Stress and Illness: A Role for Specific Emotions

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ABSTRACT

Research on stress and disease has often afforded an important role to emotion, typically conceptualized in broad categories (e.g., negative emotions), viewed as playing a causal role (e.g., anger contributing to pathophysiology of cardiovascular disease), and measured using self-report inventories. In this article, I argue for the value of evaluating specific emotions, considering bidirectional causal influences, and assessing actual emotional responding when considering the role that emotions play in the stress-disease relationship. In terms of specificity, specific emotions (e.g., anger, sadness, and embarrassment) can be linked with particular health outcomes (e.g., cardiovascular disease and musculoskeletal disease). In terms of bidirectionality, the influences of emotions on disease as well as the influences of disease on emotional functioning can be considered. In terms of assessing actual emotional responding, emotions can be studied in vivo under controlled conditions that allow behavioral, physiological, and subjective responses to be measured during different kinds of emotional functioning (e.g., responding to emotional stimuli, interacting with relationship partners, and downregulating emotional responses). With these considerations in mind, I review early theories and empirical studies in psychosomatic medicine that considered the role of specific emotions and emotion-related behaviors. Studies from our laboratory are presented that illustrate a) differences in patterns of autonomic nervous system responding associated with specific emotions, b) relationships between specific emotions and particular health outcomes in the context of social relationships, c) age as a moderator of the relationship between specific emotions and well-being, d) bidirectional influences (emotions influencing disease and disease influencing emotional functioning), and e) impact of changes in emotional functioning in individuals with neurodegenerative diseases on the health of familial caregivers.

Key words: emotion, stress, health and disease, autonomic nervous system, specificity, dementia.

INTRODUCTION

This article is based on an invited talk I gave at the October 2017 midyear meeting of the American Psychosomatic Society, which was devoted to the theme "Emotions in social relationships: Implications for health and disease." As with the original talk, my overarching goal is to consider the role that specific emotions play in the stress-disease relationship (in this article, the term *stress* primarily refers to the exposure to stressors that can result in threat or harm to the individual). To accomplish this goal, I discuss a) the history of specific emotions in psychosomatic research, b) the notion that specific emotions have different patterns of associated physiological responding, c) evidence that specific emotions and emotional behaviors that arise in social relationships are associated with particular health problems, d) changes in the relationship between specific emotions and health that occur with aging, e) influences of neurodegenerative disease on patients' emotional functioning, and f) influences of changes in emotional functioning in patients on the health of familial caregivers.

This article draws heavily on the methods and perspectives of contemporary affective science. Although emotions have often been studied using self-report inventories, new approaches enable studying emotions in vivo under conditions that allow behavioral, physiological, and subjective responses to be measured precisely during particular kinds of emotional functioning (e.g., responding to emotional stimuli, interacting with relationship partners, and downregulating emotional responses). This approach is well suited for considering the role that specific emotions play in the stress-disease relationship. Consistent with the mandate of the original talk, in this article, I present both old and new ideas, speculate on implications and future directions, and provide a number of illustrative research examples.

STRESS AND DISEASE: A BRIEF HISTORY

Fifty years ago, in a landmark study, Rahe (1) presented a classic "black box" finding. In a sample of approximately 2500 US sailors, the number of life events requiring adjustments in accustomed patterns that the sailors had encountered during a 6-month period before shipping out (measured with a self-report inventory) (2) was associated with the amount of illness they experienced during the ensuing 6 months (measured by examining medical records). Sailors in the high-risk group (i.e., top 30% of total life events) had significantly more first illnesses during the first 2 months of the cruise compared with those in the low-risk group (i.e., lowest 30% of total life events). These differences were most dramatic in the first month of the cruise during which approximately 8% of the high-risk sailors had their first illness compared with 5% of the low-risk sailors. In a subsequent review of similar studies (3), the correlations typically found between life stress and future disease (usually measured during 6- to 12-month periods) were significant but small (average $r = 0.12$).

In the period since the initial empirical studies (e.g., Ref. (4)), there has been increasing refinement in our understanding of the

ANS = autonomic nervous system, **AD** = Alzheimer's disease, **FTD** = frontotemporal dementia

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intermediate stages linking life stress to the onset of disease. Consistent with changes in the scientific zeitgeist, the "lens" model by Rahe and Arthur (3), with its inclusion of the psychodynamic concept of "psychological defenses," was supplanted by cognitive models emphasizing appraisal and coping (e.g., Ref. (5)) and ultimately by models (e.g., Refs. (6,7)) that afford a prominent role to emotions.

In the stage model proposed by Cohen and colleagues (Figure 1, redrawn from Ref. (6)), environmental events are appraised in terms of their stressfulness, leading to negative emotional responses. These negative emotions activate behavioral (health decisions and behaviors) and physiological pathways (sympathetic adrenal medullary and hypothalamic-pituitary-adrenal responding) that create disease-related physiological changes that promote disease onset and progression.

The role of emotions in this model is consistent with evolutionary/functionalist views (e.g., Ref. (8)) that envision emotions as activating biological and behavioral systems rapidly in ways that are most likely to enable the organism to deal optimally with a small set of species-typical challenges and opportunities. Inherent in these evolutionary/functionalist views is the notion that emotions are not all the same but rather differ in evoking conditions and patterns of attendant behavioral and biological responses. Thus, rather than associating all kinds of negative emotions with broad behavioral adaptations such as "fight-flight" (9), it may be useful to parse fight and flight, distinguishing among conditions involving threats to life and limb (which are most likely to elicit the emotion of fear and behavioral adaptations of "flight" or "freeze") and those that involve frustration of progress toward goals (which are most likely to elicit the emotion of anger and the behavioral adaptation of fight). To these we would add conditions that create other prototypical challenges and opportunities. For example, loss of an attachment figure might elicit the emotion of sadness and behavioral adaptations involving reaching out for comfort and support; encountering contamination might elicit the emotion of disgust and activate withdrawal and expulsive behaviors.

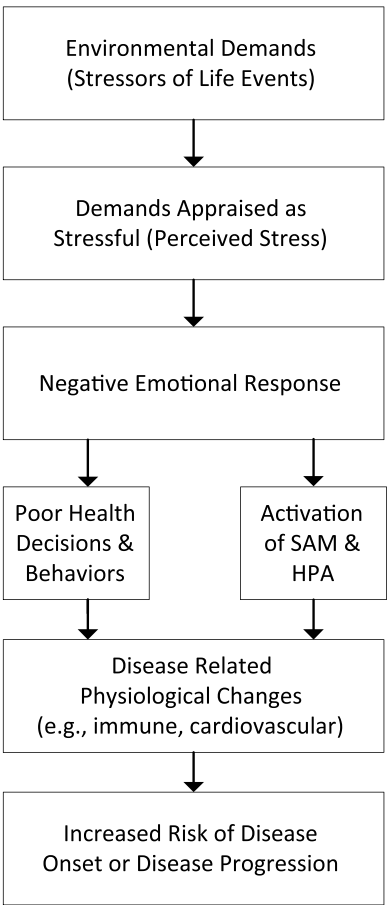

FIGURE 1. Stage model of stress and disease.

Introducing these more specific negative emotions and their different associated action patterns (10,11) sets the stage for the possibility that behaviors (e.g., facial expressions and postural changes) and physiological responses (e.g., patterns of autonomic nervous system [ANS] and endocrine activity) are different for specific emotions. Thus, the facial expressions that signal anger and the ANS and somatic changes that prepare the organism to defend its turf are likely to be quite different from the facial expressions that signal disgust and the ANS and somatic changes that prepare the organism for rapid withdrawal from sources of contamination.

Although I expect that the stage model can readily incorporate these kinds of elaborations around more specific negative emotions and the possibility that they are accompanied by different patterns of behavioral and physiological activation, it is important to realize that environmental challenges and opportunities can also produce positive emotions and self-conscious emotions (which can have positive or negative valence). Thus, for example, dealing successfully with a threat or challenge can produce the positive emotion of joy. Meeting or exceeding social expectations can produce the positive self-conscious emotion of pride; failing to meet these expectations can lead to the negative self-conscious emotion of shame. Although at one time all positive emotions were thought to share a common facial expression (i.e., the smile) (12) and most were thought to calm the ANS rather than activating it (13), more recent research indicates that positive and self-conscious emotions have much more diverse patterns of associated behavioral (14) and physiological activation (15). This greater specificity among positive and self-conscious emotions is likely to have important consequences for disease-related physiological changes and for theoretical models that link emotions and health (16).

Before considering how a more differentiated view of emotion can be applied to research on stress and disease, it is important to note that not all affective scientists embrace the functionalist/evolutionary and discrete emotions perspectives described previously. Contemporary affective science encompasses several quite different theoretical models (for alternative social constructivist and dimensional views, see Refs. (17–19)) as well as disparate views concerning the evidence supporting and disconfirming physiological and behavioral differences among specific emotions (e.g., Refs. (17,20,21)).

SPECIFIC EMOTIONS AND HEALTH

Early Studies

Although the notion that different emotions have different patterns of associated behavior and physiology is often traced back to the

19th century (22,23), its application to individual differences in health arguably began almost a century later with Alexander's (24) assertion that different diseases have their own associated emotional conflict. Alexander's model stood in stark contrast to Selye's (25) highly influential and very non-specific model that envisioned a generalized physiological response to stress that, when activated chronically, eroded diverse biological systems and created vulnerability to a range of diseases.

Although Alexander did conduct empirical studies to test his ideas—for example, using films to elicit emotional states (reported in Ref. (24))—more rigorous empirical tests of the role of specific emotions and related states (e.g., emotion-related attitudes) awaited the emergence of improved methods of psychophysiological measurement. These new methods enabled researchers to monitor and characterize the activity of multiple physiological systems during different emotional states (e.g., fear versus anger in Ref. (26)). Prominent in this era was the work of Grace and Graham (27), who viewed diseases as being associated with different "attitudes." For example, based on extensive patient interviews, they concluded that individuals with hives typically felt that they were being "unfairly treated," whereas those with hypertension typically felt that they had to be "on guard." In a classic experimental study (28), these specific attitudes were suggested to healthy individuals under hypnosis and their psychophysiological responses were measured. When the hives attitude was suggested, participants showed increases in hand temperature (consistent with hives pathophysiology); when the hypertension attitude was suggested, participants showed increases in diastolic blood pressure (consistent with hypertension pathophysiology). Although studies by Graham and colleagues focused on specific attitudes rather than specific emotions, it would not be too large a leap to assume that being "unfairly treated" (hives) was associated with the emotion of anger, whereas being "on guard" (hypertension) was more likely to be associated with the emotion of fear.

The notion of links between specific emotions and disease was also found in research on the Type A personality and cardiovascular disease (29). Although early studies focused on a broad set of behaviors, later studies identified hostility as being most important (30). Hostility is generally considered to be an emotion-related personality trait that is closely linked to habitual expression (or inhibited expression) of the emotion of anger.

Autonomic Specificity

A fundamental notion in most theories that link specific emotions with particular diseases is that different emotions produce different patterns of physiological responding. There was a spate of experimental studies of "autonomic specificity" during the 1950s and 1960s (e.g., Refs. (26,31,32)) and a revival of interest beginning in the 1980s (e.g., Refs. (33–35)). In the best of these studies, a) laboratory procedures that produce reasonably intense instances of particular emotions are used, b) within-subject designs are used so that differences between multiple emotions can be compared in the same individuals, c) emotional responses are verified in some way to ensure that "apples" are in fact being compared with "oranges" (rather than comparing unspecified varieties of emotional "fruit salad"), and d) physiological responses relevant to the emotions of interest are measured and precisely linked in time with the occurrence of emotion (36–39). Under these more stringent experimental conditions (which are unfortunately met by few studies), reliable autonomic differences among emotions are most likely to be found, belying the notion that all emotions (or all negative emotions) are physiologically the same (21,36,37,39).

Another common notion is that physiological differences among emotions "blur" as emotions become more intense. According to this view, a state of "undifferentiated physiological arousal" (9,40) is common to all highly intense emotions. This notion can be hard to evaluate in the laboratory. For both methodological and ethical reasons, emotions studied in the laboratory typically occur at mild to moderate levels of intensity (e.g., heart rate changes from pretrial baselines in the range of 5–10 beats/min). Even when larger responses are evoked (e.g., to sudden loud noises) (41), the physiological changes may be relatively short-lived. In real life, emotions often occur at much higher levels of intensity and attendant physiological changes are commensurately larger and longer-lasting.

High-Intensity Emotions: A Case Study

As part of our research program, we have periodically conducted case and group studies of individuals with specialized training and life experiences that might affect emotional functioning (e.g., highly skilled meditators, dancers, and actors) (35,42,43). One such individual, studied in collaboration with my colleague Paul Ekman, was a Bay Area therapist who had developed a method for helping clients access blocked emotions. At our initial interview, she described her ability to produce highly intense emotional states on demand. At the time, we had been primarily eliciting emotion using relived memories and directed facial actions (35), both of which produce emotions of only mild to moderate intensity. We invited her to come to the laboratory so that we could observe her method for producing emotions. She agreed and we conducted two laboratory sessions studying emotions elicited using her method and using our own eliciting methods (her emotional responses to our methods were unremarkable, quite consistent with those we had seen in others). Throughout these sessions, we videotaped her facial expressions, recorded multiple ANS measures on a second-by-second basis, and queried her about her subjective emotion experiences.

I cannot provide rich detail or insights about the method she used to produce emotional states, but she described them as accessing the emotions directly rather than via a typical indirect pathway (e.g., recalling and reliving memories, posing expressions, and imagining situations). As we observed her producing a range of discrete emotions, we saw facial expressions that were highly prototypical for these emotions (12), even when examined in slow motion using the Facial Action Coding System (44). Moreover, the facial muscle contractions were extremely intense and dynamically appropriate and coherent, not having the kind of static artificiality and temporal discoordination often seen when participants are asked to pose emotional expressions (e.g., telling someone to "look angry"). These highly intense facial muscle contractions were also accompanied by large ANS perturbations. For example, when she produced anger (Figure 2), her heart rate increased initially by more than 60 beats/min and then rose an additional 10 beats/min (around second 80) after she asked if we wanted her to allow the anger to "move toward rage." At this point, her heart rate was around 160 beats/min, and we thought it wise not to go further.

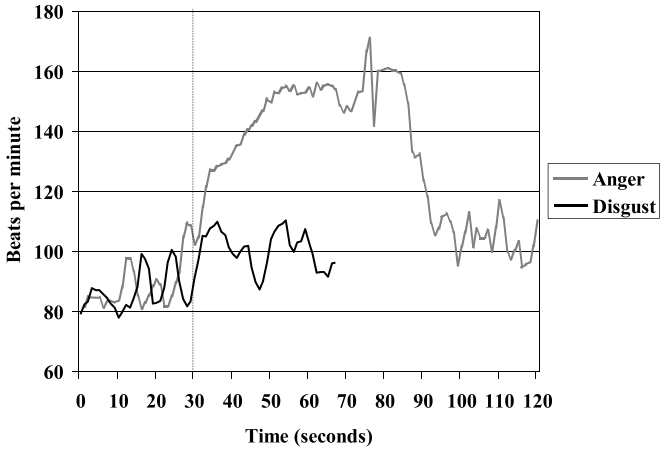

FIGURE 2. High-intensity emotions.

Needless to say, we had not seen emotions at this level of physiological intensity in any of our prior studies. Importantly, based on our collective experience, the emotions she produced appeared to be quite "real," despite their being created in a somewhat unusual way.

Comparing the heart rate changes that occurred when she produced anger versus disgust (Figure 2) is quite informative. When accessing both emotions (the emotions start at second 30), she produced high-intensity, dynamically coordinated prototypical facial expressions and large increases in the pace (respiration cycles lasting approximately 5 seconds) and depth of respiration. These elevations in somatic and respiratory activity would normally be expected to produce large increases in heart rate (45,46). However, the two emotions differed markedly in their associated magnitude and patterns of heart rate change. As noted earlier, in anger, her heart rate increased by more than 75 beats/min. Moreover, the typical rise and fall of heart rate that follows the inspiratory and expiratory phases of respiration (i.e., vagally mediated respiratory sinus arrhythmia) (47) essentially disappeared (see the "flattening" of heart rate during anger between seconds 30 and 80 compared with the higher variability before seconds 10–30 and after seconds 110–120 in Figure 2). In contrast, the heart rate during disgust increased much less markedly, and the patterns of respiratory sinus arrhythmia were quite apparent (e.g., see the clear rise and fall of disgust heart rate approximately every 5 seconds between seconds 40 and 70 in Figure 2). Although we cannot know with certainty what patterns of neural activation produced these particular heart rate responses, they are consistent with a release of vagal restraint during anger and an assertion of vagal influence during disgust. Given the magnitude and rapid onset of heart rate increase during anger, it is likely that there was sympathetic activation as well.

Clearly, these two episodes of emotion in one specially selected individual do not constitute a reliable finding. Nonetheless, similar differences in mean heart rate response during disgust relative to anger (and other negative emotions) are among the most consistent differences found in the autonomic specificity literature (21,48). For example, Figure 3 illustrates heart rate changes associated with different voluntarily produced emotional facial expressions (35). Even with this somewhat unusual and relatively mild form of emotion elicitation, a simular pattern of larger heart rate increases in anger compared with disgust can be seen.

Emotion Regulation

Although emotional *reactivity* (i.e., generating emotion in response to challenges and opportunities) has been the primary focus of research linking emotion with health, affective scientists have become increasingly concerned with emotion *regulation* (i.e., adjusting emotional responses to meet situational demands and personal goals). Emotion regulation research has focused less on the regulation of specific emotions (e.g., comparing regulation of fear with regulation of anger) and more on different kinds of regulation. For example, many studies have contrasted downregulation of emotion by *reappraisal* (changing the way the eliciting situation is construed) with downregulation by *suppression* (e.g., reducing the expressive signs of emotion). These strategies of emotion regulation differ both in their intended target (thoughts versus expressive responses) and in their temporal location in the emotion-eliciting sequence (reappraisal occurring early often before the emotion is fully formed and suppression occurring later when the emotion is being expressed). Importantly, reappraisal and suppression have quite different physiological concomitants in both the autonomic and central nervous systems (49–52). In general, suppression is seen as less "healthy" (i.e., requiring additional physiological resources to constrain the powerful expressive

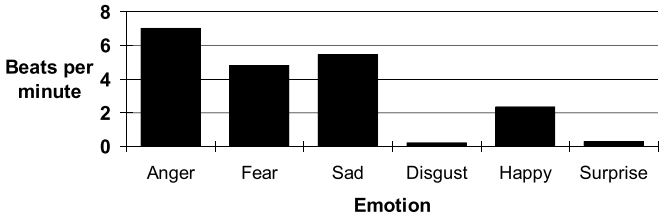

FIGURE 3. Heart rate change during directed facial actions.

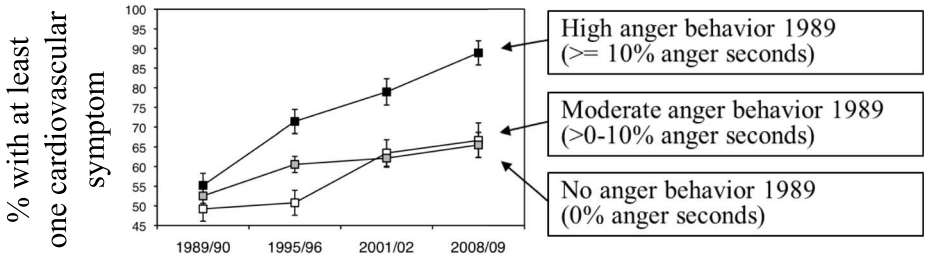

FIGURE 4. Cardiovascular symptoms and anger behavior for 20 years.

forces) than reappraisal (which requires less physiological activation). For example, in our research, we have found the cardiovascular response (e.g., increase in heart rate) associated with suppressing an emotion to be approximately twice as large as the response associated with simply expressing that emotion (41,53). Despite the greater metabolic costs associated with suppression, it would be unwise to conclude that suppression is always the unhealthy form of regulation and that reappraisal is always the healthy form (e.g., findings that the association between suppression and health can be moderated by culture) (54).

SPECIFIC EMOTIONS: SPECIFIC HEALTH PROBLEMS

A recent study from our research group (55) illustrates the potential for considering specific emotions that occur in social relationships in health research. In this study, we used data from a 20-year longitudinal study of marriage (56,57). The study began in 1989 with the recruitment of a sample of 156 middle-aged (40–50 years old, married at least 15 years) and older (60–70 years old; married at least 35 years) couples. The study had a number of features that made it particularly useful for addressing the emotion-health relationship: a) it was a laboratory-based observational study of actual marital interactions rather than a survey of attitudes and beliefs; b) the sample was recruited to be representative of the local community (e.g., in ethnicity and socioeconomic status); c) couples were observed in the laboratory repeatedly over the course of the study (every 5 years); and d) participants were moving into ages where their vulnerability to significant health problems increased.

Using a well-established procedure (58), couples came to our laboratory and engaged in three unrehearsed 15-minute conversations about different relationship topics (recent events, area of conflict, enjoyable activities). Conversations were videotaped and rated by trained coders using the Specific Affect Coding System (59), which considers facial expression, tone of voice, posture, and speech content to identify the occurrence of specific emotions (e.g., anger) and emotion-related behaviors (e.g., stonewalling and defensiveness). For this study, we focused on three negative emotions (anger, fear, sadness) and one emotion-related behavior (stonewalling: stiff frozen face, clenched jaw, rigid neck muscles) that were expressed by participants during the conflict discussion in 1989. Health (focusing on cardiovascular, musculoskeletal, and respiratory symptoms) was measured using the Cornell Medical Index (60) in 1989, 1995, 2001, and 2008.

Results indicated that emotions and emotional behaviors expressed in 1989 predicted increasing health problems over the ensuing 20 years. Importantly, there was considerable specificity in the findings: a) anger predicted increasing cardiovascular symptoms and stonewalling predicted increasing musculoskeletal symptoms, but not vice versa; b) neither fear nor sadness predicted cardiovascular or musculoskeletal symptoms; and c) none of the emotional behaviors predicted respiratory symptoms. Two striking aspects of the findings were that they only emerged over time and were strongest for husbands. Illustrating the emergence over time, in Figure 4, there were no differences in cardiovascular symptoms in 1989/1990 between participants who expressed high, moderate, or low levels of anger in their conflict discussions. However, by 1995/1996, the group expressing high levels of anger was clearly showing more cardiovascular symptoms, and these symptoms continued to increase most rapidly in this group over the final two measurement periods. Overall, the risk odds ratio of anger behavior predicting future cardiovascular symptoms was 1.5.

This finding of relationships between particular emotions and emotional behaviors and particular health outcomes is illustrative of the promise of this approach. Of course, pending replication and extension, we cannot know how robust and generalizable these findings will be. However, the linking of anger, an emotion thought to produce widespread activation of the cardiovascular system (21,35,61), with cardiovascular symptoms, and stonewalling, an emotional behavior defined by high levels of muscle tension (59), with musculoskeletal symptoms has a great deal of face validity. Studies of emotion and health typically do not observe specific emotional behaviors in interpersonal situations, do not study older samples, and either are cross sectional or, if longitudinal, span shorter periods. Studies using these more typical research designs might fail to detect the kinds of relationships between specific emotions and emotional behaviors and particular health symptoms that emerged over time in our research.

SPECIFIC EMOTIONS AND HEALTH: MODERATION BY AGE

Just as the early studies of stress and illness studied young sailors in the prime of life, it is common for contemporary laboratory research to be conducted with younger college students. Studies in which the dependent measures are related to physiological and emotional reactivity can be highly informative in younger participants, but these populations may be less well suited for studies where the dependent measure is disease occurrence (due to low base rates of illness in younger samples). Fortunately, in the realms of health and well-being, a number of population-based studies have been conducted that include participants at many different ages, and in some of these, subsamples have participated in laboratory studies of emotional functioning (e.g., Ref. (62)). Just as health risk and disease incidence clearly change with age, the relationships between emotions, health, and well-being may also change. Simply stated, it is reasonable to expect that the optimal

"emotional palette" for maintaining health and well-being for a person entering adulthood differs from that best suited for a person in the last decade of life.

We explored this issue in a study of emotional correlates of well-being in three different age groups (63). This was a cross-sectional laboratory study (participants were in their 20s, 40s, or 60s) with participants recruited to be representative of the local community. Participants viewed an excerpt from the film "Stranger Than Paradise" and rated how intensely they experienced specific emotions (e.g., anger, fear, disgust, and sadness). In the excerpt, two men struggle to maintain an extremely empty, boring, and labored conversation. In many ways, this excerpt is an "emotional Rorschach," with the viewer needing to project emotional meaning on to fairly ambiguous stimulus material. Participants also completed a standard measure of well-being (64). Findings revealed a striking moderation by age. For older participants, the more sadness that was reported in response to the film, the greater their reported well-being. For middle-aged subjects, the more anger that was reported, the greater their reported well-being. In thinking about these findings, we speculated that anger might be particularly functional in middle age as people compete for resources, defend past gains, and engage in the give and take of the workplace. In contrast, sadness might be particularly functional in old age, helping people deal with the inevitable losses encountered in that stage of life and also to signal the need for connection with others (65). The notion that life's challenges and opportunities change with age is a central tenet of many theories of life-span development (66–69). Because of this, different emotions, with their capacity to address different challenges and opportunities, may become maximally adaptive at different ages. Given the strong connections between well-being and health (70,71), it is reasonable to expect that the connections between particular emotions and health may change in similar ways.

INFLUENCES OF DISEASE ON EMOTION

Thus far, our discussion of the relationship between emotion and disease has focused on the influences of emotion on disease, a theme that is found throughout the history of psychosomatic medicine. Although there have been elegant experimental (e.g., Ref. (72)) and naturalistic longitudinal (e.g., Ref. (73)) studies showing that stress can increase susceptibility to illness and slow the pace of healing, most studies in this literature using human participants have been correlational in nature. Thus, when associations are found between emotion and disease, we cannot know whether emotions influence disease, disease influences emotion, or influences are bidirectional. There have been studies that experimentally induced illness or altered inflammation and examined the effects on emotional and/or behavioral functioning (e.g., Refs. (74–78)). Albeit and understandably rare, such studies underscore the role that disease processes play in influencing emotional functioning (e.g., the role of inflammation in the etiology and treatment of depression) (79).

NEURODEGENERATIVE DISEASE: A PATIENT MODEL FOR STUDYING INFLUENCES OF DISEASE ON EMOTIONAL FUNCTIONING

Studies of emotional functioning in individuals with particular diseases provide a "natural experiment" for exploring the influence of disease on emotion. Of course, data from these studies come with certain caveats (e.g., the research designs are not truly experimental). These inherent limitations notwithstanding, the quality of data derived from patient studies can be improved by contrasting emotional functioning across multiple patient groups with different diseases, including healthy controls, controlling for the more general effects of "illness," using longitudinal designs (which allow some disambiguation of temporal sequences of causal influence), and incorporating more precise assessments of patients' actual emotional functioning.

Neurodegenerative Disease

In recent years, we have been conducting research on late-life dementia and other neurodegenerative diseases, focusing on the ways that these diseases influence emotional functioning. In this work, we typically compare the effects of different diseases (carefully diagnosed and characterized), include healthy controls, control for disease severity, and measure patients' actual emotional functioning in the laboratory. This research is aided by laboratory procedures we have developed (80) to study specific emotions, consider particular emotional processes (including reactivity, generating emotions; regulation, altering emotional responding; and recognition, identifying emotions in others), and assess physiological, expressive, and subjective aspects of emotional responding.

Because neurodegenerative diseases are becoming increasingly common with the aging population, we have been able to go beyond case studies and small *n* studies to conduct research with sufficiently large samples of patients to obtain reasonable statistical power (e.g., 144 patients with dementia and 45 healthy controls in Ref. (81)). To date, most of our work has been cross sectional, comparing emotional functioning in different patient groups at a particular moment in time. However, we are moving to more longitudinal designs in which disease progression and emotional functioning will be assessed repeatedly over time.

Of particular interest in our research has been frontotemporal dementia (FTD), a progressive neurodegenerative disease that targets frontal and temporal brain regions critical for emotional functioning including the amygdala, insula, temporal pole, and frontal lobes. Reflecting the affected anatomy, initial symptoms in FTD include declines in ability to generate, regulate, and recognize emotion with relative preservation of many aspects of cognitive functioning such as memory (82,83). Neurodegeneration in FTD often targets ANS control centers in the brain (84,85). Given the important role the ANS plays in numerous aspects of emotion (39), this can further compromise emotional functioning in individuals with FTD.

Alzheimer disease (AD) has a very different pattern of neurodegeneration and behavioral deficits from those seen in FTD. AD targets more posterior brain regions (e.g., hippocampus, entorhinal cortex, and posterior cingulate). Reflecting this anatomy, initial symptoms in AD include declines in memory and spatial ability, with relative preservation of emotional functioning (e.g., Refs. (86–88)).

Clearly, with progressive neurodegenerative diseases, if deficits are found in emotional functioning, the notion that the disease causes changes in emotional functioning becomes more compelling than the notion that changes in emotional functioning cause the disease.

Emotional Reactivity: Specific Emotions

Emotional reactivity involves the actions of widely distributed brain regions (83). Thus, it is unlikely that there would be unique and nonoverlapping regional anatomies associated with specific emotions. Nonetheless, specific emotions may differ in terms of how much they require the involvement of different brain structures. Although FTD has widespread effects on emotional functioning, we have nonetheless found it useful to examine its effects on specific emotions, especially in the early stages of the disease when emotional deficits may be less widespread.

Embarrassment and Self-Conscious Emotions

In one line of research, we have examined embarrassment, a "self-conscious" emotion that alerts us to instances in which we have violated social norms and need to take corrective actions (89). Clinical observations suggest that individuals with FTD often engage in socially inappropriate behaviors that are quite distressing for friends and families but do not seem to bother the person with FTD (e.g., inappropriate touching of others). To determine if there are deficits in the capacity to generate embarrassment in individuals with FTD, we (90,91) used a "karaoke" laboratory task in which participants were shown a video recording of their singing "My Girl." Neurologically healthy participants find this task to be quite embarrassing and typically show facial expressions that signal embarrassment and amusement and attendant increases in ANS arousal. Figure 5 depicts the results of a study comparing the responses to this task in individuals with FTD (n = 26) and age-matched healthy controls (n = 16). In both the amount of positive emotional facial expressions (primarily amusement) shown in the left panel and the skin conductance response shown in the right panel, individuals with FTD were dramatically less reactive than controls. Lowered physiological reactivity in FTD was also seen in measures of cardiovascular (i.e., heart rate) and respiratory (i.e., respiration depth) responding (90).

In another study of embarrassment in FTD, we (91) used an unexpected acoustic startle (a sudden loud burst of white noise) stimulus. In healthy individuals, this stimulus produces a two-stage response. The initial response is a reflexive defensive response, and the secondary response is an emotional reaction that unfolds as the person becomes aware of his/her initial response (92). Using this startle stimulus, during the secondary response, we found deficits in embarrassment behavior in FTD patients compared with healthy controls, similar to our findings using the karaoke task (90). In contrast, during the initial defensive stage, FTD patients did not differ from healthy controls in their physiological or behavioral response. This suggests some specificity of the deficit in the realm of the secondary self-conscious emotional response.

In a follow-up study using structural imaging to quantify neurodegeneration, we (93) established some anatomical specificity for deficits in self-conscious emotional responding during the karaoke task. In this study, we found that greater degeneration in the right pregenual anterior cingulate cortex (a region involved in processing the social milieu) was associated with lower levels of embarrassment responding (facial expressions and physiology) in the karaoke task. This association remained significant even after statistically controlling for the association of degeneration in this region with sadness responding when viewing a sad film clip (93).

Disgust

In another line of research, we have documented marked deficits in the ability of individuals with FTD to generate disgust responses to laboratory stimuli (disgusting films) (94). As was the case with the embarrassment research reviewed in the previous section, these laboratory findings are quite consistent with clinical observations that individuals with FTD often engage in behaviors and activities that others find quite disgusting (e.g., eating unusual things). This suggests that individuals with FTD may not experience disgust (which would normally cause them to withdraw from these things rather than approaching and consuming them).

As with the embarrassment findings, the disgust findings also show some specificity in the relationships between patterns of neurodegeneration and deficits in emotional functioning. In a sample of individuals with a range of neurodegenerative diseases (n = 84) who viewed disgusting and sad films, we (95) found that lower levels of disgust responding were associated with greater degeneration in anterior insular regions (which are thought to be critical for processing visceral information) (96). The findings revealed specificity in terms of both emotions (insular volumes were not associated with sadness responding) and anatomy (disgust responding was not associated with degeneration in other regions including putamen, pallidum, and caudate).

Emotion Regulation and Recognition

To understand the impact of disease on emotional functioning more broadly, it is important to examine particular kinds of emotion regulation and emotion recognition. As noted earlier, emotional deficits become increasingly pervasive as neurodegeneration progresses. Nonetheless, in the earlier stages of disease, when patients can still participate in laboratory sessions, we have found evidence for some specificity in the influence of disease on both emotion regulation and emotion recognition.

In terms of emotion regulation, we have found that, compared with healthy controls, individuals with FTD and AD both have difficulties suppressing observable emotional responses when instructed

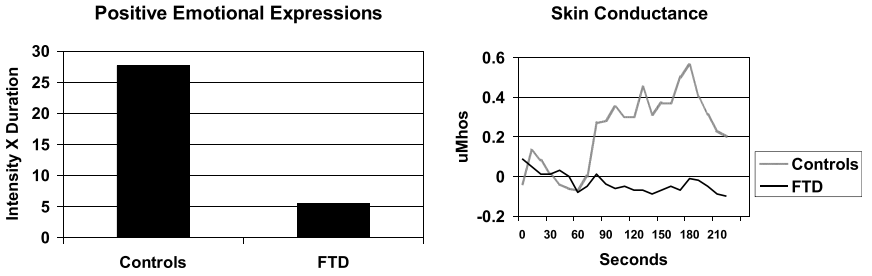

FIGURE 5. Facial and electrodermal responding during karaoke task.

to downregulate emotional responding to an aversive audio stimulus. However, when told exactly when the stimulus will occur but not given explicit instructions about regulation, FTD patients show much more profound deficits in downregulation than both AD patients and healthy controls (88). Thus, it seems that FTD patients can still follow instructions to downregulate (suggesting that their ability to downregulate is still intact) but fail to do so when they have to evaluate the situational demands and initiate downregulation on their own (suggesting problems in evaluating contextual factors and using this information to motivate appropriate behavior).

In terms of emotion recognition, we have found that individuals with FTD have greater difficulty identifying positive, negative, and self-conscious emotions displayed by characters in brief films compared with individuals with AD and healthy controls. However, deficits in emotion recognition in FTD patients are particularly pronounced in their ability to recognize self-conscious emotions such as embarrassment, pride, and shame (87).

Implications for the Influence of Other Diseases on Emotion

These examples of disease influencing emotional functioning in relatively specific ways are all drawn from our studies of individuals with neurodegenerative disease. Because neurodegenerative diseases produce different patterns of injury to emotion-critical brain circuitry, they often provide plausible explanations for the different patterns of associated change in emotional functioning. Other diseases certainly can have strong associations with changes in emotional functioning (e.g., depression and heart disease) (97,98). Based on our findings with individuals with neurodegenerative diseases, future research with other diseases should investigate links with specific emotions (e.g., heart disease and anger) and particular emotional processes (e.g., considering associations with deficits in emotional reactivity, regulation, and recognition) and consider the relative strength of bidirectional influences. Moreover, for this kind of research to be most effective, it should include studies that go beyond self-report inventories and carefully measure actual emotional functioning.

INFLUENCES OF EMOTION ON THE HEALTH OF OTHERS

Emotions are deeply embedded in the social fabric of our lives (99) providing the threads that bind us to others and the forces that drive us asunder (8). Nowhere is the role of emotion more profound than in marriage and other intimate relationships (100). Our research with individuals with neurodegenerative disease caused us to become increasingly interested in the plight of their spousal and other familial caregivers. This has led to a number of studies in which we examine the impact that deficits in specific aspects of emotional functioning in the person with dementia have on the health of their caregivers.

Dementia and Dementia Caregiving: A Growing Public Health Challenge

AD, FTD, and other forms of dementia constitute a major public health challenge worldwide. There are currently approximately 5.5 million cases of AD and 60,000 cases of FTD in the United States and approximately 16 million family members and friends who are providing 18 billion hours of unpaid care for people with dementia (101,102). Because dementia rates increase with age (e.g., 44% of individuals between the ages of 75 and 84 years have AD) (103), the worldwide "graying" of the population will make the challenges of dementia and dementia caregiving even greater in the future. In 2006, there were 700 million people worldwide older than 60 years; by 2050, this number will triple to 2.1 billion, and in the United States, 11.4% of the population will be older than 75 years (104). The staggering number of people already living with dementia; the prospects for dramatic increases in the number of future cases; the enormous associated economic, social, and personal costs; and the lack of effective preventative and curative treatments have made dementia one of the most critical public health challenges of our time.

Adverse Effects on the Health of Caregivers

Although dementia has devastating effects on the person with the disease, caregivers often experience "collateral damage." The elevated psychiatric and physical morbidity associated with caregiving is well established. In terms of mental health, caregivers have up to four-fold increases in rates of depression, three-fold increases in seeking treatment for anxiety, greater use of psychotropic medications, and greater suicidal ideation compared with noncaregiving adults of similar age (105–113). These elevations in psychiatric disorders are all the more striking given that, among people older than 65 years, the prevalence of these mental health disorders normally stabilizes or decreases (114).

In terms of physical health, dementia caregivers have greater physical morbidity (115,116), lower self-rated health (117), greater heath care utilization (118), greater decline in cellular immune functioning (73), greater heart rate reactivity to stress (119), higher rates of dementia (120), and shorter lives (121,122).

Individual Differences in Caregiver Health

Although challenging to all, some caregivers remain relatively unimpaired, whereas others spiral downward in a trajectory of declining mental health, physical health, and well-being. These individual differences are illustrated in Figure 6, which portrays depression scores (Center for Epidemiologic Studies—Depression scale) (123) in 107 consecutive familial caregivers studied in our Berkeley laboratory. The variation in depressive symptoms is striking (e.g., 27% scored above the typical clinical cutoff score of 16, but 5% reported no symptoms). Existing research indicates the promise of identifying risk factors in the external environment, in individuals with dementia, in caregivers, and in the patient-caregiver relationship that account for these individual differences (122,124–128).

The Role of Specific Emotions

Emotional changes in individuals with dementia underlie many of the problematic behaviors and psychological symptoms (e.g., aggression and agitation) (125) that create high levels of caregiver burden. Consequently, our initial studies of caregiver health focused on emotional deficits in individuals with dementia.

In one line of work, we have focused on atypical emotional responding in individuals with dementia. A person viewing a film in which a child's father dies will typically report high levels of sadness and low levels of other emotions (e.g., disgust or amusement) (129). In individuals with dementia, report of these other

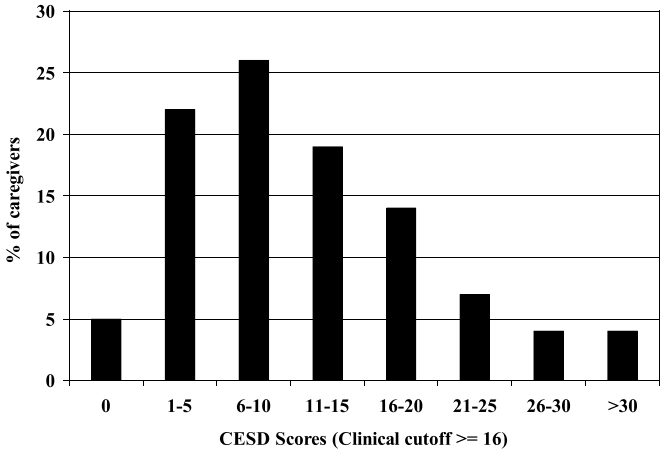

FIGURE 6. Caregivers' depression scores on CESD (n = 107). CESD = Center for Epidemiologic Studies—Depression Scale.

nontarget emotions is elevated (81). In a laboratory study of emotional reactivity (n = 178), we (126) found that greater experience of nontarget emotions by individuals with dementia in response to films that elicited either amusement or sadness was associated with greater mental illness in their caregivers.

In another line of work, we have examined the emotions that individual with dementia express during interactions with their spousal caregivers. Facial expressions provide conspecifics with emotional information that is critical for maintaining social relationships (99). Using the Facial Action Coding System (44), we (124) analyzed the smiles expressed by individuals with dementia and their spousal caregivers (n = 57 dyads) during a 10-minute naturalistic discussion of an area of marital conflict. Smiles were classified as genuine enjoyment (i.e., "Duchenne smiles") or nonenjoyment smiles using well-established morphological criteria (130). Findings revealed that low levels of genuine enjoyment smiles in individuals with dementia were associated with greater physical and mental illness in caregivers. This relationship was not found for nonenjoyment smiles in individuals with dementia or for either type of smile in caregivers.

Thus, it seems that changes in quite specific aspects of emotional responding in individuals with dementia (e.g., not producing focused emotional responses and lack of genuine smiling) assessed in the laboratory can provide important clues that help explain individual differences among caregivers in their susceptibility to the adverse health effects of caregiving. Although these initial studies have focused on fairly broad measures of mental and physical health, we expect that relationships between specific emotions and particular health problems will emerge as our samples become larger and our studies become more longitudinal. Importantly, this kind of research has the potential for revealing early indicators that identify caregivers who are at heightened risk for later health problems and for illuminating mechanisms that could become targets for focused interventions aimed at protecting caregivers' health.

CONCLUSIONS

Emotions play a critical role in explaining the well-established connections between stress exposure and disease outcomes. They provide a plausible pathway through which reactions to life's challenges and opportunities can activate biological systems in ways that increase (or decrease) vulnerability to disease. Although not present in earlier models, emotions assume more prominent roles in newer theoretical models in psychosomatic medicine (e.g., Ref. (6)). Despite this increasing prominence, emotions are often considered only in broad classes (e.g., negative emotions) rather than in terms of specific emotional states (e.g., anger and disgust) and emotional processes (e.g., different forms of emotion regulation). In this article, I have argued for a more careful consideration of the role that specific emotions and emotional processes play in health and disease. Moreover, using examples from our own research, I have tried to underscore the importance of considering bidirectional causal influences (specific aspects of emotional functioning causing particular diseases and vice versa) and the impact of changes in one person's emotional functioning on the health of intimate others (e.g., association between emotional deficits in individuals with dementia and health problems in their familial caregivers). Designing research in ways that allows specific emotions to be linked with particular health outcomes will require additional effort in a) selecting and developing emotion-eliciting stimuli; b) measuring and verifying emotional states; c) conducting longitudinal research spanning longer periods; d) studying populations at heightened risk for disease; e) assessing particular health problems; and f) measuring physiological, expressive, and subjective aspects of actual emotional responding. The payoff for these additional efforts lies in their potential for providing a deeper and more precise understanding of the emotional pathways connecting exposure to stress and disease processes.

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