007). Effortful emotion regulation refers to intentional action aimed at altering an undesirable emotional state, and would include regulatory strategies that are consciously enacted. Spontaneous emotion regulation, on the other hand, refers to unconscious processes initiated by the basic registration of sensory information, and may include spontaneously looking or turning away from negative stimuli. Given that spontaneous emotion regulation occurs without actively paying attention to the processes that alter an emotional state, spontaneous regulation may require less elaborate cognitive resources than effortful regulation, which may require more complex and intentional semantic processing or response inhibition. Lastly, attentional deployment may be important to study because attention-based emotion regulation is ubiquitous in everyday life. Work using experience sampling methodology found that adults report using attention-based emotion regulation, including distraction and behavioral activation, more frequently than they report using reappraisal-based strategies (Heiy & Cheavens, 2014).

Other forms of attentional deployment

To date, the most widely studied attentional deployment strategies are rumination and distraction. Rumination (i.e., repeatedly thinking about an emotion eliciting event) is a prominent symptom of various psychopathologies, including anxiety and depression (Aldao, Nolen-Hoeksma, & Schweizer, 2009), and has been found to negatively impact mood, thinking, and behavior. 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 & Nolen-Hoeksema, 1993; Lyubomirsky & Nolen-Hoeksema, 1995; Lyubomirsky & Nolen-Hoeksema, 1998; McLaughlin, Borkovec & Sibrava, 2007; Mor & Winquist, 2002). Physiologically, greater negative rumination is associated with increased cardiovascular activation, including elevated heart rate (McClelland, Jones & Gregg, 2009). Distraction involves mentally disengaging from negative stimuli, and greater distraction is associated with decreased self-report of emotion (Augustine & Hemenover, 2007). The vast majority of research on distraction has examined how it impacts the central nervous system by activation or deactivation of brain circuitry. Functional MRI studies have found that distraction is associated with increased activation of the prefrontal cortex (PFC) and cingulate regions, and deactivation of limbic regions (Kanske, Heissler, Schonfelder, Bongers, & Wessa, 2011; McRae et al., 2010). Presumably, this pattern emerges because regulatory structures in the PFC and cingulate cortex modulate structures implicated in emotion reactivity, such as the amygdala and anterior insula (Ochsner, Silvers, & Buhle, 2012). Importantly, past work suggests that distraction and cognitive reappraisal (an emotion regulation strategy that targets emotional knowledge rather than attention) may have distinct neural correlates. Specifically, McRae and colleagues (2010) found that cognitive reappraisal recruited neural regions involved in processing affective meaning and affect valuation (e.g., dorsal medial PFC, ventral lateral PFC and anterior temporal cortices), whereas distraction recruited prefrontal and parietal regions implicated in selective attention and attentional control. Additionally, distraction was associated with greater down-regulation of the amygdala compared to cognitive reappraisal, suggesting that attentional deployment may regulate emotional responding more powerfully. Despite this insightful work on the neural underpinnings of distraction, few studies have examined how other forms of attentional deployment impact other indices of emotion, including activation of the autonomic nervous system (ANS) and emotional facial displays.

Visual avoidance: An area in need of additional exploration

Given the potential importance of attentional deployment, it is unfortunate that limited research has examined VA in the context of emotion regulation. Research that examines VA in emotion regulatory processes has yielded inconsistent findings. Urry (2010) found that cognitive reappraisal was associated with decreased subjective experience of emotion, regardless of whether participants are instructed to look toward or away from the emotional features of negative images. Moreover, greater reappraisal ability was associated with lower corrugator activity when participants attend toward emotional features of images, suggesting that visual attention toward emotional stimuli may help down-regulate emotion. Bebko (2011) found that participants used gaze aversion during cognitive reappraisal and expressive suppression; however, looking away from the emotional features of negative images was associated with greater self-report of negative emotion, suggesting that VA may increase the subjective emotional experience (Bebko, Franconeri, Ochsner, & Chiao, 2011). Follow up work found that the regulatory success of instructed cognitive reappraisal and expressive suppression was not altered by participants' gaze, or by the valence of the visual stimuli viewed (Bebko, Franconeri, Ochsner, & Chiao, 2014).

Contrary to these findings, work by van Reekum and Manera suggest that spontaneous VA might be a part of adaptive emotion down-regulation. Specifically, uninstructed gaze aversion was found to significantly reduce the variance in amygdala activation explained by cognitive reappraisal (van Reekum et al., 2007). Moreover, Manera (2014) found that participants naturally spend less time looking at the emotional features of film clips when instructed to down-regulate compared to when they are instructed to up-regulate. In addition, spontaneous gaze aversion significantly mediated the effects of cognitive reappraisal on self-reported sadness, such that down-regulation (vs. up-regulation) was associated with greater VA, which in turn was associated with reduced experience of negative emotion.

Inconsistencies regarding the role of VA in emotion regulation may be due to several factors (Ochsner et. al., 2012). First, most studies use static images (e.g., face stimuli) to elicit emotion. Film clips that are dynamic and visually complex are more naturalistic and may elicit a fuller range of emotional responding. Second, the majority of studies examining VA use a single measure of emotional responding, typically brain activation. Overreliance on one measure of emotion is limiting, and highlights the need for a multimodal approach that examines multiple indices, such as peripheral physiology and emotional facial behavior. Furthermore, typical laboratory studies of emotion regulation have focused on instructed down-regulation of emotion (i.e., participants are instructed to down-regulate using a particular strategy). Though the merits of examining instructed emotion regulation include increased control over experimental variables including regulation strategy, valance of target emotion, and direction of regulation (i.e., down- vs. up-regulation), studying spontaneous emotion regulation may be useful in understanding how naturally occurring down-regulation impacts emotion.

Visual avoidance and neurodegenerative disease

To date, research on emotion regulation has primarily studied phenomena in either healthy individuals or individuals with psychiatric disorders. Though these populations are valuable in many ways, both come with limitations. Studying emotion regulation in healthy individuals does not allow researchers to examine how brain diseases, which may directly affect the neural circuits necessary for VA, impact regulatory phenomena. Psychiatric disorders are brain-based, however within-syndrome heterogeneity of symptoms and unclear neural underpinnings make it difficult to draw clear conclusions about the mechanisms underling regulatory impairment. For example, some individuals with obsessive-compulsive disorder (OCD) have primary symmetry obsessions (e.g., orderings and counting compulsions), while others have primary contamination obsessions (e.g., cleaning compulsions) (Bloch, Landeros-Weisenberger, Rosario, Pittenger, & Leckman, 2008). Additionally, both symptom types have been found to have distinct underlying neural circuitry (Mataix-Cols et al., 2004; Phillips et al., 2000; Rauch et al., 1998). Alternatively, the argument has been made that studying emotion-related processes in neurodegenerative diseases may offer the unique opportunity to examine basic phenomena in brain-based disorders that have well-characterized neural circuitry and well-defined behavioral symptomatology (Levenson, Sturm, & Haase, 2014).

Behavioral variant frontotemporal dementia (bvFTD) is a neurodegenerative disorder characterized by progressive deterioration of personality, socioemotional functioning, and cognition (Neary et al., 1998; Rascovsky et al., 2011). An early symptom of bvFTD is behavioral disinhibition, which manifests as socially inappropriate behavior, impulsivity, and a dysexecutive profile (e.g., difficulty planning, distractibility, and poor judgment) (Bozeat, Gregory, Ralph, & Hodges, 2000). Importantly, bvFTD targets brain regions implicated in emotion reactivity and regulation, including the anterior insula, amygdala, anterior cingulate, and dorsolateral PFC (Rosen, 2005; Seeley et al., 2009). Consistent with this pattern of brain atrophy, patients with bvFTD show marked deficits in core processes of emotion functioning, including (a) emotional reactivity (subjective experience, behavioral responding, and physiological activation/deactivation in response to an emotional stimuli) (Eckart, Sturm, Miller, & Levenson, 2012), (b) emotion regulation (use of behavioral or cognitive strategies to modify emotion) (Goodkind, Gyurak, McCarthy, Miller, & Levenson, 2010), and (c) emotion recognition (ability to know what another person is feeling accurately) (Goodkind et al., 2015).

Prior work found that patients with bvFTD showed diminished VA when watching a highly disgusting film clip compared to healthy controls and patients with Alzheimer's disease (AD) (Otero & Levenson, 2019). AD is a neurodegenerative disease characterized by progressive loss of memory and visuospatial ability, but relative sparing of emotional functioning in early disease states (Braak & Braak, 1997; Goodkind et al., 2010; Goodkind et al., 2015; Mograbi, Brown, & Morris, 2012). A possible reason why VA is diminished in bvFTD is that patients have deficits in emotion reactivity and, as such, they do not have the need to down-regulate (Eckart et al., 2012). However, prior work found that patients with bvFTD showed diminished VA compared to controls and patients with AD even after controlling for the magnitude of emotional responding, indicating that patients with bvFTD may actually have deficits in down-regulating negative emotion. Consistent with this, past work found that patients with bvFTD showed diminished suppression of the startle reflex (Goodkind et al., 2010). In the study, participants with bvFTD, AD and neurologically healthy controls were presented with an aversive acoustic startle stimulus in three conditions that assessed: (a) spontaneous startle reflex (participants were presented with an acoustic startle without warning or instruction to suppress behavioral response), (b) spontaneous emotion regulation (participants were warned that the startle would occur after a countdown, but were not given the instruction to suppress), and (c) instructed emotion regulation (participants were warned that the startle would occur after a countdown, and were given the instruction to suppress). Results indicated that all three groups showed an intact startle reflex, however, patients with bvFTD and AD showed greater deficits when instructed to regulate compared to controls. Moreover, patients with bvFTD showed less spontaneous suppression of startle reflex compared to both and healthy controls and patients with AD, suggesting that patients with bvFTD have a specific deficit in spontaneously down-regulating emotion. Patient deficits in spontaneous down-regulation may be due to atrophy of the fronto-subcortical circuits that underlie emotion regulation. One way to assess the integrity of these circuits is through measures of executive functioning, which have been found to depend on similar prefrontal, parietal, and subcortical areas (Collette, Hogge, Salmon, & Van der Linden, 2006).

Executive functioning and emotion regulation

The regulation of emotion requires the on going monitoring and modification of behavior. The higher-level cognitive processes that allow this to happen are collectively referred to as executive functioning (Goldstein & Naglieri, 2013). Broadly, these processes include thought generation, cognitive flexibility, mental manipulation of information, self-monitoring, and changing behavioral responses to meet environmental demands. Executive functioning may be divided into distinct sets of cognitive processes that help support goal-oriented behavior (Miyake et al., 2000). In the sections that follow, four major executive functions will be reviewed, with a particular focus on how each may contribute to emotion regulation.

Working Memory. Working memory refers to the maintenance, control, and mental manipulation of information in short-term memory (Baddeley, 2003; Baddeley, 1986; Smith & Jonides, 1999). A distinctive feature of working memory is its role in updating perceptual and verbal information (Baddeley, 2003; Morris & Jones, 1990). Rather than passively storing information, working memory continuously replaces old information with new task-relevant information that better serves changing situational demands (Miyake et al., 2000). Auditory working memory is typically measured by having participants memorize and mentally manipulate a series of letters or numbers. In the task, an examiner orally presents a sting of 2 to 8 digits and asks a participant to recite them back in the reverse order (i.e., backward digit-span), testing the participant's ability to retrieve and manipulate information mentally.

In the service of emotion regulation, working memory may allow for the storage and updating of perceptual and contextual information. Research on cognitive reappraisal has found that greater working memory capacity is associated with greater cognitive reappraisal ability and greater reduction of negative emotion (Hendricks & Buchanan, 2015; McRae, Jacobs, Ray, John, & Gross, 2012). Moreover, working memory was found to moderate the regulatory effect of reappraisal on subjective experience of negative emotion, ostensibly because reappraisal requires an individual to change her current perspective by updating old information with new information that better aligns with a desired appraisal (Pe, Raes, & Kuppens, 2013).

Response Inhibition. Response inhibition refers to the suppression of a dominant behavioral response that is either overly learned or triggered by an environmental stimulus (Kramer & Quitania, 2007). The suppression of a prepotent response is deliberate and thought to rely on both attentional and executive control (Friedman & Miyake, 2004; Norman & Shallice, 1986). A common task for assessing response inhibition is the Stroop test (Stroop, 1935). During the interference trial of the test, participants are presented with the names of colors printed in incongruent colors (e.g., the word "green" printed in blue ink) and asked to name the color of the ink instead of the word itself. In doing so, they must inhibit the prepotent response to read the word itself.

In the service of emotion regulation, response inhibition may facilitate the suppression of automatic aspects of emotional responding. For example, the ability to inhibit responses may enable an individual to suppress a negative appraisal in favor of a more positive one, or suppress behavioral expression of emotion. Despite its theoretical contribution to emotion regulation, prior work on cognitive reappraisal and behavioral suppression has not found an association between response inhibition and regulatory ability, suggesting that successful emotion regulation using these strategies requires more than just inhibition of responses (Gyurak et al., 2009; McRae et al., 2012; Pe et al., 2013). However, no research to date has examined how response inhibition relates to attentional deployment. The effective use of attentional deployment may require response inhibition to limit the amount of visual attention given to compelling emotional stimuli.

Set-shifting. Set-shifting (also known as task-shifting) refers to the ability to move back and forth between cognitive tasks. Set-shifting requires an individual to disengage from an irrelevant task and engage in a relevant task quickly (Miyake et al., 2000). In addition to shifting visual and mental attention, set-shifting requires an individual to perform new operations while overriding previously learned ones, thus requiring the inhibition of interfering mental sets (Friedman & Miyake, 2004). Set-shifting is typically measured by asking participants to engage in tasks that involve alternating instruction sets. For example, participants may be asked to connect alternating letters and numbers in an ascending order (i.e., 1-A-2-B). Set-shifting ability may be important for emotion regulation because it facilitates shifting visual and mental focus from one aspect of a situation to another. For instance, an individual can shift attention from an emotion-eliciting cue in the environment to other perceptual or contextual features that are less emotionally arousing.

Cognitive flexibility. In the context of executive functioning, cognitive flexibility refers to the ability to generate responses quickly (Kramer & Quitania, 2007). It is typically assessed using tasks of verbal fluency (e.g., asking participants to name as many words as they can that start with a specific letter within a set timeframe). Verbal fluency requires mentally keeping track of rules, monitoring performance, and detecting and correcting errors (Kramer & Quitania, 2007). As such, greater verbal fluency may be particularly relevant to emotion regulation because it represents the ability to strategize, monitor ongoing responses, and flexibly implement new behavioral strategies. Indeed, prior work found that greater verbal fluency but not working memory, inhibition, or set-shifting, was associated with greater emotion regulatory ability on laboratory-based measures of expressive suppression and suppression of emotion after an acoustic startle (Gyurak et al., 2009). Follow up work found that greater cognitive flexibility was also associated to more successful up-and down-regulation of emotion while viewing emotional film clips (Gyurak et al., 2012).

The modification of emotion states is said to rely on cognitive control processes (Koole, van Dillen, & Sheppes, 2011; Ochsner & Gross, 2005). Regulatory ability using some of the most commonly studied emotion regulation strategies suggests that they may be associated with performance on neuropsychological measures of executive functioning (McRae et al., 2012; Pe et al., 2013). If VA functions to regulate emotion, patient deficits in VA may relate to patient deficits in cognitive processes thought to underlie regulatory behavior. Consistent with this, patients with bvFTD show marked impairments on various measures of executive functioning, including cognitive flexibility and set-switching (Kramer et al., 2003; Katya Rascovsky, Salmon, Hansen, Thal, & Galasko, 2007). BvFTD patients also present with early dysexecutive behavior, such as reduced disinbition (e.g., socially inappropriate behavior and loss of social decorum), lack of judgment, and poor planning (Rascovsky et al., 2011).

Dysexecutive symptoms are not just hard for patients, who may put themselves at greater risk for harm; they can also be extremely difficult for caregivers. Indeed, caregivers of bvFTD patients have been found to suffer from poorer mental health compared to caregivers of patients with AD (de Vugt et al., 2006; Mioshi, Bristow, Cook, & Hodges, 2009; Wong et al., 2012). In the section that follows, research on the patient factors that contribute to caregiver mental health will be reviewed, followed by our current understanding of how VA deficits in patients impact caregiver mental health.

Patient emotional functioning and caregiver mental health

Taking care of a loved one with a neurodegenerative disease can be a meaningful, yet difficult part of adult life. Dementia caregivers typically suffer from increased rates of depression, anxiety, and stress (Joling et al., 2015; Pinquart & Sörensen, 2003). However, not all caregivers are negatively impacted, and research suggests that several patient factors may mediate the relationship between caregiving and negative mental health outcomes. One of the most consistent findings in the literature is that higher levels of patient behavioral and psychological symptoms significantly predict poorer mental health in caregivers (Arango Lasprilla, Moreno, Rogers, & Francis, 2009; Black & Almeida, 2004; Covinsky et al., 2003; Mourik et al., 2004; Rymer et al., 2002). For example, Mourik and colleagues (2004) found that higher caregiver distress was most strongly associated with higher levels of patient agitation and psychosis symptomatology, including greater experience of delusions, irritability, and hallucinations. Rymer and colleagues (2002) found that higher levels of patient disinhibition predicted greater caregiver burden, above and beyond patient disease severity or patient functional impairment. Given the impact of patient behavior on caregiver functioning, a more nuanced understanding of the specific patient behavioral deficits that contribute to caregiver mental health may help identify caregivers at risk for mental illness.

Past work found that lower VA among patients with bvFTD and AD during a disgust reactivity task predicted greater psychological distress in caregivers, above and beyond patient cognitive functioning and neuropsychiatric symptomatology (Otero & Levenson, 2017). This association was mediated by patient overall emotional functioning (as reported by the caregiver), such that patients who showed less VA were perceived by caregivers as being less emotionally functional, which in turn was associated with worse mental health in caregivers. Importantly, these associations remained significant even after controlling for overall caregiver well-being, suggesting that the effect of patient emotional functioning on caregiver mental health was not driven by negative caregiver bias. Another aspect of emotional functioning that can be negatively impacted by neurodegenerative disease is a patient's ability to recognize what another person is feeling- emotion recognition. Prior work found that patients with bvFTD have deficits in recognizing the emotion of characters in a film clip compared to patients with AD and healthy controls (Goodkind et al., 2015). Despite in negative impact of patient behavioral symptoms on caregiver well-being (Mourik et al., 2004; De Vugt et al., 2006), no prior research has directly examined how deficits in emotion recognition impact caregiver mental health compared to deficits in VA. Patient emotion regulation may play a particularly important role in caregiver mental health given the centrality of emotion regulation in interpersonal relationships. If VA functions as an emotion regulation strategy, examining how well it predicts caregiver mental health compared to patient emotion recognition may help clarify which particular aspects of patient emotional functioning contribute most to caregiver mental health.

The present study

Although interest and research in emotion regulation has burgeoned in the last two decades (Gross, 2015), there are still gaps in our understanding of attention-based regulatory strategies, including VA. Recent work indicates that spontaneous VA of highly disgusting stimuli is impacted by neurodegenerative disease (Otero & Levenson, 2019). Specifically, we found that patient with known deficits in emotional functioning showed diminished VA that was not accounted for by reduced emotion reactivity. Moreover, patient who showed less VA had caregivers who perceived them as less emotionally functional and who, in turn, were more psychologically distressed. Together, these findings suggest that VA may be a form of emotion regulation that, when compromised, negatively impacts both patients and their caregivers.

No prior work has examined the how VA impacts peripheral physiology and emotional facial behavior (two prominent indices of emotional responding), and under what conditions VA occurs. Moreover, no prior work has examined individual differences in VA such as how it relates to emotion regulation (in laboratory-based tasks and in the home), and deficits in executive functioning. Lastly, no study to date has examined whether VA deficits in patients with bvFTD and AD impact caregiver mental health independently from patient deficits in emotion recognition. The present study had three aims: (1) to examine the association between VA behavior and changes in emotional responding before and after VA onset, (2) to determine whether VA was associated with measures of regulation (in the laboratory and in the home-environment), and performance on measures of executive functioning, and (3) to determine whether patient VA deficits was associated with caregiver mental health independently from patient deficits in emotion recognition.

Methods

Participants

Data were used from 169 participants (67 with bvFTD, 67 with AD, and 35 healthy age-matched controls) who participated in an ongoing study of emotional functioning in individuals with neurodegenerative disease conducted at the Berkeley Psychophysiology Laboratory (BPL) between 2007 and 2016. The current study's sample overlapped with samples included in two earlier studies (Otero and Levenson, 2017; Otero & Levenson, 2019). Patient overlap included 56 patients with bvFTD, 43 patients with AD, and 34 healthy controls. The present study included additional data from 36 participants (11 new patients with bvFTD, 24 new patients with AD, and 1 new healthy control) that were not included in previously published work. All participants were recruited from the University of California, San Francisco (UCSF) Memory and Aging Center. Patient participants underwent extensive neurological, cognitive, and neuroimaging testing by an interdisciplinary panel of neurologists, neuropsychologists, and nurses. Patient diagnoses were based on consensus criteria that were current at the time of the assessment: (a) bvFTD (Neary et al., 1998; Rascovsky et al., 2011), and (b) AD (McKhann et al., 1984). Healthy controls were recruited by UCSF using local newspaper advertisements and were screened to ensure no prior history of neurologic, psychiatric or cognitive disturbances. A caregiver accompanied each patient participant. Caregivers were close family members or friends (typically spouses) who identified themselves as the patient's primary care taker. Each caregiver completed a packet of questionnaires assessing various domains, including the patient's social and emotional functioning, and their own mental health.

Staging of dementia severity was assessed using the Clinical Dementia Rating Scale (CDR; Morris, 1997). The CDR is a semi-structured interview with an informant (typically a patient's spouse or close relative) conducted by a trained evaluator. Patients were assessed for impairment in six cognitive domains (Orientation, Memory, Judgment and Problem Solving, Community Affairs, Home and Hobbies, and Personal Care). A CDR box score was computed by summing scores for each of the CDR subtests, with higher box scores indicating greater functioning impairment.

Laboratory procedure

Participants came into the BPL and participated in a 6-hour comprehensive assessment of emotional functioning (Levenson et al., 2008). The lab battery included various tasks designed to assess different aspects of emotional functioning, including emotion reactivity (i.e., the type, magnitude, and duration of a response in reaction to changes in the internal or external environment), emotion regulation (i.e., a change in the type, magnitude, and duration of an emotional response to meet situational demands or personal goals) and emotion recognition (i.e., an understanding of emotion in self and others) (Levenson, 2007; Levenson et al., 2008). A subset of tasks from this assessment (see Laboratory Tasks below) was used in the present study. Upon arriving to the lab, participants completed consent forms (approved by the University of California Berkeley, Committee for Human Subjects) and were seated in a well-lit, 3x6 experimental room. A trained experimenter applied non-invasive physiological sensors that monitored autonomic nervous system activity during the tasks (see Measures below). Participants were videotaped while participating in the day's tasks and at the end of the study, provided written consent for the use of their video recordings. Participants received $30, in addition to any transportation costs that they might have incurred.

Apparatus

Audiovisual. Experimental stimuli were presented on a 21-inch LCD computer monitor positioned directly in front of the participant. Task instructions and post-task questions were audio-recorded and played for the participant. A remotely controlled high-resolution color video camera was used to record participants' facial behavior and body movement during the tasks. The camera was placed behind darkened glass on a bookshelf directly facing participants.

Physiology. Autonomic and somatic activity was continuously collected and monitored using a 23-channel Biopac polygraph, a computer, and an online data acquisition and analysis software package written by Robert W. Levenson. The software package calculated the second-by-second averages of all physiological measures.

Laboratory tasks

Visual avoidance. VA behavior (see Measures below) was examined during a disgust reactivity trial where participants were asked to view a film clip known to elicit disgust reliably in neurologically intact adults (Shiota & Levenson, 2009). The 101-second clip was taken from the show *Fear Factor,* and shows a man sucking fluids from cow intestines. Before watching the clip, participants were instructed to sit quietly for 60-seconds, while baseline physiological activation and disgust expressivity were recorded. After viewing the film clip, participants were asked to rate how they felt while viewing the film clip (see Measures below).

Laboratory-based tasks of emotion regulation. Laboratory-based emotion regulation was examined using two trials from an acoustic startle task (Goodkind et al., 2010; Gyurak et al., 2009) and a disgust suppression task (Gyurak et al., 2012). During the startle task, participants were presented with a loud noise (115-dB 100-msec-long burst of white noise) played from speakers placed behind the participant's head. Data from two trials were used in the present study: (1) anticipated startle with no instruction to suppress (participants were warned that they would hear a loud noise at the end of a 10-second countdown but were not explicitly instructed to inhibit emotion), and (2) anticipated startle with instruction to suppress (participants were warned that they would hear a loud noise at the end of a 10-second countdown and asked to try their best not to let their feelings show). At the start of the each trial, participants received the following instruction, "For this next task, you will hear the loud noise again. This time, you will know exactly when the noise is coming. You will see a countdown from 10-0. The loud noise will come at 0." The anticipated startle with instruction to suppress condition had the additional instruction, "HIDE your reaction so that no one would know how you feel when you hear the noise." Following instructions for each trial, participants were then asked to sit quietly for a 60-second baseline period, after which they were reminded that the loud noise would come at 0 and the countdown was presented on a computer monitor directly in front of them. Given that instructions to down-regulate involved the behavioral suppression of the startle response, I focused on emotional facial behavior and somatic activity as indices of regulatory performance. Following previously published procedures (Goodkind et al., 2010; Gyurak et al., 2009), regulatory performance was operationalized as the somatic activity and emotional facial behavior occurring in the 5-seconds immediately following startle onset, with smaller responses representing greater regulatory ability (see Measures below).

During the disgust suppression task, participants were asked to view an 85-second film clip taken from the movie *Pink Flamingos.* In the clip, an actor dressed in drag follows a dog down a street. After the dog defecates, the actor picks up the dog's feces, spreads it over his face and tongue, chews and then eats the fecal matter. Before the start of the task, participants were given the following instructions, "For the next task, you will watch another film. This time HIDE your reactions so that no one would know how you feel while watching the film." To ensure that participants understood the instructions, they were also asked, "Do you understand the instructions for this task? … (a) *Yes*, (b) *I'm not sure*." If a participant responded, "*I'm not sure*", a graduate student experimenter went into the room and explained the procedure again. Prior to the start of the film, participants were instructed to sit quietly and watch an "X" for a 60-second baseline period. Immediately before the start of the film, participants were reminded of the instruction to suppress. Following previously published procedures (Gyurak et al., 2012), regulatory ability was measured as the change in physiological activation and disgust expressivity in this suppression task, controlling for emotional responding in the disgust reactivity task (see Measures below).

Emotion recognition. The ability to recognize emotion was assessed by asking participants to identify the emotion experienced by target characters in 11, 37-second film clips. This task has been validated as a measure of emotion recognition in patient and healthy controls (Goodkind et al., 2015). The use of film clips to assess emotion recognition may be more ecologically valid than the traditional use of static images given that emotion recognition in the real world occurs with multimodal sensory stimuli that are dynamic. Identification of 11 target emotions was assessed: 4 positive emotions (i.e., affection, amusement, calm, enthusiasm), 4 negative emotions (i.e., anger, fear, sadness, disgust), and 3 self-conscious emotions (i.e., pride, shame, embarrassment). Prior to viewing the film clip, participants were asked to sit quietly for a 30-second baseline period and instructed to watch an "X" on the screen. Following the clip, participants were asked to identify the emotion experienced by a target character in the film (see Measures below).

Laboratory measures

Visual avoidance. VA behavior was coded using the Attentional Control Coding System (ATCO; Otero & Levenson, 2017; Otero & Levenson, 2019), which is comprised of 13 codes capturing 2 broad types of attentional control behaviors: (a) visual avoidance (i.e., movements of the eyes, head and upper torso that limit the intake of visual information) and (b) distancing (i.e., body movements or verbal utterances that indicate physical or mental distancing from a stimuli, including pulling the body backwards, eye rolls, disapproving speech [e.g., "Ugh", "Jeez" and explicit requests to have the film stopped). Given the present aims, the study focused on data from the VA codes (head turn, head down, head up, head shakes, eye closures, gaze aversion, and blinks). Past work found that the 2 remaining codes (squints and eyes covered) occur infrequently among patients and controls, thus they were excluded (Otero & Levenson, 2017). 6 out of the 7 VA codes (head turn, head up, head down, head shake, eye closures, gaze aversion) were rated for intensity on a second by second basis, and 1 code (blinks) was rated for frequency across the task. Each code rated for intensity was coded using one of three intensity scales: (a) a 4-point scale assessing the intensity of head movements (head turn, head down, head up, head shakes), with 0 indicating no head movement, 1 indicating slight head movement, 2 indicating moderate head movement, and 3 indicating extreme head movement, (b) a 3-point scale assessing the intensity of eye closure (eyes closed), with 0 indicating no eye closure, 1 indicating partial eye closure, and 2 indicating complete eye closure, or (c) a 2-point intensity scale assessing the presence or absence of gaze aversion. Blinks were coded for frequency across the entire film clip (i.e., each blink was counted as 1 and summed to create an overall blink score for each participant).

A team of 3 undergraduate research assistants participated in 6 weeks of formal training consisting of studying the ATCO manual, weekly practice assignments, and a weekly 1-hour meeting to discuss coding disagreements. Coders were blind to participant diagnostic group and task stimulus. To assess rater reliability for the study, coders had a 20% overlap in assignments. Inter-rater reliability for VA behavior was high (intra-class correlation coefficient = .84).

Physiology. The following physiological measures were used: (1) heart rate (electrodes with conductive paste were placed on both sides of the participant's torso to obtain the electrocardiogram [EKG]. Inter-beat interval was measured by the interval, in milliseconds, between successive R waves); (2) finger pulse amplitude (a UFI photoplethsmograph was used to record the amplitude of blood volume in the finger using a photocell taped 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 distal phalanx of the non-dominant hand's index 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. Transition time in milliseconds was measured between the R wave of the EKG and the upstroke of the peripheral pulse at the ear site); (5) 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 to calculate sweat response); (6) finger temperature (a thermistor was attached to the distal phalange of the non-dominant hand's little finger and recorded temperature in degrees Fahrenheit); (7) general somatic activity (an electromechanical transducer attached to a platform under the participant's seat generates an electrical signal proportional to the amount of movement in any direction); (8) respiration period (a rubber belt was stretched around the thoracic region; the inter-cycle interval was computed in milliseconds as the time between successive inspirations); (9) systolic and (10) diastolic blood pressure (an Ohmeda Finapress 2300 was used to measure blood pressure on each heart beat. The Finapress uses a small cuff placed on the middle phalange of the middle finger of the participant's non-dominant hand). These 10 physiological measures were selected to provide a broad index of the major physiological systems (cardiovascular, respiratory, electrodermal, and somatic) found to be important in emotional responding (Cacioppo, Berntson, Larsen, Poehlmann, & Ito, 2000; Kreibig, 2010).

Emotional facial behavior. Emotional facial behavior was coded during the disgust reactivity task, the two acoustic startle conditions (anticipated startle with and without instruction to suppress) and the disgust suppression task. Trained coders (independent from the VA raters) coded participant emotional facial behavior using the Emotional Expressive Behavior Coding System (EEB; Gross & Levenson, 1993). Six emotions were coded including, anger, disgust, fear, sadness, surprise, and amusement. Coders were blind to the participant's diagnosis and the task's stimulus. Inter-rater reliability for facial emotional behaviors was high (intra-class correlation coefficient = .92).

Self-report data.

Self-reported emotional experience. At the end of each task, 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 to 2 point scale (0= not at all; 1= a little; 2= a lot). Additionally, at the end of both acoustic startle trials, participants were asked how surprised they were when they heard the loud noise on a 0 to 2 point scale (0= not at all; 1= a little; 2= a lot).

Emotion recognition. After viewing each emotion recognition film clip, participants were shown a picture of a target character and asked to identify the emotion the character was experiencing during the clip. A list of the 11 emotions (affection, amusement, calm, enthusiasm, anger, fear, sadness, disgust, pride, shame, and embarrassment) was shown on a computer monitor and orally presented using a pre-recorded audio clip. Participants were instructed to say their responses aloud.

Caregiver-Completed Measures

Patient emotion regulation in the home. Patient use of emotion regulation in the home was assessed using the Caregiver Assessment of Socio Emotional Functioning (CASEF; Ascher, 2012). The CASEF is a 44-item questionnaire covering four domains of emotional functioning (emotional reactivity, regulation, empathy, and emotional memory) and six domains of social functioning (interpersonal warmth, pro-social behavior, adherence to social norms, self-centeredness, insight into disease state, and social interest). The current study only used data from the emotion regulation subscale. Caregivers were asked to rate the patient's emotion regulation (without mention of any particular regulatory strategy) in the past month (e.g., "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). Given the present study's focus on the regulation of negative emotion, scores from the negative emotion regulation item were used.

Caregiver mental health. Caregiver mental health was assessed using the Symptom Checklist 90-Revised (SCL-90-R; Derogatis & Unger, 2010), a well-validated and widely-used inventory of psychopathological symptoms. The SCL-90-R is comprised of 90-items and assesses 9 domains of psychopathology (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism). The current study used data from the anxiety (ANX) and depression (DEP) subscales. Example items for ANX scale include, "Nervousness or shakiness inside" and "Worrying too much about things". Example items for DEP scale include, " Feeling blue" and "Feeling no interest in things". For each item, caregivers rate themselves on a 5-point scale of distress from 0 (none) to 4 (extreme). The Global Severity Index (GSI) is the average score of all 90 items, and was used as a measure of overall psychological distress (Derogatis & Savitz, 2000). SCL-90-R subscale and summary scores have been found to have good predictive and construct validity, and high internal consistency (Derogatis & Unger, 2010; Morgan, Wiederman, & Magnus, 1998; Schmitz, Kruse, Heckrath, Alberti, & Tress, 1999). Reliability among DEP, ANX, and GSI scores in the present sample was high (Cronbach's α coefficient = .92).

Executive functioning

Neuropsychological measures were administered at the UCSF Memory and Aging Center within 3 months of the laboratory visit at the BPL. The 3-month time window was used to ensure that performance on measures of neuropsychological functioning accurately represented patients' cognitive ability at time of laboratory visit. Trained staff at UCSF evaluated participants in a testing room using standard neuropsychological testing procedures. The measures below are part of a bedside screen developed by the UCSF Memory and Aging Center to assess executive functioning in patient (Kramer et al., 2003).

Working memory. Auditory working memory was assessed using the backward digit span subtest of the Wechsler Adult Intelligence Scale, Third Edition (Wechsler, 1997). Participants were orally presented with a sting of numbers ranging from 2 to 8 digits, after which they were asked to repeat them verbally in the reverse order. A total score was computed by summing the number trials completed correctly, with higher scores indicating greater working memory capacity.

Response inhibition. Response inhibition was assessed using the Stroop subtest of the Delis-Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001). The Stroop test consists of a control condition during which participants were asked to name the color of a color patch, and an interference condition during which participants were asked to name the color of ink in which an incongruent color word is printed (e.g., word "red" printed in the color blue). Participants were asked to name the color as quickly as they can. A total score was computed by summing the number of correct responses made in 60-seconds, with higher scores indicating greater response inhibition ability.

Set-shifting. Set-shifting ability was assessed using an adapted version of Trail Making subtest, Condition B of the D-KEFS (Delis et al., 2001). Participants were asked to connect ascending numbers and days of the week in an alternating sequence (i.e., 1-Sunday-2-Monday-3-Tuesday) as quickly as they could. If a participant made a mistake while working on the task, the evaluator pointed out the error and instructed the participant to start at the last correct connection while the clock was kept running. A total score was computed by inverse scoring time to completion in seconds, with faster times indicating greater set-shifting ability.

Cognitive flexibility. Cognitive flexibility was assessed using an adapted version of verbal fluency subtest of the D-KEFS (Delis et al., 2001). Participants were given one minute to generate as many words as possible that started with the letter D. A total score is computed by tallying the number of correct words generated, with higher scores indicating greater cognitive flexibility.

Data Reduction

Visual avoidance. VA behavior was coded second-by-second throughout the entire disgust reactivity task (101-seconds). Data reduction was as follows: first, second by second raw data was averaged for head turn, head up, head down, head shakes, eye closed, and gaze aversion. To do this, second-by-second codes was summed and divided by 101 (total number of seconds coded). Blinks (the only code not coded for second by second) was tallied and divided by 101 to create an average blink score. Second, the averaged scores were standardized (using mean and standard deviation from the entire sample) to account for differences in intensity scaling. Lastly, the standardized scores were summed to create a composite score representing total VA behavior throughout the entire disgust reactivity task, with higher scores indicating greater use of VA. Internal consistency of the 7 codes was moderate for a new behavioral coding system (Cronbach's α coefficient = .57) (Nunnally & Bernstein, 1978). To increase internal reliability, each item was removed from the Cronbach's α systematically to determine which code brought down overall reliability the most. Results indicated that reliability among the 7 VA codes (across all diagnostic groups) was greatest after removing headshake (Cronbach's α coefficient = .60), thus it was removed from further analyses. Other codes were not removed because their inclusion resulted in acceptable internal reliability.

Physiological activation. Second by second values for each physiological measure was averaged during the 60-second pre-task baseline periods, and during the following time frames (per task):

Task	Seconds of Physiological Data Used
Disgust Reactivity	101-seconds (entire task)
Anticipated startle: No instruction to suppress	5-seconds immediately following startle presentation
Anticipated startle: Instruction to suppress	5-seconds immediately following startle presentation
Disgust Suppression	85-seconds (entire task)

Baseline averages were subtracted from the task average to create a difference score. For eight of the 10 measures (all measures except for skin conductance and finger temperature) the entire 60-seconds of the baseline period were used. The last ten seconds of the pre-task periods were used to compute the baseline averages for skin conductance and finger temperature because these measures often show slow linear trends. Each change score was normalized using means and standard deviations from the entire sample. Normalized scores for inter-beat interval, finger pulse amplitude, ear pulse transmission times, and respiration period were inverse scored by multiplying values by -1 so that for all measures larger standardized scores indicate greater activation. A composite score representing overall physiological activation that was created by averaging the standardized scores for all ten measures. This composite score was used for Aim 2 analyses and Exploratory Aim 1 analyses to control for Type 1 error. Aim 1 analyses used IBI and SCL data only because of their focus on the relationship between VA and changes in ANS activation before and after VA onset. IBI and SCL were selected because they are the two most commonly used measures of ANS activation in the study of emotion.

Emotional facial behavior. For each emotion code (anger, disgust, fear, sadness, surprise, and amusement), rates per second were computed by summing the second-by-second intensity scores and dividing them by the total number of seconds coded. Thus, each participant had 6 emotion codes per task.

Emotional recognition. For each emotion recognition film clip, correct identification of the target emotion was assigned the numeric value of 2; naming another emotion that was the same valence as the target emotion was assigned a score of 1; and naming another emotion that was a different valence was assigned a score of 0. Subscores scores were derived for three groups of films: positive (affection, amusement, calm, enthusiasm), negative (anger, fear, sadness, disgust), and self-conscious (shame, embarrassment, pride). An overall emotion recognition score was computed by summing correct answers across the films and dividing by the total number of films.

Aims and Hypotheses

Aim 1. To examine the association between total VA behavior (coded across the disgust reactivity task) and change in emotional responding before and after the onset of VA.

Hypothesis 1.1a: Greater increases in IBI and SCL activation and disgust facial behavior *before* the onset of VA will be associated with greater VA behavior across the disgust reactivity task.

Rationale: If VA is an emotion regulation strategy, it should occur when emotional responding is increasing (thus indicating a need to down-regulate emotion).

Hypothesis 1.1b: Greater decreases in IBI and SCL activation and disgust facial behavior *after* the onset of VA will be associated with greater VA behavior across the disgust reactivity task.

Rationale: If VA is an emotion regulation strategy, it should lead to decreasing emotional responding following the onset of VA.

Hypothesis 1.2*:* Greater increases in IBI and SCL activation and disgust facial behavior *before* the onset of VA, and greater decreases in IBI and SCL activation and disgust facial behavior *after* the onset of VA will be associated with greater VA behavior across the disgust reactivity task in healthy control participants and patients with AD, but not in patients with bvFTD.

Rationale: Although prior findings suggest that VA is reduced in bvFTD, it is not completely absent (Otero & Levenson, 2019). As such, it is important to examine the relationship between VA and indices of emotional responding (ANS activation and emotional facial behavior) the context of bvFTD. BvFTD is characterized by diminished connectivity in neural networks implicated in emotion reactivity and regulation (i.e., salience and executive networks; Seeley et al., 2007). Moreover, past work found disruption of frontal-temporal white-matter tracts connecting frontal and limbic structures (Zhang et al., 2009). Given connectivity loss between frontal regulatory centers and limbic regions, greater VA should not be associated with increased emotional responding before the onset of VA or down-regulatory effects in the bvFTD patients compared to patients with AD or healthy control participants.

Aim 2. To determine whether greater deficits in VA are associated with worse performance on laboratory-based measures of emotion regulation, emotion regulation in the home, and measures of executive functioning.

Hypothesis 2.1*:* Greater VA deficits during a disgust reactivity task will be associated with greater deficits in spontaneous down-regulation on a laboratory-based measure (i.e., anticipated acoustic startle task with no instruction to suppress).

Rationale: Different forms of spontaneous emotion regulation are theorized to rely on similar cognitive control mechanisms to down-regulate emotional responding (Ochsner & Gross, 2005; Ochsner & Gross, 2008; Ochsner et al., 2012). If VA is a form of spontaneous emotion regulation, lower VA should relate to lower down-regulation in a laboratory-based measure of spontaneous emotion regulation, but not with lower down-regulation in laboratory-based measures of instructed emotion regulation (i.e., anticipated acoustic startle with instruction to suppress and disgust suppression).

Hypothesis 2.2*:* Greater patient deficits in VA during the disgust reactivity task will be associated with greater patient deficits in emotion regulation of negative emotion in the home (as rated by their caregiver).

Rationale: If VA is helps down-regulate negative emotion, it should be associated with a measure of negative emotion regulation in the home environment. Furthermore, its association with non-regulatory emotional processes, such as emotion recognition, may be insignificant.

Hypothesis 2.3: Greater deficits in VA during the disgust reactivity task will be associated with greater deficits in cognitive flexibility (i.e., lower verbal fluency scores), above and beyond dementia severity and deficits in working memory, response inhibition and set-shifting.

Rationale: Emotion regulation relies on goal-oriented cognitive processes. Consistent with this, prior work finds that emotion regulation ability is associated with performance on tests of executive functioning (Gyurak et al., 2009; Gyurak et al., 2012; McRae et al., 2012; Pe et al., 2013). Cognitive flexibility may be particularly important for VA because it underlies the ability spontaneously organize and plan behavior, and monitor and update behavioral responses- all potentially necessary for the execution of VA. Working memory may not be important to VA because VA may not require previous knowledge to be retrieved. Response inhibition may not be important to VA because VA may rely more on directing visual attention *away* from stimuli rather than inhibiting proponent responses. Lastly, set-shifting may not be important in VA given that VA may not require disengaging from a mental set.

Aim 3. To determine whether patient VA deficits predict worse caregiver mental health independently from patient emotion recognition.

Hypothesis 3*:* Greater VA deficits among patients will predict greater caregiver psychological distress, depression, and anxiety above and beyond patient deficits in emotion recognition.

Rationale: Emotion regulation is an important part of intimate relationships. Given its hypothesized regulatory function, we expect that greater patient VA deficits will predict worse caregiver mental health independently from patient emotion recognition ability.

Results

Demographic and clinical variables

The distribution of males and females among diagnostic groups was compared using a chi-square test. A significant sex difference among diagnostic groups was found, χ_2 (3, N =169) = 6.39, p = .041, with proportion of women in the control group being larger than the proportion of woman in the patient groups. Age differences between diagnostic groups were examined using analysis of variance (ANOVA). An age difference among diagnostic groups was found, F (2, 130) = 3.402, p = .036. Bonferroni-corrected pairwise comparisons showed that patients with AD were younger than healthy controls (M_{diff} = - 4.39). No age differences were found between patient groups or between patients with bvFTD and healthy controls. ANOVAs were also used to examine diagnostic group differences in global cognitive functioning, as assessed by the MMSE total score, and disease severity as assessed by the CDR box score. Results revealed significant group differences in global cognitive functioning, F (2, 130) = 30.599, p < .001, with bvFTD patients showing the greatest levels of cognitive impairment followed by AD patients and healthy controls. Results showed significant group differences in disease severity, F (2, 130) = 87.664, p < .001, with patients with bvFTD showing greatest disease severity followed by patients with AD. Descriptive statistics for demographic and clinical variables are presented in Table 1.

Aim 1: To examine the association between total VA behavior (coded across the disgust reactivity task) and change in emotional responding before and after the onset of VA.

Analytic Approach: To examine the relationship between VA behavior and rates of change in emotional responding before and after onset of VA, a series of bivariate correlations were performed on total VA scores and the slopes of IBI, SCL, and disgust facial behavior before and after VA onset. Data restructuring and computation of standardized beta values was conducted using the Python programming language (Python Software Foundation, https://www.python.org/). For each participant, the onset of VA behavior was identified as the first transition from a score of 0 to 1 or greater on each of the 6 VA codes. Pre-VA rates of change for IBI, SCL, and disgust facial behavior were computed using second-by-second data taken from the 15 seconds immediately preceding the onset of VA. Post-VA rates of change were computed using second-by-second data taken from the 15 seconds immediately following the onset of VA. Beta values for each variable (pre-and post-VA IBI, SCL, and disgust facial behavior) were estimated using ordinary least squares (OLS) regression. This created 6 new beta values for pre- and post-VA IBI, SCL, and disgust facial expressivity. Unstandardized beta values were standardized using the mean and standard deviation of the entire sample. Intercorrelations for Aim 1 main variables across all groups are presented in Table 2. Intercorrelations for variables separated by diagnostic group are presented in Tables 3 and 4.

To examine whether diagnosis moderated the association between total VA behavior and pre-and-post VA rates of change in emotional responding, 6 moderated hierarchical regressions were performed using PROCESS (Model 1) for SPSS (Hayes, 2013). Age, gender, and dementia severity scores were entered as covariates, and total VA behavior was entered as the dependent variable. Diagnosis (1= controls, 2= AD, 3= bvFTD) was coded with Helmert contrasts (D_1: control= -.667; AD= .333; bvFTD= .333, D_2: control = .000; AD= -.500; bvFTD= .500). Helmert coding is a coding system for ordinal multicategorical variables that computes regression coefficients representing the difference in means for one group against all groups in ascending order on the multicategorical variable (Hayes & Montoya, 2017). Resulting contracts included (1) controls vs. all patients, and (2) patients with AD vs. patients with bvFTD. Independent variables included, 2 Helmert coded diagnosis variables, 2 interaction terms (created by multiplying each Helmert coded variable with standardized beta values of each index of emotional responding), and standardized beta values of each index of emotional responding. Simple slope analyses were used to examine significant interaction affects using values at +/− 1 SD from the mean (Aiken & West, 1991).

Increasing emotional responding before VA onset. Regarding IBI, collapsing across groups, increasing heart rate before the onset of VA was marginally associated with greater VA across the entire task, $r = 0.151$, $p = 0.058$. No moderation of diagnosis was found for IBI. Regarding SCL, moderation analyses revealed a significant main effect of pre-VA SCL slope, $\beta = 0.26$, $t(136) = 3.16$, $p = 0.002$, such that the more SCL activation increased before the onset of VA, the greater VA behavior across the task. This effect was moderated by group membership, $\Delta R^2 = 0.12$, $\Delta F\ (2, 127) = 10.09$, $p < 0.001$, $\beta = -1.02$, $t(136) = -4.47$, $p < 0.001$, such that greater increases in SCL before the onset of VA was associated with greater total VA in controls, $\beta = 0.97$, $t(136) = 4.61$, $p < 0.001$, but not in patients with AD, $\beta = -0.12$, $t(136) = 0.13$, $p = 0.365$, or patients with bvFTD, $\beta = 0.01$, $t(136) = 0.12$, $p = 0.905$ (see Figure 1). No differences were found as a function of AD vs. bvFTD diagnosis. No association was found between disgust facial behavior and total VA or moderation effect of diagnosis.

Thus, results supported the hypothesis that increasing emotional responding (i.e., SCL activation) *before* the onset of VA would be associated with greater VA behavior across a disgust reactivity task. Results also supported the partial hypothesis that the increasing ANS activation before the onset of VA would be associated with greater total VA in healthy control participants, but not in patients with bvFTD.

Decreasing emotional responding after VA onset. Collapsing across groups, rates of change of IBI, SCL, or disgust facial behavior after the onset of VA was not associated with total VA behavior. Follow up moderation analyses did not indicate a significant interaction effect of diagnosis. Thus, results did not support the hypothesis that greater VA behavior across the disgust reactivity task would be associated with decreasing emotional responding following VA onset after the onset.

Summary: Aim 1 addressed the question of whether VA behavior occurred in the context of increasing emotional responding and whether, after VA onset, emotional responding decreases. Supporting Hypothesis 1.1a, the present study showed that the more SCL increases prior to the onset of VA, the more VA is used during the disgust reactivity task. This effect was moderated by diagnosis, such that greater increase in SCL before the onset of VA predicts greater VA in healthy control participants, but not in patients with bvFTD or AD. Rate of change of disgust facial behavior before the onset of VA was not associated with total VA behavior. Contrary to Hypothesis 1.1b, current data did not support the notion that greater VA behavior is associated to decreasing physiological activation and disgust facial expressivity following VA onset.

Aim 2: To determine whether greater deficits in VA are associated with worse performance on laboratory-based measures of emotion regulation, emotion regulation in the home, and measures of executive functioning.

Analytic Approach: To examine the relationship between VA behavior during the disgust reactivity task and performance on laboratory-based tasks of emotion regulation, 6 bivariate correlations were conducted on total VA scores (coded across the entire task) and: (a) performance on the anticipated startle task with no instruction to suppress; (b) performance on the disgust suppression task; and (c) performance on the acoustic startle task with instruction to suppress. Intercorrelations for all Aim 2.1 variables are presented in Table 5.

To examine whether diagnosis moderated the relationship between total VA behavior and performance on laboratory-based measures of emotion regulation, 6 moderated hierarchical regressions were performed. Age, gender, and dementia severity scores were entered as covariates, and total VA behavior was entered as the dependent variable. Independent variables included, 2 Helmert coded diagnosis variables, 2 interaction terms (created by multiplying each Helmert coded variable with scores from each measure of laboratory-based emotion regulation), and scores from each measure of laboratory-based emotion regulation. Simple slope analyses were used to examine significant interaction affects using values at +/− 1 SD from the mean.

To assess whether VA behavior was associated with caregiver-reported patient negative emotion regulation in the home, a bivariate correlation was performed between total VA behavior (coded across the entire task) and CASEF negative emotion regulation scores. Additionally, a bivariate correlation was performed on total VA and emotion recognition ability to examine whether VA behavior was uniquely associated to emotion regulation in the home. Intercorrelations for all Aim 2.2 variables (across entire patient sample) are presented in Table 6.

Lastly, to examine whether VA behavior was associated with performance on measures of executive functioning, 4 bivariate correlations were conducted on total VA behavior (coded across the entire task) and: (a) WAIS- III backwards digit span scores (working memory), (b) D-KEFS Stroop test, interference trial scores (response inhibition), (c) adapted DKEFS verbal fluency scores (cognitive flexibility), and (d) adapted DKEFS trail making test, condition B (set-shifting). Intercorrelations for all Aim 2.3 variables across all groups are presented in Table 7. Intercorrelations for variables separated by diagnostic group are presented in Tables 8 and 9.

To examine whether diagnosis moderated the relationship between total VA behavior and performance on measures of executive functioning, 4 moderated hierarchical regressions were performed. Age, gender, and dementia severity scores were entered as covariates, and total VA behavior was entered as the dependent variable. Independent variables included, 2 Helmert coded diagnosis variables, 2 interaction terms (created by multiplying each Helmert coded variable with scores from each measure of executive functioning), and scores from each measure of executive functioning. Simple slope analyses were used to examine significant interaction affects using values at +/− 1 SD from the mean.

VA and laboratory-based measures of emotional regulation. Collapsing across groups, results showed that greater VA behavior across the disgust reactivity task was associated with greater suppression of facial behavior during the acoustic startle task with instruction to suppress ($r = 0.181$, $p = 0.027$). This association did not survived family-wise error correction (Bonferroni= $p < .008$), computed by dividing 0.05 by the total number of correlations (6). Moderation analyses did not indicate a significant interaction effect of diagnosis. Thus, the hypothesis that greater VA behavior would be associated with better performance on laboratory-based measures of spontaneous emotion regulation was partially supported; specifically greater VA across the disgust reactivity was associated with greater regulatory ability during a task of instructed expressive suppression.

VA and caregiver-reported negative emotion regulation. Collapsing across patient groups, results showed that greater VA behavior throughout the disgust reactivity task was associated with greater CASEF negative emotion regulation scores, $r = 0.222$, $p = 0.029$. Greater patient VA was also associated with greater patient emotion recognition ability ($r = 0.197$, $p = 0.015$). Thus, the hypothesis that greater VA behavior would be associated with greater regulation of negative emotion in the home was supported.

VA and measures of executive functioning. Collapsing across groups, results from correlation analyses indicated that VA behavior throughout the disgust reactivity task was not associated with any measure of executive functioning. However, moderation analyses revealed a significant main effect of verbal fluency, $\beta = 0.30$, $t(127) = 2.45$, $p = 0.016$, such that participants with greater verbal fluency showed greater VA behavior across the task. A significant interaction effect between group membership and verbal fluency was also found, $\Delta R^2 = 0.06$, $\Delta F\ (2, 118) = 4.38$, $p= 0.015$, $\beta = -0.91$, $t(127) = -2.88$, $p = 0.005$, with greater verbal fluency associated with greater total VA in controls, $\beta = 0.90$, $t(127) = 3.03$, $p = 0.003$, but not in patients with AD, $\beta = 0.07$, $t(127) = 0.53$, $p = 0.599$, or patients with bvFTD, $\beta = -0.08$, $t(127) = -0.55$, $p = 0.583$ (see Figure 2). Thus, the hypothesis that greater deficits in VA would be associated with greater deficits in cognitive flexibility was partially supported. Specifically, greater cognitive flexibility predicted greater overall VA behavior in controls, but not in either patient group.

Summary: Aim 2 addressed the question of whether VA behavior was associated with emotion regulation (in the laboratory and in the home), and performance on measures of executive functioning. Contrary to Hypotheses 2.1, VA behavior during the disgust reactivity task was not associated with performance on a laboratory-based task of spontaneous emotion regulation, however it was associated with performance on a task of instructed expressive suppression. Consistent with Hypothesis 2.2, greater patient VA was associated with greater caregiver-reported negative emotion regulation in the home. Additionally, consistent with Hypothesis 2.3, greater VA behavior was associated with greater cognitive flexibility. This effect was moderated by diagnosis, such that greater cognitive flexibility ability predicted greater VA behavior in healthy control participants, but not in either patient group.

Aim 3. To determine whether patient VA deficits predict worse caregiver mental health independently from patient emotion recognition.

Analytic Approach: To examine the relationship between caregiver mental health and patient VA behavior and patient emotion recognition ability, a series of bivariate correlations were conducted. Caregiver mental health measures included: (a) psychological distress (GSI); (b) depression symptomatology (DEP); (c) anxiety symptomatology (ANX). Intercorrelations for all Aim 3 variables are presented in Table 10.

Following the correlation analyses, three stepwise linear regressions were performed to examine whether patient VA deficits predicted caregiver mental health independently from patient deficits in emotion recognition. GSI, DEP, and ANX scores were entered as the criterion variables in each regression. For all analyses, dementia severity scores were entered in the first step as a covariate. In the second step, patient VA and emotion recognition ability were entered as predictor variables. Results for the regression equations are presented in Tables 11, 12, and 13.

Patient VA deficits and caregiver mental health. Results showed that greater patient VA behavior throughout the disgust reactivity task was associated with lower caregiver anxiety (r = -0.243, p = 0.009), lower caregiver depression (r = -0.240, p = 0.010), and lower caregiver psychological distress (r = -0.231, p = 0.012). Thus, the hypothesis that greater VA behavior would be associated with greater caregiver mental health was supported.

Patient emotion recognition deficits and caregiver mental health. Results showed that greater patient emotion recognition was associated with lower caregiver anxiety, r = -0.320, p = .001, lower caregiver depression, r = -0.219, p = .026, and lower caregiver psychological distress, r = -0.265, p = 0.006. The relationship between patient emotion recognition and caregiver depression symptomatology did not survived family-wise error correction (Bonferroni= $p < 0.016$), computed by dividing 0.05 by the total number of correlations (3).

Patient VA deficits caregiver mental health independently from patient emotion recognition deficits.

Caregiver psychological distress. Results indicated that patient VA behavior and emotion recognition ability accounted for significant additional variance of caregiver psychological distress, *adjusted* R^2 = 0.098, ΔF (2, 103) = 6.84, p = 0.010. In this second step, greater dementia severity and deficits in emotion recognition among patients significantly predicted greater caregiver psychological distress (CDR-BS: β = 0.22, p = 0.021; emotion recognition: β = -0.24, p = 0.010), but greater patient deficits in VA did not (β = -0.15, p = 0.128). Thus, the hypothesis that greater patient deficits in VA behavior would predict greater caregiver psychological distress independently from patient deficits in emotional recognition was not supported.

Caregiver anxiety symptomatology. Results indicated that patient VA behavior and emotion recognition ability accounted for significant additional variance of caregiver anxiety, *adjusted* R^2 = 0.13, ΔF (2, 99) = 10.42, p = 0.002. In this second step, greater dementia severity and deficits in empathic accuracy among patients significantly predicted greater caregiver anxiety (CDR-BS: β = 0.23, p = 0.017; emotion recognition: β = -0.30, p = 0.002). Greater patient deficits in VA did not (β = -0.12, p = 0.212) predict greater caregiver anxiety. Thus, the hypothesis that greater patient deficits in VA behavior would predict greater caregiver anxiety independently from patient deficits in emotion recognition ability was not supported.

Caregiver depression symptomatology. Results indicated that patient VA behavior and empathic accuracy accounted for significant additional variance of caregiver depression, *adjusted* $R^2 = 0.11$, ΔF (2, 99) = 4.89, $p = 0.029$. In this second step, greater dementia severity and deficits in VA behavior among patients significantly predicted greater caregivers depression (CDR-BS: $\beta = 0.28$, $p = 0.002$; total VA: $\beta = -0.21$, $p = 0.029$). Thus, the hypothesis that greater patient deficits in VA behavior would predict greater caregiver depression independently from patient deficits in emotion recognition ability was supported.

A follow up moderation analysis was conducted to examine whether dementia diagnosis moderated this effect. A moderated hierarchical regression was performed with patient emotion recognition ability and dementia severity entered as covariates, and caregiver depression scores entered as the dependent variable. Independent variables included, a dummy coded diagnosis variables (AD=0, bvFTD=1), 2 interaction terms (created by multiplying each dummy coded variable with total VA behavior), and total VA behavior. Simple slope analyses were used to examine significant interaction affects using values at +/− 1 SD from the mean.

Results revealed a significant interaction effect between dementia diagnosis and deficits in VA behavior, $\Delta R^2 = 0.09$, ΔF (1, 77) = 8.81, $p = 0.004$, $\beta = -0.33$, $t(81) = -2.97$, $p = 0.004$, with greater patient VA deficits predicting greater caregiver depression in bvFTD caregivers, $\beta = -0.33$, $t(79) = -3.20$, $p = 0.002$, but not in AD caregivers, $\beta = 0.01$, $t(79) = 0.14$, $p = 0.890$ (see Figure 3).

Summary: Aim 3 addressed the question of whether patient VA behavior impacted caregiver mental health independently from patient emotion recognition ability. Findings partially supported Hypothesis 3. Specifically, greater patient VA deficits during a disgust reactivity task predicted greater caregiver depressive symptoms independently from patient deficits in emotion recognition and dementia severity. Dementia diagnosis moderated this effect, with diminished VA behavior being particularly detrimental to the depressive symptomatology of bvFTD caregivers.

Exploratory Analyses

1. Visual "sipping"

Behavioral observation indicated that individuals sometimes look toward and then away from film stimuli ("visual sipping") when presented with the disgust reactivity task film stimuli. In order to examine whether this pattern of behavior was meaningful, exploratory analyses were conducted to assess how the behavior related to 5 indices of emotional responding: (1) a composite score of physiological activation during the hot spot (i.e., 30 most emotionally intense seconds of the disgusting film clip as rated by independent observers), (2) hot spot SCL activation, (3) hot spot IBI activation, (4) hot spot disgust facial behavior, and (5) self-report of disgust experienced while viewing the disgusting film clip. Data from the hot spot was selected to represent emotional responding from the peak emotional moments of the film clip.

"Visual sipping" behavior was quantified as follows: (a) first, second-by-second moments of gaze aversion (i.e., GV) were identified for each participant; b) second, a total "visual sipping" frequency score was computed for each participant by tallying discrete transitions from the presence of GV (indicated by a GV score of 1), to the absence of GV (indicated by a GV score of 0), and back to the presence of GV. Given that "visual sipping" may also include first looking *away* and then *toward* a film stimulus, an alternative frequency score was quantified by tallying discrete transitions from the absence of GV (indicated by a GV score of 0), to the presence of GV (indicated by a GV score of 1), and back to the absence of GV.

Analytic Approach: A series of bivariate correlations were conducted to examine the relationship among the new "visual sipping" code and the aforementioned indices of emotional responding. Intercorrelations for main variables are presented in Table 14. To test the hypothesis that diagnosis moderates the relationship between "visual sipping" and indices of emotional responding, a series of moderated hierarchical regressions were performed using PROCESS (Model 1) for SPSS (Hayes, 2013). Age, gender, and dementia severity scores were entered as covariates. Hot spot scores for composite physiological activation, SCL, IBI, disgust facial behavior, and disgust self-report were entered as separate dependent variables in 5 analyses. Independent variables included, 2 Helmert coded diagnosis variables, 2 interaction terms (created by multiplying each Helmert coded variable with "visual sipping" score), and "visual sipping" scores. Simple slope analyses were used to examine significant interaction affects using values at +/− 1 SD from the mean.

Frequency of "visual sipping" behavior and emotional responding. Preliminary descriptive statistics revealed that "visual sipping" quantified as presence-to-absence-to-presence of GV only occurred in 4.7% of the participant sample. "Visual sipping" quantified as absence-to-presence-to-absence of GV occurred in 25.4% of the participant sample and was used in subsequent analyses.

Collapsing across groups, results showed that greater frequency of "visual sipping" during the disgust reactivity task was associated with greater SCL activation during the hot spot, $r = 0.289$, $p = 0.001$. Greater frequency of "visual sipping" was also associated with greater hot spot disgust facial behavior, $r = 0.199$, $p = 0.012$, and composite physiological activation, $r = 0.182$, $p = 0.031$. These associations did not survive family wise error correction (Bonferroni= $p < 0.01$), computed by dividing 0.05 by the total number of correlations (5).

Moderation analyses indicated that there was a significant main effect of "visual sipping" on hot spot SCL activation, $\beta = 0.28$, $t(126) = 2.69$, $p = 0.008$, with greater "visual sipping" predicting greater SCL activation during the hot spot. Diagnosis moderated this effect, $\Delta R^2 = 0.040$, ΔF (2, 126) = 3.33, p= 0.039, with greater "visual sipping" predicting greater hot spot SCL activation in healthy control participants, $\beta = 0.47$, $t(126) = 4.23$, $p < 0.001$, but not in patients with AD, $\beta = 0.09$, $t(126) = 0.90$, $p = 0.372$, or patients with bvFTD, $\beta = 0.266$, $t(126) = 1.00$, $p = 0.321$ (see Figure 4). No difference as a function of AD vs. bvFTD diagnosis. No interaction effects were found in moderation analyses for composite physiological activation, hot spot IBI, hot spot disgust facial behavior, or disgust self-report.

Summary: Exploratory Aim 1 assessed the association between frequencies of "visual sipping" behavior and indices of emotional responding. Results revealed that greater frequency of "visual sipping" across the disgust reactivity task was associated with greater SCL activity in the 30 most emotionally intense seconds of the film clip. This association was moderated by diagnosis, with greater hot spot SCL activation predicting greater frequency of visual "sipping" in neurologically health controls, but not in patients with bvFTD or AD. Results also showed an association between greater frequency of "visual sipping" and greater disgust facial behavior and physiological activation during hotspot that was not moderated by diagnosis.

2. Coding for intensity of VA behavior versus frequency of VA behavior alone.

Lastly, we addressed the question of whether scoring for intensity of VA behavior adds any value to coding for its frequency alone. Data restructuring was conducted using the Python programming language (Python Software Foundation, https://www.python.org/). The following data structuring steps were taken: a) raw second-by-second scores of each of the 4 visual avoidance codes rated for intensity (i.e., head turn, head down, head up, eye closures) were recoded on a 0-1 scale, with 0 indicating absence of a code and 1 indicating the presence of a code; b) a frequency score for each of the 4 visual avoidance codes was computed by tallying the total number of instances each code was present and z-scoring these scores using the means and standard deviations from the entire sample; c) an overall VA frequency score was computed for each participant by summing the 6 frequency scores for head turn, head down, head up, eyes closed, gaze aversion, and blinks.

Analytic Approach: A series of multiple regressions were conducted to examine the relationship between VA intensity and frequency scores and 5 indices of emotional responding: a) composite physiological activation during the hot spot, b) hot spot SCL activation, c) hot spot IBI activation, d) hot spot disgust facial expressivity, and e) self-report of disgust experienced while viewing the disgusting film clip. Age, gender, and dementia severity were entered in the first step as covariates. Each index of emotional responding was entered as a dependent variable in 5 separate regressions. In the second step of all regressions, VA frequency scores were entered in the second step, and VA intensity scores were entered in the third step, both as predictor variables.

Incremental validity of coding for intensity. Results indicated that adding VA intensity scores did not significantly improve the model fit of any of the regression equations used to predict the 5 indices of emotional responding (hot spot composite physiological activation: $\Delta R^2 = 0.00$, $\Delta F\ (1, 135) = 0.38$, $p = 0.541$; hot spot SCL activation: $\Delta R^2 = 0.00$, $\Delta F\ (1, 129) = 0.28$, $p = 0.559$; hot spot IBI: $\Delta R^2 = 0.00$, $\Delta F\ (1, 128) = 0.05$, $p = 0.826$; hot spot disgust facial behavior: $\Delta R^2 = 0.00$, $\Delta F\ (1, 136) = 0.06$, $p = 0.813$; disgust self-report: $\Delta R^2 = 0.01$, $\Delta F\ (1, 137) = 1.89$, $p = 0.172$). Thus, results revealed that coding for intensity of VA behavior did not increase the predictive ability of VA on indices of emotional responding beyond coding for frequency of VA behavior alone.

Discussion

In the present dissertation, I sought to examine visual avoidance (VA) a common yet understudied form of attentional deployment, in patients with two kinds of neurodegenerative disease (i.e., bvFTD and AD), and neurologically healthy controls. The three major aims included better understanding: (a) when VA occurs (Aim 1), (b) how VA relates to other measures of regulation (in the laboratory and in the home-environment), and measures of executive functioning (Aim 2), and (c) how deficits in VA in patients relate to the mental health of caregivers (Aim 3).

Findings indicated that increasing physiological activation, particularly increasing skin conductance level (SCL), *before* the onset of VA, predicted subsequent VA behavior during the task. The effect was moderated by diagnosis, such that increasing SCL activation before the onset of VA predicted greater VA behavior in neurologically healthy control participants, but not in patients with bvFTD or AD. SCL is a well-established indicator of ANS activation. The eccrine sweat glands that produce SCL are predominantly innervated by the sympathetic nervous system (Stern, Ray, & Quigley, 2001), and unlike other sweat glands that respond to increased temperature, eccrine sweat glands primarily respond to psychological stress (Dawson, Schell, & Filion, 2007). Prior work has found increased SCL activation in response to a variety of emotional stimuli, including anger-eliciting personal memories (Foster & Webster, 2001), fear-eliciting still images (Williams et al., 2005), and disgust-eliciting film clips (Codispoti, Surcinelli, & Baldaro, 2008). The current findings provide evidence that VA occurs in the context of increasing ANS activation in response to disgusting stimuli in the environment (Aim 1). The ANS is theorized to prepare the body for changing internal and external states via coordinated action of experiential, physiological, and behavioral responding (Ekman, 1992; Lazarus & Lazarus, 1991; Levenson, 1994; Plutchik, 1982). This coordinated action includes adaptive behavioral responding, such as the fighting, fleeing, and freezing responses, which can support survival. Viewed in this way, VA may represent a basic behavioral response that promotes the down-regulation of ANS activation. Consistent with this, emotion scholars have posited that individuals engage in VA when presented with negative triggers in their environment (Frijda, 1986; Frijda, 1987; Frijda et al., 1989).

In the context of disgust, VA is conceptualized as a basic response tendency that reduces the risk of contamination by limiting exposure to possible pathogens, supporting physical heath (Curtis, de Barra, & Aunger, 2011; Rozin & Fallon, 1987; Rozin, Haidt, & McCauley, 2008). The current findings indicate that VA behavior also may also promote psychological health. Specifically, VA may serve as an intermediary step between increasing sympathetic nervous system activation to disgust-eliciting stimuli, and fully formed behavioral avoidance. The fact that greater VA was associated with increasing SCL activity before VA onset, in health control participants but not either patient group, suggests that diminished neuronal integrity impacts the initiation of VA. In line with this, prior work has shown that patients with bvFTD show a number of emotional deficits compared to healthy controls including, diminished emotional reactivity (Sturm et al., 2008; Eckart et al., 2012), diminished ability to recognize emotion in others (Goodkind et al., 2015), and diminished suppression of the startle reflex (Goodkind et al., 2010). Patients with bvFTD also show lower VA compared to patients with AD and healthy controls (Otero & Levenson, 2019). VA behavior may be impacted by bvFTD because its initiation could rely on frontal and limbic regions implicated in emotion reactivity (i.e., amygdala, anterior insula) and emotion regulation (i.e., prefrontal cortex, cingulate cortex) that are effected by bvFTD pathology (Rosen, 2005; Seeley et al., 2009). Although emotional functioning is relatively spared in the early stages of AD, emotional symptoms are still found in up to 78% of patient (Spalletta et al., 2010), with anxiety and depression symptoms being the most common. Turning attention to specific emotional processes, past work has found increased emotional contagion (i.e., the automatic synchronizing of physiological and behavioral activation with another person that promotes helping behavior; Decety, 2004) in patients with AD (Sturm et al., 2013) compared to patients with mild cognitive impairment, AD's clinical prodromal stage. The emotional symptoms of AD, including heightened emotional contagion, are thought to be associated with atrophy of medial temporal regions, such as the ventral hippocampus, which have projections to the autonomic and endocrine systems associated with emotion reactivity (Krettek & Price, 1977; Moser & Moser, 1998). Diminished neuronal integrity in hippocampal regions associated in emotion reactivity and the inhibition of emotion (Fanselow & Dong, 2010; Femenía, Gómez-Galán, Lindskog, & Magara, 2012) may interfere with the connection between increasing ANS activation and the initiation of regulatory behavior, including VA.

Contrary to hypotheses, no associations were found between VA behavior and increases in disgust facial behavior before VA onset. An explanation for this may be differences in how SCL activation and emotional facial expression are processed and their behavioral impact. Given excitatory and inhibitory influences on SCL, its neural mechanisms are broad, and include pathways in cortical regions (e.g., premotor cortex), basal ganglia, hypothalamus, amygdala regions, and the reticular formation in the brainstem (Dawson, Schell, & Filion, 2017). Excitatory limbic influences from the amygdala are particularly relevant for SCL activation in the context of emotion reactivity. For example, prior research on fear-conditioning found greater SCL to be associated with greater amygdala activation, particularly in the right amygdala (LaBar, Gatenby, Gore, LeDoux, & Phelps, 1998; Phelps, Delgado, Nearing, & LeDoux, 2004). Increased amygdala activation and associated increases in the sympathetic nervous system activation might contribute to the initiation of regulatory behavior, such as VA, to restore homeostasis in the physiological milieu. Though also associated with amygdala activation, disgust facial behavior has been found to rely on brain regions related to sensory and face processing, including the premotor cortex, inferior occipital gyrus, fusiform gyrus, and posterior superior temporal sulcus (Goldin, McRae, Ramel, & Gross, 2008; Ousdal, Andreassen, Server, & Jensen, 2014; Skelly & Decety, 2012). Increased disgust facial expressivity, in isolation, may not trigger VA because it may be less imperative for an individual to down-regulate facial behavior given its social utility (e.g., sharing valuable information about the environment to conspecifics) (Darwin, 1965; Ekman, 1993; Ekman & Oster, 1979).

Current findings only provide evidence for a physiological condition that accompanies the initiation of VA (i.e., increasing SCL activation)- the regulatory effect of VA is less clear. Contrary to Hypothesis 1.1b, greater VA was not associated with decreasing emotional responding following VA onset. An explanation may be that VA leads to down-regulation of emotional responding when an individual has control over their environment via situation modification. For example, turning away from negative stimuli may be effective if you are simultaneously able to modify the situation. Though speculative, this suggests that VA might work in concert with other forms of emotion regulation to regulate negative emotion. Aligning with this, prior work has found that gaze aversion mediates the down-regulatory effects of cognitive reappraisal on subjective experience of negative emotion (Manera et al., 2014; Sanchez, Everaert, & Koster, 2016), and significantly reduces the variance in amygdala activation explained by cognitive reappraisal alone (van Reekum et al., 2007). The re-positioning of the eyes, head, and body away from aversive stimuli may function to create a psychological distance that allows other antecedent-focused regulatory strategies to take place, such as situational selection and modification, cognitive reappraisal, or distraction.

Interestingly, the current study found an association between VA behavior during a disgusting film and performance on laboratory-based tasks of instructed behavioral suppression (a response-based regulatory strategy) (Aim 2). Though this association did not survive family-wise error correction it provides early evidence that VA behavior is tied to emotion regulation ability on laboratory-based tasks. Future work would benefit from examining VA's association with antecedent-based strategies, in addition to response-based strategies. Specifically, past studies have found links between gaze aversion and both cognitive reappraisal and distraction in neurologically healthy individuals (Manera et al., 2014; Strauss et al., 2016; van Reekum et al., 2007). Two other antecedent-based strategies that may be associated with VA are situation selection and situation modification. Viewed as an early indicator of the intent to down-regulate emotion by physically withdrawing from the environment, it is plausible that VA may be related to regulatory strategies that target an individual's physical exposure to one's surroundings. Future work on VA would benefit from further examination the boundary conditions in which VA might be useful, including when used flexibly with other antecedent-based emotion regulation strategies.

The current study also tested the hypothesis that deficits in executive functioning, which are believed to support regulatory behavior, would be associated with deficits in VA behavior. Partially consistent with hypotheses, the current study found that greater verbal fluency (a measure of cognitive flexibility) predicted greater VA in healthy controls (Aim 2). This finding is consistent with prior work that found that deficits in cognitive flexibility were associated with worse behavioral suppression when instructed to down-regulate in response to an acoustic startle (Gyurak et. al., 2009). The lack of association between VA and other measures of executive functioning (i.e., working memory, response inhibition, and set-shifting) underscores the idea that executive functioning may be divided into distinct sets of cognitive processes (Miyake et al., 2000). Greater verbal fluency may be relevant to VA because it represents the ability to strategize, monitor ongoing responses, and flexibly implement new behavioral strategies, whereas it may not require previously stored knowledge to be retrieved (working memory), inhibition of behavioral responses (response inhibition), or disengagement from mental sets (set-shifting).

Lastly, findings from the current study have clinical implications for caregivers of patients with bvFTD and AD. Specifically, the study found that greater patient deficits in VA predicted greater caregiver depression independently from patient deficits in emotion recognition. This effect was moderated by diagnosis, with greater patient deficits in VA being particularly detrimental to the mental health of bvFTD caregivers (Aim 3). Prior work has linked caregiver depression to patient anger and aggression (Covinsky et al., 2003; Schulz, O'Brien, Bookwala, & Fleissner, 1995). Current findings extend such work by suggesting that specific deficits in regulating negative emotion may contribute to caregiver depression most heavily. Examining VA in patients with bvFTD and AD could help detect caregivers, who are at risk for depression early on, which would allow them to seek mental health treatment before depression symptoms become costly to caregiver health and quality of life. Early detection of depression in caregivers is particularly crucial considering the sizeable and growing number of individuals caring for a loved one with dementia (Schulz & Eden, 2016), and the link between caregiver mental health and patient mortality (Lwi, Ford, Casey, Miller, & Levenson, 2017).

The current study assessed emotion recognition by asking participants to identify target emotions of characters in film clips. Although film clips are more ecologically valid than static images because they use dynamic stimuli whose emotional content unfolds overtime (similar to real life), the forced-choice format of identifying target emotions is limited in its ability to capture how well patients can track other person's emotional state moment by moment. Moreover, recent work found that greater patient deficits in emotion recognition using a rating dial task, which requires patients to turn a dial to rate the affective valence of another person's emotional state second-by-second, was associated with greater caregiver depression, above and beyond patient deficits in identifying a film character's emotion using the forced-choice format (Brown et al., 2018). Future work would benefit from examining how patient VA deficits impact caregiver depression compared to patient deficits in emotion recognition using the rating dial task as well, to assess how VA compares in predicting caregiver mental health compared to a more nuanced measure of emotion recognition.

The association between patient VA and caregiver-reported patient negative emotion regulation in the home suggests concordance between spousal perception of patient emotion regulation and laboratory-based measurement of VA. Given the importance of emotion regulation in interpersonal relationships (Gross & John, 2003; Lopes, Salovey, Côté, Beers, & Petty, 2005), the perception that patients are less likely or able to regulate negative emotion likely negatively impacts the quality of the caregiver-patient relationship by reducing the number of social interactions patients have with others due to anticipated behavioral disturbances. This might increase risk of social isolation for both patients and caregivers, and limit their access to social resources that can maintain or improve quality of life and physical and mental health. Future work on VA and caregiver mental health should examine the possible mechanisms through which diminished patient VA impacts caregiver depression, including increased aggression and agitation in patients and lower quality social interactions between partners. Lastly, the current work may inform treatment development for caregivers of patients with dementia. Specifically, future interventions aimed at increasing or maintaining caregiver mental health may benefit addressing patient deficits in emotion regulation given its negative impact on caregiver depression.

Strengths and Limitations

The present study has several strengths, including the use of an objective observational coding system for quantifying VA behavior with high interrater reliability, a multi-method approach (using physiology, objectively coded behavior, and questionnaire data), and the use of well-validated laboratory-based tasks of emotion reactivity, emotion regulation, and emotion recognition. Additionally, the current study used dynamic video stimuli to elicit emotion, which is more ecologically valid than static images because daily emotion occurs in sensory rich environments with dynamic visual and auditory stimuli. Lastly, the study included a relatively large sample of two of the most common types of neurodegenerative disease (i.e., bvFTD and AD) and a neurologically healthy comparison group.

The study also has limitations, including the use of a single negative emotion (disgust) and the use of a single disgust-eliciting film clip. Additionally, the present study did not experimentally manipulate VA behavior by instructing participants to use it more or less, thus, causal inferences about the directionality of findings cannot be made. The study also only examined the relationship between VA behavior and response-based emotion regulation, and did not examine its links to antecedent-based emotion regulation, including other forms of attentional deployment, situation modification, or situation selection. Lastly, caregiver mental health, including depression and anxiety, was assessed using self-rated questionnaire data, and not by clinical interview, which has the advantage of being a less biased and more rigorous assessment of psychopathology compared to subjective report alone.

Summary and Conclusion

The present study examined VA behavior in response to a disgust eliciting film and its relationship to indices of emotional responding and performance on laboratory-based tasks of emotion regulation and executive functioning, using a sample of patients with two kinds of neurodegenerative disease (i.e., bvFTD and AD) and neurologically intact control participants. Additionally, the study examined how patient deficits in VA contributed to caregiver mental health compared to emotion recognition, a domain of emotional functioning known to be impaired in patients. Results revealed that VA behavior occurred in the context of increasing physiological activation, particularly SCL activity, in neurologically healthy participants but not in either patient group. Regarding executive functioning, cognitive flexibility significantly predicted greater VA while watching a disgusting film clip, in neurologically healthy individuals, but not in patient groups. Lastly, results showed that deficits in patient VA behavior significantly predicted caregiver depressive symptoms independently from patient deficits in emotion recognition and dementia severity. Dementia diagnosis moderated this effect, with diminished VA behavior being particularly predictive of depression symptomatology among bvFTD caregivers. The present study extends our understanding of the emotional context in which VA occurs (i.e., increasing SCL activation) and the cognitive functions that may help support it (i.e., cognitive flexibility). It also highlights a link between VA deficits in patients and lower mental health among bvFTD caregivers, which might be useful for identifying caregivers at risk for depression and allow for earlier psychosocial intervention.

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Table 1

Descriptive Statistics for Demographic and Clinical Variables

	bvFTD (n=67) *M* (SD)	AD (n=67) *M* (SD)	Controls (n=35) *M* (SD)	Statistical test value
Sex	25(F) 42(M)	28(F) 39(M)	13(F) 22(M)	X^2 (2, N=169) = 6.38, p < .05
Age	62.22 (7.81)	61.61 (8.21)	66.00 (7.80)	F (2, 130)= 3.32, p < .05
MMSE	24.36 (5.10)	21.86 (5.20)	29.59 (0.61)	F (2, 130)= 30.60, p < .001
CDR-BS	6.96 (2.97)	4.622 (2.50)	.00 (0.00)	F (2, 130)= 87.66, p < .001

Note. MMSE = Mini-Mental State Exam. CDR-BX = Clinical Dementia Rating – Box Score

Table 2

Summary of Intercorrelations for Scores of Visual Avoidance and Rates of Change in Indices of Emotional Responding Across Entire Sample

Measure	1	2	3	4	5	6	7
Visual avoidance							
1. VA total	-						
Autonomic physiology							
2. Pre-VA IBI	.151	-					
3. Pre-VA SCL	.084	-.161*	-				
4. Post-VA IBI	-.061	-.102	.065	-			
5. Post-VA SCL	-.133	-.051	.015	-.009	-		
Disgust facial behavior							
6. Pre-VA disgust	-.020	-.126	.036	-.002	-.117	-	
7. Post- VA disgust	-.105	.034	-.109	-.218	-.121	-.180	-

Note. *N*= 169. VA Total = composite score of visual avoidance behavior coded during the entire disgust reactivity task (101-seconds). Pre-VA IBI = rate of change in interbeat interval in the 15-seconds immediately preceding the onset of VA. Pre-VA SCL = rate of change in skin conductance level in the 15-seconds immediately preceding the onset of VA. Pre-VA Disgust = rate of change in disgust facial behavior (coded using the Emotional Expressive Behavior Coding System; EEB, Gross & Levenson, 1993) in the 15-seconds immediately preceding the onset of VA. Post-VA IBI = rate of change in interbeat interval in the 15-seconds immediately following the onset of VA. Post-VA SCL = rate of change in skin conductance level in the 15-seconds immediately following the onset of VA. Post-VA Disgust= rate of change in disgust facial behavior (EEB-coded) in the 15-seconds immediately following the onset of VA. Pre-VA and post-VA scores of emotional responding represent beta values indicating rates of change. Higher beta values indicate greater rate of change; higher scores of visual avoidance indicate greater VA behavior across the task. * p <.05

Table 3

Summary of Intercorrelations for Scores of Visual Avoidance and Emotional Responding Rates of Change in Neurologically Intact Controls

Measure	1	2	3	4	5	6	7
Visual Avoidance							
1. VA total	-						
Autonomic physiology							
2. Pre-VA IBI	.185	-					
3. Pre-VA SCL	.584***	.091	-				
4. Post-VA IBI	-.213	.245	-.310	-			
5. Post-VA SCL	-.148	-.019	-.163	.004	-		
Disgust facial behavior							
6. Pre-VA disgust	.140	-.175	.237	.089	-.418	-	
7. Post- VA disgust	-.195	.088	-.019	-.173	.361	-.164	-

Note. $n = 35$. Pre-VA and post-VA values of emotional responding are beta values indicating rates of change. Higher beta values indicate greater rate of change; higher scores of visual avoidance indicate greater VA behavior across the task. *** $p < .001$

Table 4

Summary of Intercorrelations for Scores of Visual Avoidance and Emotional Responding Rates of Change in Patients with Neurodegenerative Disease

Measure	1	2	3	4	5	6	7
Visual avoidance							
1. VA total	-	.299*	.043	-.211	-.214	-.137	.373
Autonomic physiology							
2. Pre-VA IBI	.024	-	-.316	-.389	-.063	-.163	.273
3. Pre-VA SCL	-.152	-.107	-	.162	-.424	-.122	.121
4. Post-VA IBI	.032	.005	.057	-	-.024	.167	-.075
5. Post-VA SCL	-.076	-.057	.495***	-.003	-	-.047	.124
Disgust facial behavior							
6. Pre-VA disgust	-.068	-.067	.014	-.027	-.043	-	-.305
7. Post- VA disgust	-.077	-.103	-.226	-.362*	-.453**	-.218	-

Note. Intercorrelations for bvFTD participants (n=67) are presented above the diagonal, and intercorrelations for AD participants (n=67) are presented below the diagonal. Pre-VA and post-VA values of emotional responding are beta values indicating rates of change. Higher beta values indicate greater rate of change; higher scores of visual avoidance indicate greater VA behavior across the task. * $p < .05$. ** $p < .01$. *** $p<.001$

Table 5

Summary of Intercorrelations for Scores of Visual Avoidance and Performance on Laboratory-based Measures of Emotion Regulation Across Entire Sample

Measure	1	2	3	4	5	6	7
Visual avoidance							
1. VA total	–						
Anticipated startle without instruction to suppress							
2. Somatic activity	.019	–					
3. Emo facial behavior	.052	.491***	–				
Instructed behavioral suppression of disgust reactivity							
4. Physio activation	-.052	-.037	-.015	–			
5. Emo facial behavior	-.181	.094	-.026	-.091	–		
Anticipated startle with instruction to suppress							
6. Somatic activity	-.027	.553***	.143	.085	.100	–	
7. Emo facial behavior	.135	.111	.007	.033	-.060	-.061	–

Note. *N*= 169. Higher scores on all laboratory-based measures of emotion regulation indicate greater emotion regulation; higher scores of visual avoidance indicate greater VA behavior across the task. Anticipated startle without regulation instruction = task assessing spontaneous down-regulation of emotion following presentation of acoustic startle stimulus. Anticipated startle with regulation instruction = task assessing instructed down-regulation of emotion following presentation of acoustic startle stimuli. Behavioral suppression of disgust with regulation instruction = task assessing instructed behavioral suppression of emotion during a disgust-eliciting task. Emo facial behavior = composite score of 6 emotions (anger, disgust, fear, sadness, surprise, and amusement) coded during the 5-seconds immediately following startle onset for startle based down-regulation tasks, and throughout the entire behavioral suppression task (85-seconds). Physio activation = composite score of 10 physiological measures (interbeat interval, finger pulse amplitude, finger pulse transmission time, ear pulse transmission time, skin conductance level, finger temperature, general somatic activity, respiration period, systolic and diastolic blood pressure) during the 5-seconds immediately following startle onset for startle based down-regulation tasks, and throughout the entire behavioral suppression task (85-seconds).
*** $p < .001$

Table 6

Summary of Intercorrelations for Scores of Visual Avoidance and Emotion Recognition and Caregiver-reported Emotion Regulation (Negative Emotion) Across Entire Sample

Measure	**1**	**2**	**3**
1. VA total	-		
2. Emotion recognition	.190*	-	
3. CASEF negative emotion regulation	.226*	.447***	-

Note. *N = 96*. CASEF = Caregiver Assessment of Socioemotional Functioning. Higher scores on all variables indicate greater emotion functioning. * *p* < .05. ***p < .001

Table 7

Summary of Intercorrelations for Scores of Visual Avoidance and Performance on Measures of Executive Functioning Across Entire Sample

Measure	1	2	3	4	5
1. VA total	-				
2. Modified trail making test, number-day sequencing	-.022	-			
3. Verbal fluency	.048	-.425***	-	.	
4. Backward digit span	-.028	-.464***	.613***	-	
5. Stroop inhibition	.038	-.619***	.530***	.611***	-

Note. $N = 169$. Higher scores on modified trail making test, number-day sequencing indicate greater time to completion (i.e., poorer performance); higher scores on all other executive functioning variables indicate greater performance. Higher scores on VA total indicate greater VA behavior across the entire task. *** $p < .001$

Table 8

Summary of Intercorrelations for Scores of Visual Avoidance and Performance on Measures of Executive Functioning in Neurologically Intact Controls

Measure	1	2	3	4	5
1. VA total	-				
2. Modified trail making test, number-day sequencing	.302	-			
3. Verbal fluency	.488*	-.002	-		
4. Backward digit span	-.190	.081	.081	-	
5. Stroop inhibition	.170	.395	.395	.047	-

Note. $N = 35$. Higher scores on modified trail making test, number-day sequencing indicate greater time to completion (i.e., poorer performance); higher scores on all other executive functioning variables indicate greater performance. Higher scores on VA total indicate greater VA behavior across the entire task. *$p < .05$

Table 9

Summary of Intercorrelations for Scores of Visual Avoidance and Performance on Measures of Executive Functioning in Patients with Neurodegenerative Disease

Measure	1	2	3	4	5
1. VA total	-	.029	-.148	-.083	.011
2. Modified trail making test, number-day sequencing	-.017	-	-.464***	-.386**	-.543***
3. Verbal fluency	-.007	-.075	-	.691	.678
4. Backward digit span	-.103	-.446**	.451***	-	.742
5. Stroop inhibition	-.147	-.501***	.192	.548***	-

Note. Intercorrelations for bvFTD participants (n=67) are presented above the diagonal, and intercorrelations for AD participants (n=67) are presented below the diagonal. Higher scores on modified trail making test, number-day sequencing indicate greater time to completion (i.e., poorer performance); higher scores on all other executive functioning variables indicate greater performance. Higher scores on VA total indicate greater VA behavior across the entire task **$p < .01$. *** $p < .001$

Table 10

Summary of Intercorrelations for Scores of Visual Avoidance, Empathic Accuracy, and Caregiver Mental Health Across Patient Sample

Measure	1	2	3	4	5
1. VA total	-	.190*	-.231*	-.243**	-.240*
2. Emotion recognition	.190*	-	-.265**	-.320**	-.219*
3. SCL GSI	-.231**	-.265**	-	.855**	.905**
4. SCL ANX	-.243*	-.320**	.855**	-	.777**
5. SCL DEP	-.240*	-.219*	.905**	.777**	-

Note. *N= 103*. SCL GSI = Symptom Checklist – 90 Revised Global Severity Index. SCL ANX = Symptom Checklist- 90 Revised Anxiety subscale. SCL DEP = Symptom Checklist – 90 Revised Depression subscale. Higher scores on VA total and Empathic accuracy scores indicate greater patient visual avoidance and empathic accuracy; higher scores on SCL GSI, SCL ANX, and SCL DEP indicate greater self-reported caregiver psychopathological symptoms. * p <.05 ** p < .01

Table 11

Standardized and Unstandardized Coefficients for Regression of Patient Visual Avoidance and Emotion Recognition on Severity of Psychopathological Symptoms in Caregivers

	Caregiver Severity of Psychopathological Symptoms						
	B	*SE B*	*LB*	*UB*	β	*R*	*F* for change in *R*
Model 1							
CDR- BS	.516	.040	.437	.595	.238	.238	6.229*
Model 2							
CDR-BS	.017	.007	.003	.030	.219		
Emotion recognition	-.025	.009	-.043	-.006	-.243	.340	6.843*

Note. Lower and upper bounds represent 95% confidence intervals. * $p < .05$.

Table 12

Standardized and Unstandardized Coefficients for Regression of Patient Visual Avoidance and Emotion Recognition on Caregiver Anxiety

	Caregiver Anxiety						
	B	*SE B*	*LB*	*UB*	β	*R*	*F* for change in *R*
Model 1							
CDR- BS	.027	.058	.006	.048	.249	.249	6.625*
Model 2							
CDR-BS	.024	.010	.004	.044	.225		
Emotion recognition	-.044	.014	-.071	-.017	-.300	.389	10.419**

Note. Lower and upper bounds represent 95% confidence intervals. * $p < .05$. ** $p < .01$.

Table 13

Standardized and Unstandardized Coefficients for Regression of Patient Visual Avoidance and Emotion Recognition on Caregiver Depression

	Caregiver Depression						
	B	*SE B*	*LB*	*UB*	β	*R*	*F* for change in *R*
Model 1							
CDR- BS	0.033	0.011	0.011	0.055	0.283	0.249	6.625**
Model 2							
CDR-BS	0.033	0.011	0.011	0.055	0.280		
VA total	-0.022	0.01	-0.041	-0.002	-0.208	0.351	4.888*

Note. Lower and upper bounds represent 95% confidence intervals. * $p < .05$. ** $p < .01$.

Table 14

Summary of Intercorrelations for Scores of Frequencies of "Visual Sipping" and Indices of Emotional Responding Across Patient Sample

Measure	1	2	3	4	5	6
1. "Visual sipping"	-	-.150	.185	-.167	.199	.090
2. Physio activity (composite)	-.150	-	.229	.572***	.167	.044
3. SCL	.185	.229	-	.026	0	0
4. IBI	-.167	.572***	.026	-	.146	.069
5. Disgust facial expression	.199	.167	.000	.146	-	.166
6. Disgust self-report	.090	.044	.000	.069	.166	-

Note. *N*= 157. All variables were collected during the disgust reactivity task. Variables collected throughout the entire task were sampled across 101-seconds. Variables collected during the "hot spot" were sampled during the 30 most emotionally intense second of the disgust film clip as rated by a panel of independent observers. "Visual sipping" = frequency of discrete transitions from the presence of gaze aversion to the absence of gaze aversion and back to the presence of gaze aversion during the entire task. Physio activity (composite) = composite score of 10 physiological measures (interbeat interval, finger pulse amplitude, finger pulse transmission time, ear pulse transmission time, skin conductance level, finger temperature, general somatic activity, respiration period, systolic and diastolic blood pressure) collected during the hot spot. SCL = skin conductance levels during the hot spot. IBI = interbeat interval during the hot spot. Disgust facial behavior = second-by-second EEB-coded disgust facial behavior during the hot spot. Disgust self-report = subjective rating of disgust experienced while viewing the disgusting film clip. Self-report rating was on a 0-2 point scale, with greater numbers indicating greater subjective experience of disgust. Higher scores on VA variables indicate higher frequency of behavior; higher scores of emotional responding variables indicate greater emotional responding.
*** $p < .001$

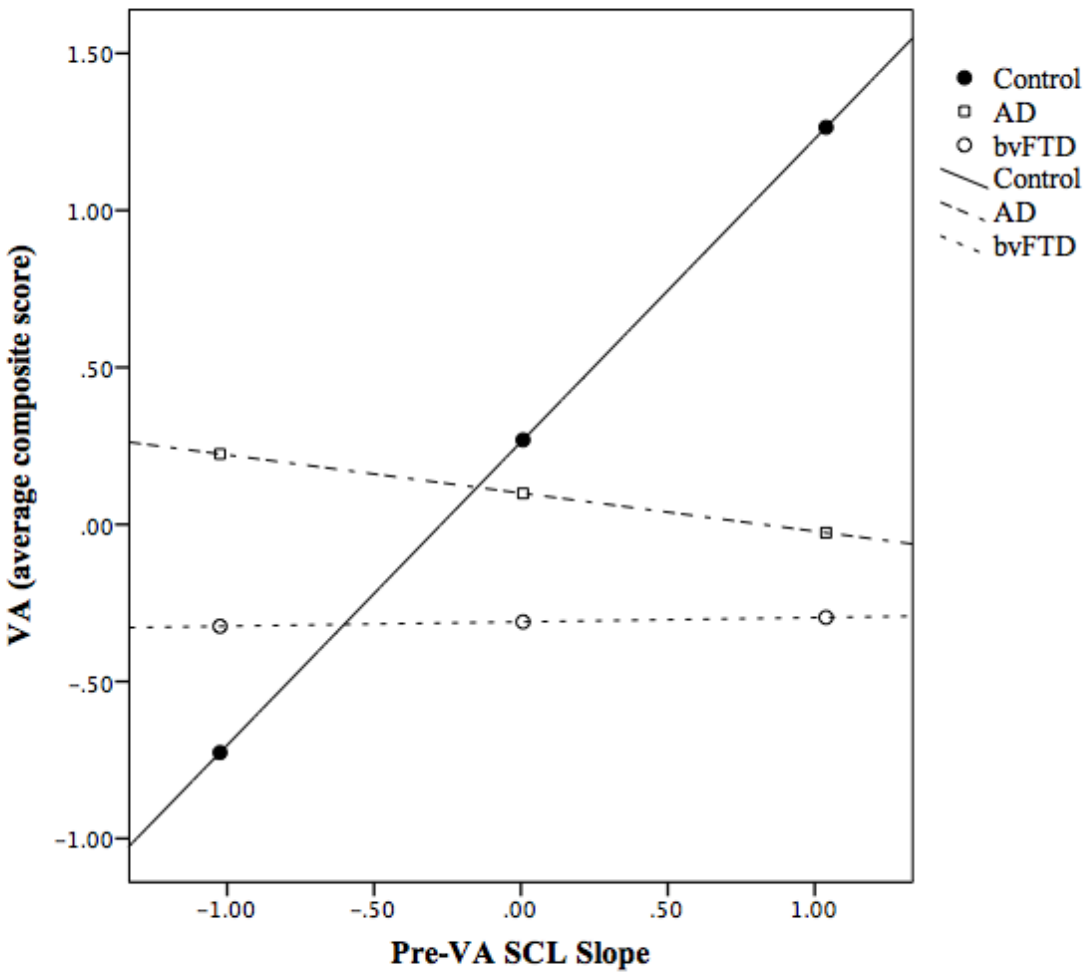

Figure 1. A visual depiction of the interaction between group membership (control vs. AD vs. bvFTD) and rate of change in skin conductance levels before the onset of visual avoidance in predicting total visual avoidance behavior across the disgust reactivity task (+/− 1 SD from the mean).

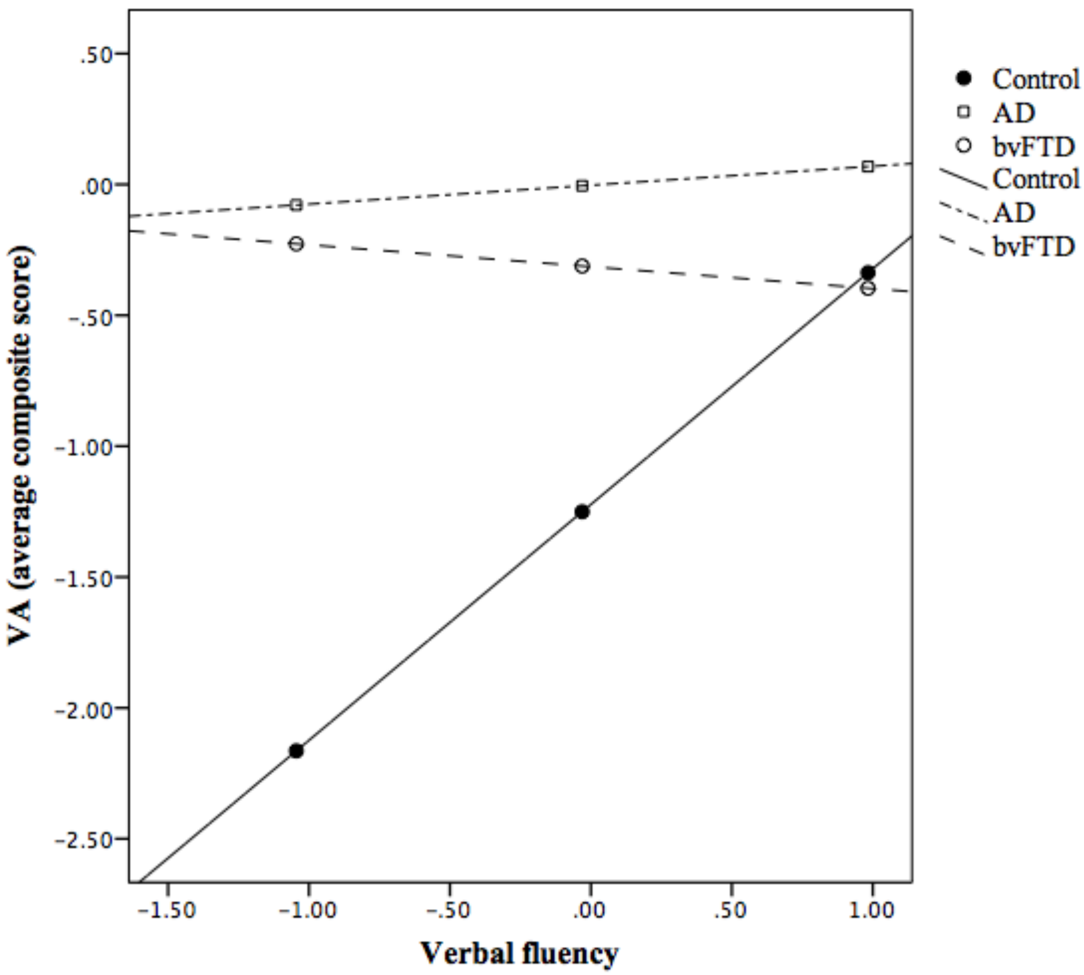

Figure 2. A visual depiction of the interaction between group membership (control vs. AD vs. bvFTD) and verbal fluency in predicting total visual avoidance behavior across the disgust reactivity task (+/− 1 SD from the mean).

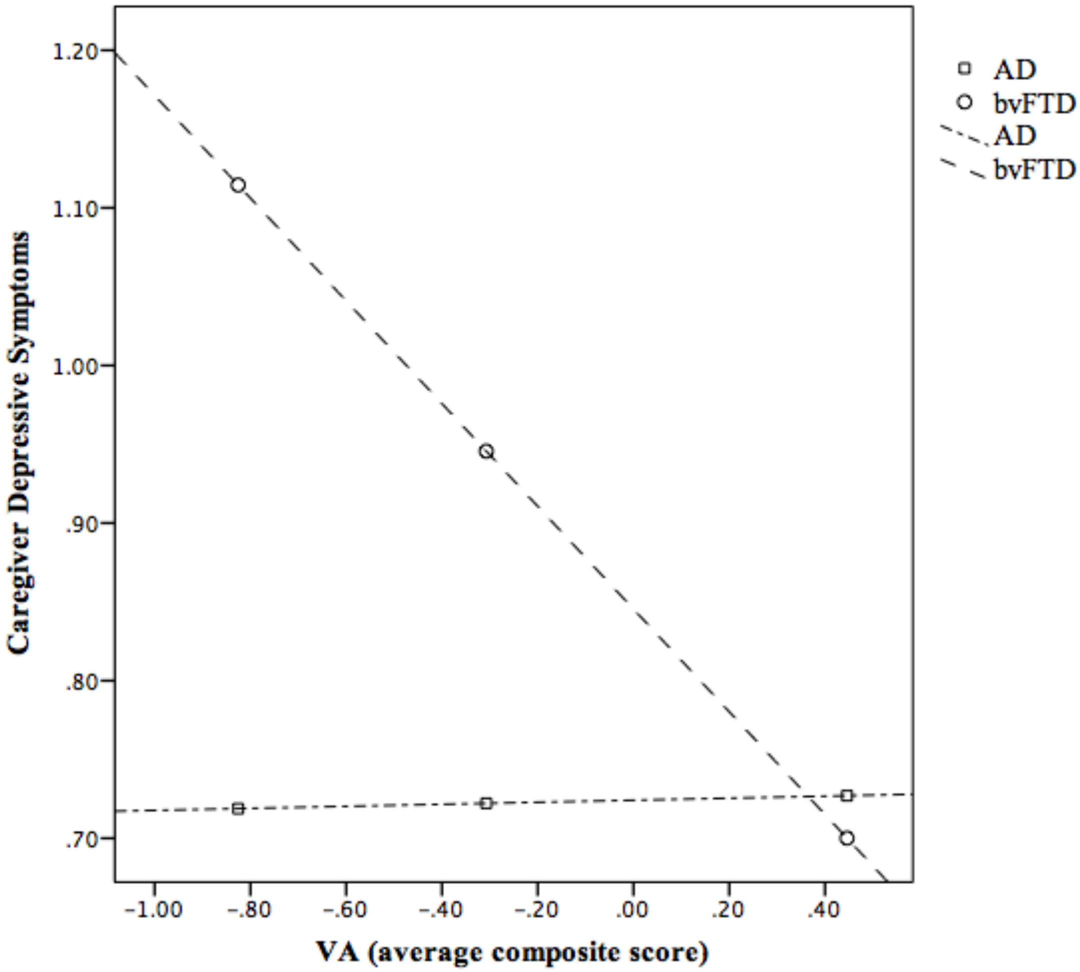

Figure 3. A visual depiction of the interaction between group membership (AD vs. bvFTD) and total visual avoidance behavior across the disgust reactivity task in predicting caregiver depressive symptoms (+/− 1 SD from the mean).

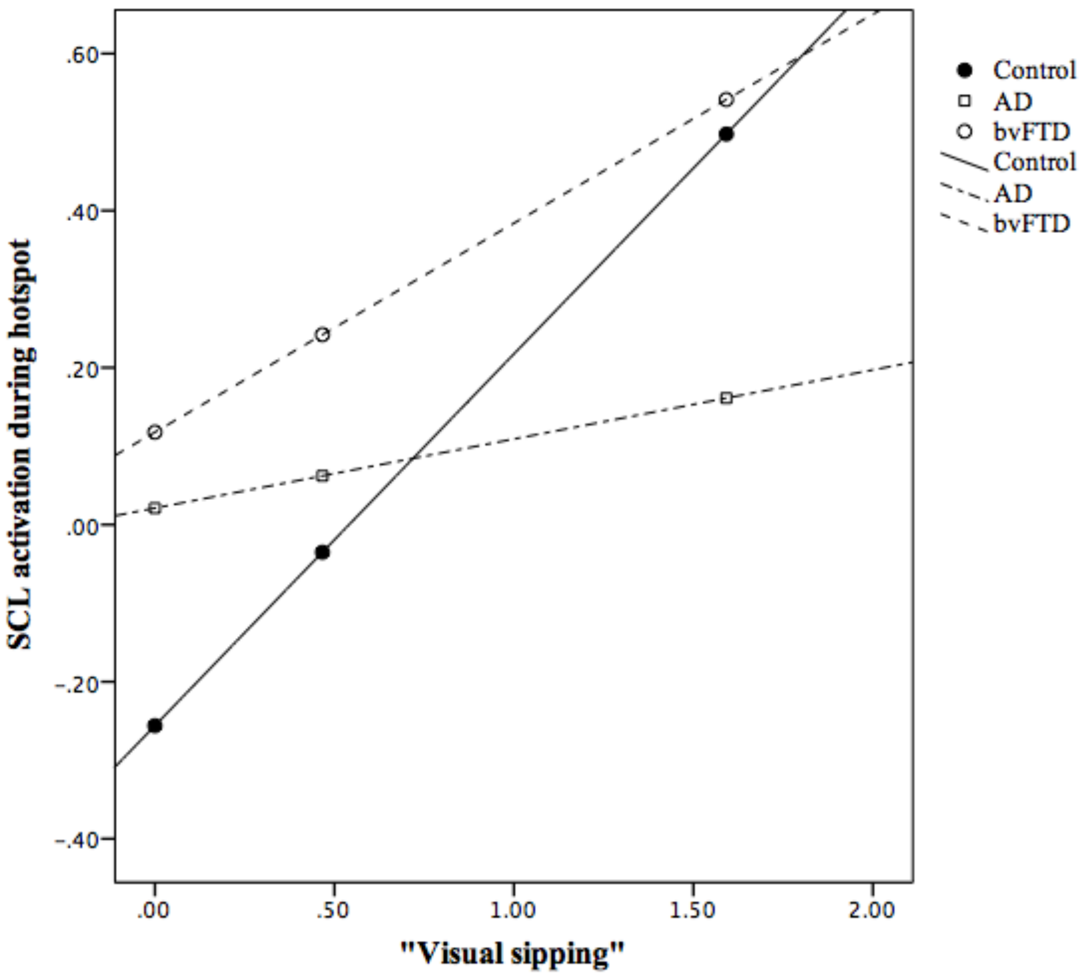

Figure 4. A visual depiction of the interaction between group membership (control vs. AD vs. bvFTD) and "visual sipping" while watching a disgusting film-clip in predicting SCL (skin conductance levels) during the hot spot (30 most emotionally intense seconds of the film) (+/− 1 SD from the mean).