

SELFLESS CELLS

FRONTOTEMPORAL LOBAR DEGENERATION AND EMOTIONAL FUNCTIONING

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Dementia is a common age-related disorder resulting from degenerative synaptic loss and neuronal death. The associated progressive disability causes enormous psychological and social burdens for patients and their loved ones. Among the dementias, Alzheimer's disease (AD) is the most common. Estimates are that approximately 5 million people are affected with AD in the United States alone. Frontotemporal lobar degeneration (FTLD), once relatively unknown, is now thought to account for approximately 10% of primary degenerative dementias (Brun, 1987; Neary et al., 1998) and a significantly higher percentage of early-onset dementias (Ikeda, Ishikawa, & Tanabe, 2004). Current demographic trends toward a "graying" population mean that our society will be faced with an increasing number of individuals with dementia. Different dementias convey different kinds of disability and burden. Accordingly, it is important to understand the associated areas of lost and preserved function so that available resources can best be applied to serve the needs of patients and their families. Moreover, when therapies for dementia become available, they are more likely to slow or halt the course of neurodegeneration rather than reverse its effects. Thus, there is a need to develop more effective and sensitive means for making early diagnoses, which will allow therapies to be applied before neural damage becomes widespread and debilitating.

The cognitive symptoms that define the early stages of AD have long been recognized, and there are many excellent comprehensive tests for assessing cognitive symptoms in domains such as memory and visuospatial functioning. In contrast, consensus as to the symptoms that define the early stages of FTLD was not reached until relatively recently (Neary et al., 1998; Rascovsky et al., 2011), causing many cases to go unrecognized or misdiagnosed (Mendez, Selwood, Mastri, & Frey, 1993). Unlike AD, where symptoms occur largely in cognitive domains, many of the criteria for diagnosing FTLD are behavioral in nature and involve deterioration in socioemotional functioning. For example, in the Neary criteria (Neary et al., 1998), four of

the five core diagnostic features involve changes of this sort: (1) decline in social interpersonal conduct; (2) impairment in regulation of personal conduct; (3) emotional blunting; and (4) loss of insight. Consistent with this, in the newly proposed international research criteria for behavioral variant frontotemporal dementia (Rascovsky et al., 2011), changes in socioemotional functioning again are featured, with apathy, disinhibition, and loss of sympathy or empathy for others representing core signs of the disease.

CHALLENGES IN ASSESSING DEFICITS IN EMOTIONAL FUNCTIONING

In cognitive realms, functional modularity is well accepted. Thus, in documenting cognitive deficits, distinctions are typically made among short- and long-term memory, executive functioning, language production and recognition, praxis, and a host of other functions. Historically, there has been an unfortunate tendency to think of emotion as a monolith, with functionality in all aspects thought to rise and fall together. However, as affective science and the associated measurement methodologies have matured, it has become increasingly apparent that accurately assaying emotional functioning requires much more differentiated models and metrics.

PROCESSES

A reasonable account of socioemotional functioning requires a number of different emotional processes that include, at minimum, (1) emotional "reactivity"—the type, magnitude, and duration of emotional responses that occur in reaction to changes in the internal and external environments that have significance for our goals and well-being; (2) emotional "regulation"—the adjustments in emotional response that are made to meet situational demands; and (3) "empathy." Within empathy, it is important to assess recognition of emotion in other people ("cognitive empathy"),

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emotional reactions to the plight of others (“emotional empathy”), and action to help others in distress (“prosocial behavior”). These processes are illustrated schematically in Figure 40–1. In assembling this catalog of functions, there is an assumption that these processes are somewhat independent, subserved by different brain circuitry (Adolphs, 2002), and susceptible to different patterns of preservation or loss, depending on patterns of neural degeneration.

SPECIFIC EMOTIONS

A related and similarly problematic notion is that “what holds for one emotion holds for all.” Instead, emotional functioning should, at minimum, be assessed within three broad “families” of emotion: (1) positive (e.g., amusement, affection), (2) negative (e.g., sadness, disgust), and (3) self-conscious (e.g., embarrassment, pride). Differences between these emotional families and among specific emotions within them are supported by research on emotional ratings (Watson, Clark, & Tellegen, 1988), expression (Ekman & Friesen, 1982; Keltner, 1995; Keltner & Buswell, 1996), and physiology in the central (Davidson & Fox, 1982) and autonomic (Ekman, Levenson, & Friesen, 1983; Fredrickson & Levenson, 1998) nervous systems.

RESPONSE SYSTEMS

Emotions are manifest in multiple response systems including peripheral and central physiology, facial expression,

body posture, and voice tone. Subjective emotional experience (measured by self-report) is also an important part of the emotional response (specific emotions “feel” different to us, and that information has important signal value for influencing our behavior; Damasio, Tranel, & Damasio, 1991; Sze, Gyurak, Yuan, & Levenson, 2010). A full accounting of emotion benefits from measurement in multiple domains (Lang, 1979); thus, it is important to assess peripheral physiology, facial expression, and subjective emotional experience. Where appropriate, it also is useful to examine emotional language (e.g., analyzing the use of emotion words in transcripts of conversations between spouses; Ascher et al., 2010). In assessing emotional functioning in patient populations, measuring multiple response systems is essential because disease processes may cause impairments that make particular response systems less reliable (e.g., compromised semantic knowledge affecting self-reported emotional experience).

OBJECTIVE MEASUREMENT OF ACTUAL EMOTIONAL FUNCTIONING

Emotional functioning is often assessed by asking individuals to report on their *beliefs* about their own emotional reactivity, regulation, and empathy or by asking significant others to provide these reports. Although self-perceptions and other-perceptions provide extremely important information, they are not always accurate proxies for objective measurement of actual socioemotional behavior

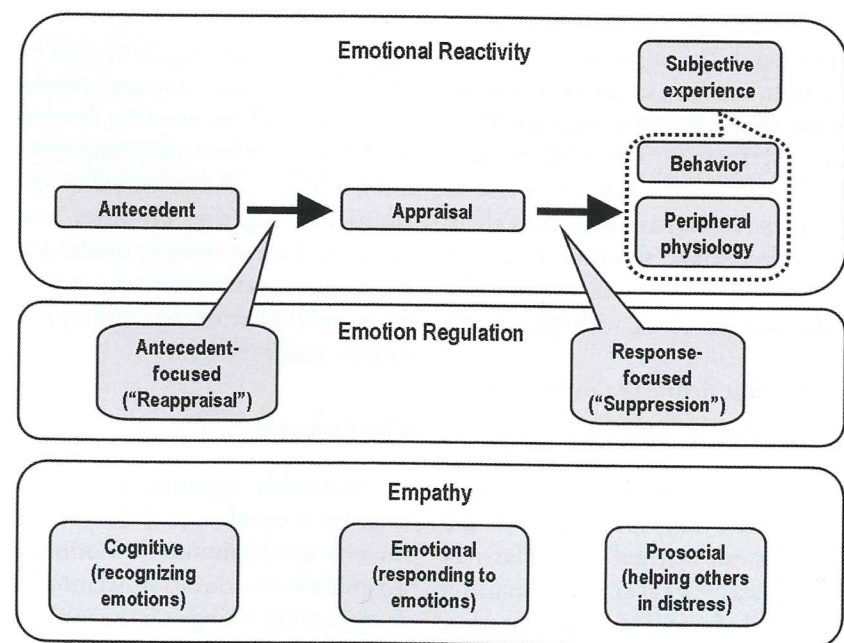


Figure 40–1 Overview of assessment of emotional processes, including (1) emotional reactivity (generating subjective behavioral and physiological responses to significant antecedent events), (2) emotion regulation (adjusting emotional responses to meet situational demands; the figure illustrates two kinds of regulation, one that targets appraisals and one that targets responses), and (3) empathy (cognitive empathy involves recognizing another person’s emotions; emotional empathy involves responding emotionally to another person’s emotions; prosocial behavior involves helping another person who is in distress).

(e.g., Ickes, Stinson, Bissonnette, & Garcia, 1990; Levenson & Ruef, 1992; Reisenzein, Bordgen, Holtbernd, & Matz, 2006). In various dementias, deficits in memory, language, and insight are among the many factors that can increase discrepancies between patient self-reports and objective measures. Observer reports are important for assessing real-world emotional functioning, but observers vary greatly in their ability to provide accurate descriptions and in their objectivity. This may be particularly true when caregivers serve as observers. Their reports may be unduly influenced by the stresses of caregiving, premorbid characteristics of the patient, and the desire to present the patient’s functioning in particular ways. Despite the convenience of obtaining these kinds of reports of emotional functioning by self and others, the gold standard for assessing emotional functioning is arguably only achieved by observing and objectively quantifying *actual* emotional functioning.

LABORATORY ASSESSMENT OF EMOTIONAL FUNCTIONING

When we assess patients’ emotional functioning in our laboratory, we use a series of tasks designed to reveal areas of impaired and preserved functioning in a comprehensive sampling of emotional processes, emotion families, and emotional response systems. This approach uses structured laboratory tasks to assess emotional reactivity, regulation, and empathy (for additional details, see Levenson, 2007).

At first consideration, saying that a patient has “emotional blunting” might seem quite precise. However, an affective scientist would want to know which emotions are blunted (e.g., positive, negative, self-conscious emotions), what aspects of the emotional response are blunted (i.e., emotional experience, physiology, behavioral expression), and the conditions under which the blunting occurs (e.g., when emotions are self-generated, when they occur in response to external sensory input, when they occur in response to other people). Similar concerns have been raised by dementia researchers. In the recent report from the International bvFTLD Criteria Consortium (Rascovsky et al., 2011), the “ambiguity of behavioral descriptions” was viewed as one of the limitations of the existing research criteria for diagnosing FTL D. These concerns would be less critical if emotional deficits in neurodegenerative diseases occurred in an all-or-none fashion. However, as socioemotional functioning in neurodegenerative diseases is studied with greater precision, a number of quite specific deficits have been documented in terms of particular emotions (e.g., deficits in disgust in patients with Huntington’s disease; Sprengelmeyer et al., 1997) and particular processes (e.g., preservation of low-level emotional reactivity but loss of reactivity in more complex self-conscious emotions in FTL D; Sturm, Rosen, Allison, Miller, & Levenson, 2006; Werner et al., 2007).

THE BACKDROP OF NORMAL AGING

In most areas of cognitive and physical functioning, normal aging involves gradual losses that become significant over time. For example, Salthouse (2004) has documented a monotonic decline in a number of cognitive functions (e.g., processing speed, reasoning, memory) across the decades between ages 20 and 80. Because many of these same functions are negatively impacted by mild cognitive impairment and by AD, deciding whether a particular individual’s cognitive decline is associated with these disease processes or with normal aging is diagnostically challenging.

Early theories of lifespan development suggested that there is a similar pattern of broad decline in emotional functioning associated with normal aging (Cumming & Henry, 1961; Jung, 1933; Looft, 1972). However, modern developmental theories (Carstensen, 1995; Labouvie-Vief, 1999) and contemporary studies of emotional functioning in healthy elders (Levenson, 2000) present a quite different picture, with preservation of many aspects of emotional functioning throughout life.

We have studied emotional reactivity in young, middle-aged, and elderly individuals using films (Kunzmann, Kupperbusch, & Levenson, 2005; Tsai, Levenson, & Carstensen, 2000), relived memories (Levenson, Carstensen, Friesen, & Ekman, 1991), directed facial actions (Levenson, Carstensen, Friesen, & Ekman, 1991), and marital interaction (Carstensen, Gottman, & Levenson, 1995; Levenson, Carstensen, & Gottman, 1993, 1994). Aggregating across the findings from these studies, our general conclusion is that subjective emotional experience and emotional behavior do not show marked age-related decline. Rather, in healthy individuals, both seem to be well preserved throughout middle age and late life. In contrast, some physiological responses, especially in the cardiovascular system, do show age-related decline.

In the realm of emotion regulation, questionnaire studies indicate that people *believe* that they gain greater control over their emotions with age (e.g., Gross et al., 1997; Lawton, Kleban, Rajagopal, & Dean, 1992). We (Kunzmann et al., 2005) have studied emotional regulation in the laboratory in young (mean age = 21) and old (mean age = 71) individuals who were instructed to either suppress or amplify their behavioral responses to emotion-eliciting films. Results indicated that young and old individuals did not differ in their ability to regulate behavioral expression or in the physiological or subjective consequences of this regulation. A more recent study by our group that examined the impact of aging on multiple emotion regulation strategies revealed additional complexities. In that study (Shiota & Levenson, 2009) we found that older individuals show *greater* ability to regulate their emotions using *positive appraisal* strategies (i.e., viewing something negative in a more positive light) than middle-aged and younger

individuals but show *less* ability to regulate using *detachment* strategies (i.e., minimizing involvement).

Finally, in the realm of empathy, studies in which participants have to identify the emotion portrayed in a photograph or sound suggest that older people perform more poorly (Ruffman, Henry, Livingstone, & Phillips, 2008). However, we have recently found evidence that older people show greater ability to track changing emotions of others in complex social situations (Sze, Goodkind, Gyurak, & Levenson, in press a) and greater likelihood of engaging in helping behavior when confronted with others in distress (Sze, Gyurak, Goodkind, & Levenson, in press b).

FTLD AND EMOTIONAL FUNCTIONING

As noted in the preceding section, empirical studies largely confirm newer theories that envision normal aging as leaving much of the emotional apparatus intact. In contrast, FTLN creates the kinds of devastating declines and disengagement that were envisioned in the earlier models of aging. In our work over the past decade, we have tried to document precisely where these declines occur and also to identify areas of relatively preserved functioning.

In terms of *emotional reactivity*, we have found that simple forms of emotional reactivity (e.g., responding to seeing others display strong emotions of happiness and sadness) are preserved in FTLN even when reactivity in more complex self-conscious emotions (e.g., becoming embarrassed by seeing yourself singing in a video) is dramatically diminished. Self-conscious emotions serve important social functions by motivating reparative action to bring behavior back in line with normative expectations. Thus, dementia patients with deficits in self-conscious emotions are likely to behave in socially inappropriate ways without engendering these correction-inducing emotional responses.

In terms of *emotion regulation*, we have found that both FTLN and AD patients have difficulty downregulating emotional responses when instructed to do so, but FTLN patients are particularly deficient in situations in which they have to read social cues and downregulate spontaneously (Goodkind, Gyurak, McCarthy, Miller, & Levenson, 2010). Our studies of the relationship between emotion regulation and executive functioning in a range of patients (Gyurak et al., 2009; Gyurak, Goodkind, Kramer, Miller, & Levenson, 2012) have revealed a consistent relationship between deficits in the ability to regulate emotion in our laboratory tasks and poor performance on tests of verbal fluency (generating lists of words). Interestingly, we have found emotion regulation abilities to be unrelated to other tests of executive functioning that focus on response inhibition, working memory, or set-shifting. It may be that verbal fluency tests better capture the full range of planning and monitoring activities that are necessary for successful emotion regulation.

In terms of cognitive *empathy*, we have found that FTLN patients have difficulty identifying emotions in others (Werner et al., 2007). Recently, using an expanded set of emotional stimuli that allowed testing of a full range of positive, negative, and self-conscious emotions, we found that both FTLN and AD patients had trouble recognizing specific positive and self-conscious emotions, but that deficits in recognizing self-conscious emotions were particularly profound in FTLN patients (Goodkind & Levenson, 2012a). Examining more dynamic kinds of emotion recognition, we (Goodkind et al., 2012b) found that the ability to track dynamically changing emotions in social contexts was dependent on the integrity of right lateral orbitofrontal structures, the nidus of early degeneration in behavioral variant FTLN (see Figure 40-2).

We have conducted several studies of the *patient-spouse relationship* using our laboratory procedures for studying the emotional qualities of marital interaction, which are based on observing couples' unrehearsed conversations about marital issues (Levenson & Gottman, 1983). In a study focusing on patterns of mutual gaze, we (Sturm et al., 2011) found that couples in whom the patient had the semantic dementia variant of FTLN showed more mutual gaze than normal controls. Couples with the behavioral variant of FTLN showed less mutual gaze than controls. We also found that lower levels of mutual gaze predicted greater levels of apathy and greater levels of disinhibition, as measured by the Neuropsychiatric Inventory (Cummings, 1997). In another study, we (Ascher et al., 2010) examined emotional language using text analysis methods (Mergenthaler, 1985; Pennebaker, Francis, & Booth, 2001). Results indicated that spouses of FTLN patients used significantly more negative emotion words ("angry," "sad," etc.) and reported significantly lower marital satisfaction than spouses of AD patients, who did not differ from age-matched control couples.

FTLD: A DEVASTATING DISEASE THAT PRODUCES HIGH LEVELS OF CAREGIVER BURDEN

The review of emotion in normal aging presented earlier supports the conclusion that most aspects of emotional functioning are well preserved with age and that some even improve. Thus, there is essentially nothing in the realm of normal aging that even remotely resembles the devastating declines in emotional functioning that occur in FTLN. Whereas, to some extent, AD can be reframed as a dramatic acceleration and intensification of the cognitive declines that are associated with normal aging, the changes that occur in FTLN cannot be viewed as normative. Rather, FTLN is experienced as robbing patients and their loved ones of the emotional richness that they could have expected in late life. Although all dementias are

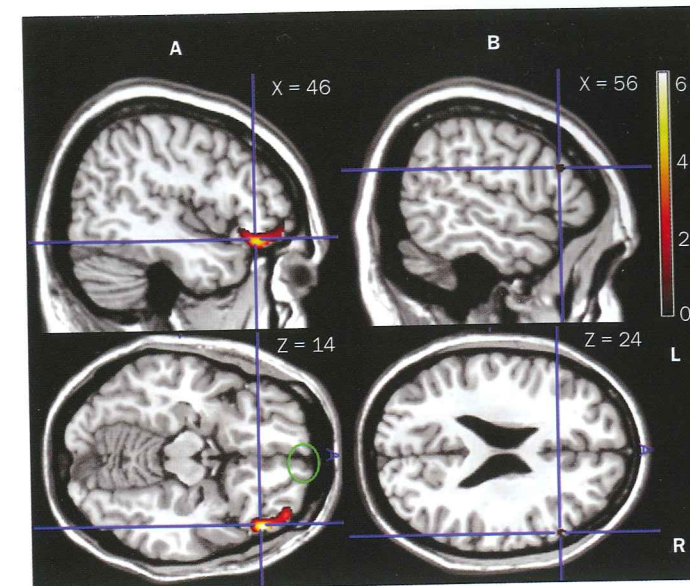


Figure 40-2 Colored areas are regions where brain atrophy was significantly correlated with impairment on the emotion tracking task. The analysis controlled for age, sex, total intracranial volume, Mini-Mental State Examination, control task performance, and diagnostic group membership. Results of the analysis are superimposed on sagittal and axial slices of a standard brain from a single normal subject and corrected for family-wise error across the whole brain at a significance level of $p < .05$ shown as a T-score range on the left. (A) The blue crosshairs indicate the regions of the right lateral orbitofrontal cortex with significant correlations ($T = 5.62$); the green circle indicates the region of the right gyrus rectus with significant correlations ($T = 5.11$). (B) The blue crosshairs indicate the region of right pars triangularis with significant correlations ($T = 5.05$).

devastating and create significant burden, the few existing comparative studies underscore the profound caregiver burden associated with FTLN (de Vugt et al., 2006).

Our findings (Ascher et al., 2010) that FTLN is associated with more emotionally negative patient-spouse interactions and lower marital satisfaction than AD are indicative of the kind of schism between spouses that FTLN causes. In marriage, the sense of partnership or "we-ness" is a critical component of marital strength and stability (Seider, Hirschberger, Nelson, & Levenson, 2009). In the natural course of events, spouses have many occasions to work together on life's problems, both large and small. Thus, in healthy, happy marriages, the sense of partnership between spouses builds over time. In contrast, FTLN often creates a sense of isolation, abandonment, aloneness, and resentment in the healthy spouse. Thus, emotions and emotional language become more negative and satisfaction with the marital relationship declines. In AD, couples often follow a different course. As devastating as the disease is, in the early stages when patients' insight and awareness are still somewhat intact, partners often display a profound sense of partnership and work together on strategies that help them compensate for some of the losses and take advantage of areas of preserved functioning. In FTLN, the patient's loss of insight and self-knowledge combine with the emotional losses to make this kind of partnership impossible. Ironically, the preservation of many areas of cognitive functioning in FTLN only adds to the frustration ("You can do this, so why can't you do that?"). This combination of preserved and lost functioning constitutes a blueprint for frustration and distress.

SUMMARY

In this chapter, I have argued for a more differentiated view of emotional functioning that encompasses multiple emotional processes, multiple emotional families, and multiple emotional response systems. With this as a framework, I reviewed the trajectory of changes in emotional functioning that occurs in normal aging. The resultant picture of preservation and growth of functioning is quite different than the age-related declines found in many cognitive and physical domains. I then reviewed the results of applying our laboratory methods for comprehensively assessing emotional functioning to dementia patients, which have revealed patterns of loss and preservation of function that are quite different in FTLN and AD. The losses in emotional functioning associated with FTLN are particularly devastating to spouses and families because they occur in domains that are typically spared in normal aging.

DISCLOSURE STATEMENT

R.W.L. has no conflicts of interest to disclose.

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