

Emotion Regulation Therapy and Its Potential Role in the Treatment of Chronic Stress-Related Pathology Across Disorders

Chronic Stress
Volume 4: 1–10
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DOI: 10.1177/2470547020905787
journals.sagepub.com/home/css
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Abstract

Although stress is an inevitable part of everyday life, its chronicity, severity, and perceived burden can result in enduring distress, which may manifest as heightened emotionality, contributing to a number of self-regulatory failures. Specifically, distress disorders are characterized, in part, by heightened sensitivity to underlying motivational systems related to threat/safety, reward/loss, or both. Further, individuals suffering from these conditions typically engage in perseverate negative thinking (e.g., worry, rumination, self-criticism) in an effort to manage motivationally relevant distress and often utilize these processes at the detriment of engaging in new contextual learning. Distress disorders are often brought on by enduring chronic stress, coupled with these maladaptive emotional, cognitive, and behavioral responses and ensuing impairment which contribute to and in turn worsen the deficits from these purported mechanisms. Emotion regulation therapy is a theoretically derived treatment that is based upon affective science to offer a blueprint for improving intervention by focusing on targeting the motivational responses and corresponding regulatory failures of individuals with distress disorders. Open and randomized controlled trials have demonstrated considerable preliminary evidence for the utility of emotion regulation therapy and its proposed mechanisms in treating the distress conditions.

Keywords

chronic stress, emotion regulation, distress disorders, treatment, allostasis

Received 14 October 2019; accepted 22 January 2020

Conceptualizing Mood and Anxiety Difficulties in the Context of Chronic Stress

Stress brought about by physical, environmental, and/or interpersonal challenges is an inevitable part of life and many organisms have developed means to adapt to these stressors when they arise. McEwen¹ refers to this active and dynamic process of confronting and adapting to stressors as *allostasis* and quantifies the cumulative physiological cost or burden caused by this adaptation to the stress as *allostatic load*. A primary goal of organisms is to maintain *homeostasis*, which refers to an attempt to maintain an internal state within the body in service of optimizing survival. Although stressors are taxing to the organism, ideally the burden is temporary or cyclical and the organism can reestablish homeostasis.² However, stress can lead to dysfunction and pathophysiological states (i.e., *allostatic overload*) when adversities arise unexpectedly, are extreme, and protracted—thereby causing an imbalance as the available energy or resources are insufficient to address the burden brought on by the stressor. McEwen's¹ allostasis model provides an

important heuristic for understanding the normative and adaptive aspects associated with managing stress. In essence, this model is predicated on *self-regulation*, which commonly refers to the behavioral, cognitive, and emotional control responses emitted by an organism to optimally address circumstances that arise in daily life.² This model also helps to account for when and how severe and persistent stress can lead to dysfunction and disease as regulatory systems can no longer

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withstand the burden caused by the intensity of one or more stressors.

Consistent with McEwen's³ allostasis model, contemporary emotion regulation theories⁴ also view an organism's responses to an emotionally evocative situation from a self-regulation perspective. Gross adopts a functional emotion perspective in positing that optimal regulation represents the coordination of attentional, cognitive, and behavioral responses to the arising of emotionally evocative situations so that an individual is constantly adjusting and/or course correcting his or her appraisals of a situation and corresponding behavioral responses to fit one's personal goals or objectives.⁵ Beyond achieving a personally relevant outcome, optimal emotion regulation results in an economy of resource involvement that tries to match the amount of effort exerted (e.g., attentional, cognitive, behavioral) to the situation and emit the least taxing response necessary to achieve the desired goal.

Drawing upon these models of allostasis and emotion regulation, we have sought to characterize and empirically investigate *distress*, which is commonly regarded as a maladaptive internal response to stressors that arise in one's life. Our program of research is predicated on a neurobehavioral model that conceptualizes distress as an imbalance of neural circuitry subserving cognition, emotion, and decision-making.⁶ For instance, distress often manifests as intense emotionality⁷⁻⁹ that affects the experience of negative and positive emotions as well as cognitive and behavioral factors that actually cause, worsen, and prolong the stressful situations that patients struggle to tolerate. One such factor that commonly accompanies this intense emotionality in distress is perseverative negative thinking (PNT; e.g., worry, rumination^{10,11} self-criticism,¹² loneliness,^{13,14} and perceived discrimination¹⁵⁻¹⁹). PNT complicates treatment responsiveness, increases unhealthy habits,²⁰ and interferes with life-style and treatment engagement. Importantly, distress is also a transdiagnostic experience in that it is not specific to a particular disorder but rather characterizes several prevalent psychiatric disorders that are often comorbid with one another and have led to the moniker of *distress disorders*.²¹

The Distress Disorders

The experience of chronic and enduring distress over time typifies the phenomenological experience of psychiatric disorders that structural emotion scholars (e.g., Krueger, 1999, Watson, 2009)^{22,23} have termed the "distress disorders" comprised of generalized anxiety disorder (GAD), major depressive disorder (MDD), persistent depressive disorder (DYS), and posttraumatic stress disorder (PTSD). In contrast to the rationally derived categories found in the Diagnostic and

Statistical Manuals (DSM; e.g., anxiety disorders, mood disorders, etc.), structural emotion scholars adopt an atheoretical and actuarial approach to vertically organize diagnostic entities into superordinate categories of broad emotional features that align with constructs of negative emotionality. Findings from these various studies revealed that many of the DSM anxiety disorders coalesce into a grouping that is typically referred to as *fear disorders* (consisting of specific phobia, social anxiety disorder, and panic disorder) and the aforementioned *distress disorders*. Collectively, distress disorders are impactful psychiatric conditions which pose a significant public health burden. For instance, distress disorders are among the most commonly occurring and impairing psychiatric disorders.^{24,25} Lifetime and 12-month prevalence of these conditions are considerable: GAD (5.7%/3.1%), PTSD (6.8%/3.5%), MDD (16.6%/6.7%), and DYS (2.5%/1.5%). Distress disorders demonstrate a chronic and persistent course and are not likely to spontaneously remit without intervention.²⁶ They also complicate the presentation and treatment of medical conditions throughout the lifespan, contributing to both an increased risk of cardiovascular disease^{27,28} and metabolic syndrome.²⁸ The burden of distress disorders is particularly prevalent among older adults.³⁰ A recent study examining the world disease burden from all medical conditions in 2010 estimated that mood disorders including MDD and DYS were the second leading cause of years lived with disability (YLD) throughout the world.³¹ Further, a 2010 study estimated that anxiety disorders (which included GAD and, at the time, PTSD) were named as the fifth leading cause of YLD.³¹ Individuals diagnosed with distress disorders also are likely to engage in numerous health risk behaviors.²⁰ Individuals experiencing depression and anxiety are more likely to smoke tobacco, consume greater quantities of alcohol, be more sedentary, and consume an unhealthy diet.³² Findings have indicated that both veterans and nonveterans diagnosed with PTSD are more likely to smoke tobacco, consume alcohol, be sedentary, and be medication nonadherent compared to individuals without PTSD.^{33,34}

Applying an Affective Science Approach to the Nature and Treatment of Distress Disorders

The burgeoning field of affective science seeks to elucidate the emotional processes that underlie adaptive and maladaptive responses to stressors³⁵ and consequently provides a strong empirical basis for how to best target distress and distress disorders. Normative emotional processing and regulation models^{4,36} are a core

component of affective science and when applied to understanding psychopathology align with the growing multidisciplinary field of intervention science and with National Institute of Mental Health priorities,³⁷ which seeks to elucidate biobehavioral markers that are reliably dissociable in patient subgroups as compared to healthy controls so as to hone interventions to better target central determinants of distress and dysfunction.³⁸

Using an affective science framework of emotion processing and regulation, we have delineated a model that targets motivational, regulatory, and resultant behavioral components of adaptive and maladaptive stress responding. We have argued that effective responding to stress involves (1) activation of motivational systems that mobilize the pursuit of safety/reducing perceived threat, reward/minimizing loss,^{39–41} or both; regulatory mechanisms comprised of (2) attentional capacities including the ability for broadening, shifting, and sustaining attention to interoceptive and exteroceptive emotional stimuli^{42–44} and (3) metacognitive capacities including decentering (e.g., the ability to observe items that arise in the mind with healthy psychological distance, greater self-awareness, and perspective-taking)^{45–47} and cognitive reappraisal (e.g., the ability to change one's evaluation of an event so as to alter its emotional significance)⁴⁸; and (4) resultant broad and flexible behavioral repertoires, which are comprised of maximal emotional clarity⁴⁹ and subsequent effectively implemented and goal-relevant responses that produce optimal behavioral outcomes (see part a of Figure 1).

Conversely, as we have argued,⁵⁰ individuals with distress disorders often experience motivational conflicts for which they are unable to resolve and effectively act on impetuses for risk and reward, fail to flexibly place and maintain their attention on percepts that are personally relevant to one's goals, and resort to more cognitively elaborative and resource intensive perseverative strategies (e.g., worry, rumination, self-criticism) as a way of managing distressing emotions and motivations. This pattern of motivational and regulatory deficits results in short-term maladaptive behavioral consequences (i.e., reassurance seeking, compulsive behaviors, drinking, smoking, maladaptive eating behavior) and long-term impact on threat and reward learning⁵⁰ (lack of approach behavior in favor of greater perceived safety, withdrawing pursuit of potentially rewarding outcomes).

Emotion regulation therapy (ERT) is a brief psychotherapy that was focally developed to help ameliorate the impact of distress disorders using the functional affective science model delineated above as a framework for targeting interventions. Although ERT's approach to treating distress disorders is uniquely packaged within an affect science framework, it integrates principles

from traditional^{51,52} and contemporary cognitive behavioral therapies^{53–55} to target motivational mechanisms (i.e., security system; reward system) and regulatory mechanisms (particularly self-referential; e.g., worry, rumination, self-criticism) that lead to short-term behavioral (e.g., avoidance, reassurance-seeking, compulsive behaviors; maladaptive coping) responses and long-term contextual learning consequences (i.e., generalized threat, diminished reward sensitivity) that are hypothesized to comprise the distress disorders.^{50,56} ERT has been delivered in 20-, 16-, and 8-session formats as part of manualized open label and randomized controlled trials.^{57–59} In each of these formats, the treatment is divided into two different phases, with the first phase of treatment focusing on increasing momentary clarity of motivational responses during emotional episodes and the cultivation of mindful emotion regulation skills with the goal of promoting counteractive responding to intense emotional experiences. Skills are presented in a specific order focusing on less cognitively elaborative skills (e.g., attention regulation skills) followed by more cognitively elaborative skills (e.g., metacognitive regulation skills). Metacognitive regulation skills focus specifically on decentering and reappraisal. Collectively, these attention and metacognitive skills are introduced to promote more adaptive responding to one's internal (e.g., emotional) and external (e.g., contextual) environments. Each skill is meant to target a different point along the temporal emotional cascade that occurs during a distress episode, particularly in the presence of PNT. Clients are taught to utilize these skills in the moment when they first notice the arising of emotional and motivational cues. Further, the cultivation of these skills aid individuals in increasing their ability to identify pulls towards both security (e.g., safety-seeking, avoidance) and reward (e.g., moving towards potentially satisfying and values-consistent stimuli and experiences in one's environment) motivations and created more balanced responding to their motivational impetuses.

Once clients have developed some competency with identification of motivations and applying mindful emotion regulation skills in maladaptive momentary responding in the first half of treatment, the focus of the second phase of ERT seeks to proactively engage motivational states through the promotion of behavioral approach informed by clients' identification of what is meaningful and intrinsically rewarding in their lives⁵³ and how they would like to be living if distress associated with negative emotions and PNT were not holding them back. Motivation is targeted through the utilization of imaginal risk/reward exposures and conflict dialogue tasks, during which clients commit to taking actions between sessions that, rather than relying on seeking security and avoiding, promote approaching intrinsically rewarding situations threat in service of

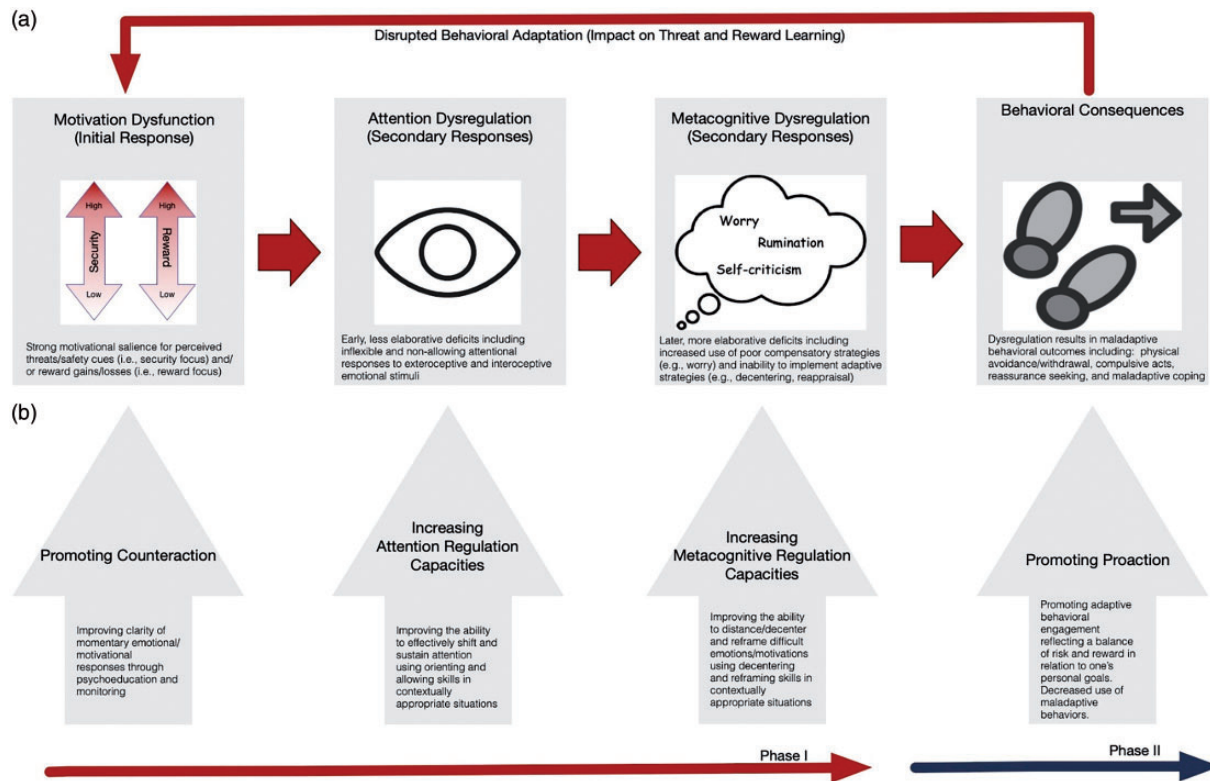


Figure 1. Functional emotion regulation model of distress disorders and corresponding ERT targets.

gaining a wider behavioral repertoire congruent with personal values. ERT concludes with the therapist and patient reviewing the progress made during the course of treatment and encouraging the patient to continue utilizing mindful emotion regulation skills to address distressing situations when they arise (i.e., “being counteractive”) as well as when planning important but potentially stressful future endeavors (i.e., “being proactive”). See part b of Figure 1 for a summary of this emotion regulation model and how ERT targets each of the model’s components.

ERT Clinical Outcomes

Efficacy Findings

ERT has established efficacy through an initial open trial (OT; $N = 20$; M age = 32, $SD = 10.96$; 75% women) of patients diagnosed with GAD with and without co-occurring major depression⁵⁸ and in a randomized controlled trial (RCT; $N = 53$; M age = 38, $SD = 14.46$; 81% women) examining symptom changes throughout ERT in comparison to a minimal attentional control condition.⁶⁰ Patients in this initial OT demonstrated reductions in GAD severity,⁶¹ worry,⁶² trait anxiety,⁶³ depression symptoms,⁶⁴ and corresponding

improvements in quality of life,⁶⁵ with within-subject effect sizes well exceeding conventions for large effects (Hedges’ g ’s = 0.5 to 4.0). These gains were maintained for nine months following the end of treatment.⁵⁸ The Time \times Group interaction findings from the RCT evidenced significant reductions in GAD severity,⁶¹ worry,⁶² trait anxiety,⁶³ and depression symptoms,⁶⁴ and corresponding improvements in social disability⁶⁶ and quality of life⁶⁵ for patients who received immediate ERT compared to a modified attention control condition, with between-subject effect sizes in the medium to large range (g ’s = 0.5 to 1.5). Similar to the OT findings, these gains were maintained for nine months following the end of treatment.⁶⁰ Furthermore, depression-related outcomes such as rumination⁶⁷ and anhedonia were reduced considerably (g ’s = 0.6 to 0.9).

More recently, ERT has been tested in an OT of ethnically diverse and disadvantaged young adults ($N = 31$; M age = 22, $SD = 2.48$; 71% women) diagnosed with a primary diagnosis of any anxiety or mood disorder.⁵⁷ Results demonstrated a comparably severe sample to the previous trials and similarly strong ameliorative changes from pre- to posttreatment in worry,⁶² rumination, generalized anxiety, anhedonic depression, clinician-rated severity of GAD and MDD,⁶¹ social disability,⁶⁶ and quality of life⁶⁵ with within-subjects

Hedges' g 's ranging from 1.5 to 4.0. These gains were maintained at a 3-month and 9-month follow-up. Most recently, we have examined the efficacy of the 8-session format of ERT compared to the 16-session version. Preliminary analyses have revealed no significant differences in completer status between the two groups ($\chi^2 = 1.29$, $p = .27$), highlighting that both versions were tolerable for participants. Across all outcomes, although both treatment versions produced significant main effect improvements from pre- to posttreatment (all Cohen's f^2 s $> .52$), the magnitude of gains was comparatively larger for the 16-session version. Commensurately, findings revealed significant group by time interactions for the majority of outcomes from pre- to posttreatment. Beyond these indices of clinical response, all of these ERT trials resulted in an impressive percent of patients achieving high endstate functioning, which corresponds to whether patients' scores on clinician-assessed and self-reported symptom measures are restored to within one standard deviation of healthy norms. High end state functioning is a rigorous standard of clinical improvement than simply examining change over time given that it necessitates normalization of self-reported symptoms rather than reductions alone. Achieving high endstate functioning essentially means that ERT was associated with restoration of normative symptom and functioning levels on a combination of GAD (range = 55% to 85%) and MDD (range = 56% to 80%) indicators that were maintained or increased into the posttreatment follow-up.^{56,57,59}

ERT has subsequently also been evaluated in the context of cancer caregivers.^{68,69} The contextual demands of caregiving for a loved one with a chronic illness has been found to lead to heightened emotional distress.^{70,71} At times, the distress experienced by these caregivers may surpass that of the actual cancer patient.⁷²⁻⁷⁴ Psychosocial interventions containing efficacious treatment principles (e.g., CBT) show disappointing results in reducing anxiety and depression in informal caregivers.⁷⁵ In an initial open trial, 32 informal caregivers (87% women; mean age = 55; 61% partner, 19% children, and 16% parent of patient with cancer) who endorsed significant distress and either elevated worry or rumination received the 8 session version of ERT, which was adapted to the caregiver context (ERT-C). Caregivers receiving ERT-C evidenced reductions in worry,⁶⁰ rumination,⁶⁵ and anxiety and depression symptoms⁷⁶ (within-subject effect sizes g 's = 0.4-0.9).⁶⁸ A follow-up RCT in 81 informal caregivers (75% women; mean age = 48; 75% were female caring for male patients) comparing the 8-session ERT-C protocol versus a waitlist control condition further found strong between-subject effects for these indices as well as a measure of caregiver burden (g 's = 0.5-1.0). Further, patients whose informal caregivers attended ERT-C

experienced a large increase in quality of life posttreatment compared to those whose informal caregiver were in the waitlist condition ($g = 0.9$).⁶⁹

Model-Related Changes

In addition to establishing strong effects for clinical outcomes, the above trials also demonstrated significant treatment-related change from pretreatment to posttreatment and through the follow up in self-reported measures of target mechanisms with moderate to large within (g 's = 0.6-2.6)^{55,57,68} and between-subjects effect sizes (g 's = 0.5-1.0).^{57,69} Further, we tested mediational models and found that measures of overall and specific attentional and metacognitive regulatory ability demonstrated indirect effects on primary outcomes of diagnostic anxiety severity,⁵⁹ worry,⁶⁰ depression,⁶² social disability,⁶⁴ and quality of life⁶³ when comparing ERT to the modified attention control comparator.⁵⁷

To examine the relationship of these changes to outcomes, we have utilized multiple indices of emotion functions including subjective report, behavioral tasks, and biological indices that have established reliability and validity in lab and analogue studies. Below, we describe a set of pilot studies that examined the relationship between ERT implementation, changes in the proposed target mechanisms, and clinical outcomes using multi-method assessment. These studies provide important preliminary multi-method evidence that ERT achieves clinical response via changes in motivational and regulatory mechanisms as theorized.

To test changes in attention regulation in response to treatment and its relation to treatment outcome, participants completed a modified emotional Stroop (1935) task consisting of happy or fearful facial expressions with emotion words (e.g., "fear" or "happy") overlaid on the image to test emotional conflict adaptation.^{77,78} Participants were instructed to respond as quickly and accurately as possible to whether the person in the image displayed a fearful or happy expression. Overall, participants evidenced pre- to mid-treatment improvements in their ability to shift their attention in the face of emotional conflict (pre to mid Cohen's $d = 0.74$) to levels comparable to healthy controls.⁷⁷ Further, these pre- to mid-treatment changes were associated with gains in patients' ability for greater mindful observing which in turn was associated with reductions in social disability.⁷⁹ In a subsequent study, we have also examined changes in neural correlates of this conflict adaptation and found that dorsal medial prefrontal cortex activation at pretreatment (potentially reflecting elaborative self-referential processing) significantly disengaged at posttreatment and this change was associated with decreases in clinician-rated anxiety severity and increases in self-reported attentional shifting and focusing abilities. The

Emotional Interference Task⁸⁰ was also completed by a subset of trial patients to assess ERT-linked gains in attentional flexibility. This task requires participants to differentiate between low- and high-pitched tones and press the corresponding keys quickly and accurately as possible while viewing images (e.g., neutral, negative arousing, positive arousing) from the International Affective Picture System.⁸¹ Findings indicated that patients receiving ERT increased their ability to sustain attention despite emotional distraction from pre- to mid-treatment, when attention skills are specifically cultivated. Further, this attention regulation change from pre- to mid-treatment significantly predicted reductions in anxiety and worry in addition to increases in mindful nonreactivity and social disability at posttreatment.⁷⁹

With respect to metacognitive regulation, in the 16-session open trial⁵⁷ self-reported reappraisal and decentering were examined as causally preceding symptom change throughout treatment. Findings indicated that improvements in decentering temporally preceded changes in worry and trait anxiety while improvements in reappraisal preceded reductions in worry, trait anxiety, and generalized anxiety symptoms⁸² were associated with increases in decentering and commensurate reductions in worry. Further, in another study,⁶⁰ we examined a commonly used explicit emotion regulation task⁸³ and found increased activation in neural areas associated with regulatory ability and corresponding increases in metacognitive abilities and decreased clinician-rated severity of MDD.

Finally, two recent publications derived from the 16-session ERT open trial⁵⁷ revealed ERT-linked patterns of resting state functional connectivity (rsFC) associated with areas of the salience network (SN; involved in orienting attention to external and internal stimuli and facilitating the integration of sensory, emotional, and cognitive information in service of optimal communication, social behavior, and self-awareness)⁸⁴ and areas of the default mode network (DMN; involved in autobiographical, self-monitoring, and social cognition functions).⁸⁵ Using seed-based rsFC with seeds placed in the SN (i.e., insular cortex) and DMN (i.e., posterior cingulate cortex [PCC]), pretreatment patterns of neural activation predicted clinical response to ERT with respect to gains in decentering and reductions in worry.⁸⁶ A recent follow-up once again using seed-based rsFC with seeds in the insula and PCC revealed ERT-linked changes in resting state connectivity which were associated with decreases in GAD and MDD diagnostic severity (r 's = 0.4–0.6) and increases in both attention and metacognitive regulation (r 's = 0.3–0.5).⁸⁷ Taken together, these preliminary findings provide initial support for our hypotheses that the salutatory effects of ERT result in part through normalization of emotion regulatory mechanisms.

Limitations

This review presents a contemporary conceptualization of distress disorders using an affective science framework. Our conceptualization is consistent with nosological models that group disorders based on similarities in observable surface level characteristics (e.g., anxiety vs. depression symptoms) but find conceptual utility in grouping disorders on the basis of fear versus distress symptoms.^{88,89} Given the more conceptual classification of distress disorders within the context of ERT, continued work is needed to test whether each of these disorders respond favorably to the treatments that focally target hypothesized underlying and shared characteristics. Although GAD and MDD have been extensively tested in previous trials of ERT with favorable outcomes, these trials have not examined PTSD specifically (although it was often comorbid). The mechanism studies described above are preliminary and do not fully test the mediating role of target mechanisms in producing ERT's ameliorative effects given limits in the number of assessment points, small sample size, and the absence of a comparison condition to control for maturation effects. Although ERT findings to date are promising, larger, more definitive trials with rich mechanism assessments across the entire range of distress disorders are an important next step.

Conclusions and Future Directions

Distress disorders are prevalent, result in considerable suffering and public health burden, are highly comorbid with one another, and are challenging to treat even when patients receive demonstrated medication and psychosocial interventions. Distress disorders are particularly difficult to treat given the presence of salient emotional responses and subsequent negative self-referential processes that exacerbate and maintain the symptoms associated with these conditions. We have emphasized the public health significance of distress disorders such as GAD, DYS, MDD, and PTSD given their prevalence and impact on functioning, economic burden, and health outcomes. Individuals who experience these conditions are more vulnerable to engaging in emotional and behavioral processes that may exacerbate the presence and experience of chronic stress in their lives. This process, in turn, reinforces the symptomology present in distress disorders, particularly the processes of worry, rumination, and self-criticism. ERT offers a blueprint based on affective science for improving intervention for these individuals by focusing on the motivational responses and corresponding regulatory characteristics common to their symptomology. This emphasis on affective science permits identification of mechanisms of treatment in terms of core disruptions of normative

motivational, regulatory, and resultant behavioral/learning factors, which in turn helps generate more targeted solutions to help clients utilize adaptive ways to cope or compensate for these core deficits. Although future research is needed to further identify the specific ways that it may ameliorate the psychological, physiological, and contextual aspects of chronic stress, previous trials of ERT have demonstrated considerable preliminary evidence for its ability to treat distress disorders and potential mechanisms that may underlie this efficacy. We also plan to use a dismantling approach to identify the way that specific skills in ERT may contribute to improvements in the purported mechanisms by examining whether briefer tailored intervention components can more precisely and specifically target the purported mechanisms of action. This work will allow us to better hone the treatment in identifying the way in which specific ERT skills, in isolation, promote changes in each purported mechanism of the intervention and thus independently contribute to reduction of symptom burden, distress, and impairment in distress disorders.


Declaration of Conflicting Interests


The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Dr. Renna was supported by NRSA T32CA229114-01 (PI: Shields). Dr. Fresco was supported by NHLBI Grant R01HL119977, NCCIH Grant R61AT009867, NIMH Grant R01MH118218, and NICHD Grant R21HD095099.

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References

1. McEwen BS. Stress, adaptation, and disease. Allostasis and allostatic load. *Ann N Y Acad Sci.* 1998; 840: 33–44.
2. McEwen BS. *Encyclopedia of Neuroscience. Subject Classification: Neural Basis of Behavior Stress and the Nervous System: Article Titles.* Academic Press, Cambridge, MA, USA; 2009: 557–561.
3. McEwen BS. Protective and damaging effects of stress mediators. *New Engl J Med.* 1998; 338: 171–179.
4. Gross JJ. Emotion regulation: current status and future prospects. *Psychol Inq.* 2015; 26: 1–26.
5. Gross JJ. The extended process model of emotion regulation: elaborations, applications, and future directions. *Psychol Inq.* 2015; 26(1): 130–137.
6. McEwen BS. Neurobiological and systemic effects of chronic stress [published online ahead of print April 10, 2017]. *Chronic Stress.* doi: 10.1177/2470547017692328.
7. Barlow DH, Ellard KK, Sauer-Zavala S, Bullis JR, Carl JR. The origins of neuroticism. *Perspect Psychol Sci.* 2014; 9(5): 481–496.
8. Mineka S, Watson D, Clark LA. Comorbidity of anxiety and unipolar mood disorders. *Ann Rev Psychol.* 1998; 49(1): 377–412.
9. Shackman AJ, Tromp DPM, Stockbridge MD, Kaplan CM, Tillman RM, Fox AS. Dispositional negativity: an integrative psychological and neurobiological perspective. *Psychol Bull.* 2016; 142(12): 1275.
10. Mennin DS, Fresco DM. What, me worry and ruminate about DSM-5 and RDoC? The importance of targeting negative self-referential processing. *Clin Psychol: Sci Pract.* 2013; 20(3): 258–267.
11. Ottaviani C, Thayer JF, Verkuil B, Lonigro A, Medea B, Couyoumdjian A, et al. Physiological concomitants of perseverative cognition: a systematic review and meta-analysis. *Psychol Bull.* 2015; 142(3): 231–259.
12. Blatt SJ. The destructiveness of perfectionism: implications for the treatment of depression. *Am Psychologist.* 1995; 50(12): 1003–1020.
13. Cacioppo S, Grippo AJ, London S, Goossens L, Cacioppo JT. Loneliness: clinical import and interventions. *Perspect Psychol Sci.* 2015; 10(2): 238–249.
14. Eisenberger NI, Cole SW. Social neuroscience and health: neurophysiological mechanisms linking social ties with physical health. *Nature Neurosci.* 2012; 15(5): 669–674.
15. Jackson JS, Knight KM, Rafferty JA. Race and unhealthy behaviors: chronic stress, the HPA axis, and physical and mental health disparities over the life course. *Am J Public Health.* 2010; 100(5): 933–939.
16. Sims M, Diez-Roux AV, Gebreab SY, Brenner A, Dubbert P, Wyatt S, et al. Perceived discrimination is associated with health behaviours among African-Americans in the Jackson Heart Study. *J Epidemiol Community Health.* 2016; 70(2): 187–194.
17. Greer TM, Brondolo E, Brown P. Systemic racism moderates effects of provider racial biases on adherence to hypertension treatment for African Americans. *Health Psychol.* 2014; 33(1): 35–42.
18. Greer TM. Perceived racial discrimination in clinical encounters among African American hypertensive patients. *J Health Care Poor Underserved.* 2010; 21(1): 251–263.
19. Forsyth JM, Schoenthaler A, Ogedegbe G, Ravenell J. Perceived racial discrimination and adoption of health behaviors in hypertensive Black Americans: the CAATCH trial. *J Health Care Poor Underserved.* 2014; 25(1): 276–291.
20. Clancy F, Prestwich A, Caperton L, O'Connor DB. Perseverative cognition and health behaviors: a systematic review and meta-analysis. *Front Human Neurosci.* 2016; 10: 534.
21. Watson D. Rethinking the mood and anxiety disorders: a quantitative hierarchical model for DSM-V. *J Abnormal Psychol.* 2005; 114(4): 522–536.

22. Krueger RF. The structure of common mental disorders. *Archives of general psychiatry*. 1999; 56(10): 921–926.
23. Watson D. Differentiating the mood and anxiety disorders: A quadripartite model. *Annual Review of Clinical Psychology*. 2009; 5: 221–247.
24. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch General Psychiatry*. 2005; 62: 593–602.
25. Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch General Psychiatry*. 2005; 62: 617–628.
26. Tyrer P, Baldwin D. Generalised anxiety disorder. *Lancet*. 2006; 368(9553): 2156–2166.
27. Hare DL, Toukhsati SR, Johansson P, Jaarsma T. Depression and cardiovascular disease: a clinical review. *Eur Heart J*. 2014; 35(21): 1365–1372.
28. Cohen BE, Edmondson D, Kronish IM. State of the art review: depression, stress, anxiety, and cardiovascular disease. *Am J Hypertension*. 2015; 28(11): 1295–1302.
29. Skilton MR, Moulin P, Terra JL, Bonnet F. Associations between anxiety, depression, and the metabolic syndrome. *Biol Psychiatry*. 2007; 62(11): 1251–1257.
30. Wolitzky-Taylor KB, Castriotta N, Lenze EJ, Stanley MA, Craske MG. Anxiety disorders in older adults: a comprehensive review. *Depression Anxiety*. 2010; 27(2): 190–211.
31. Murray CJ, Lopez AD. Measuring the global burden of disease. *New Engl J Med*. 2013; 369(5): 448–457.
32. Strine TW, Mokdad AH, Dube SR, Balluz LS, Gonzalez O, Berry JT, et al. The association of depression and anxiety with obesity and unhealthy behaviors among community-dwelling US adults. *Gen Hosp Psychiatry*. 2008; 30(2): 127–137.
33. Zen AL, Whooley MA, Zhao S, Cohen BE. Post-traumatic stress disorder is associated with poor health behaviors: findings from the heart and soul study. *Health Psychol*. 2012; 31(2): 194–201.
34. Rheingold AA, Acierno R, Resnick HS. Trauma, posttraumatic stress disorder, and health risk behaviors. In: Schnurr PP & Green BL, eds. *Trauma and health: Physical health consequences of exposure to extreme stress*. American Psychological Association; 2004: 217–243.
35. Davidson RJ, Sherer KR, Goldsmith HH. *Handbook of Affective Sciences*. Oxford, UK: Oxford University Press; 2009.
36. Barrett LF. The theory of constructed emotion: an active inference account of interoception and categorization. *Soc Cogn Affect Neurosci*. 2017; 12(1): 1–23.
37. Craske MG. The R-DoC initiative: science and practice. *Depression Anxiety*. 2012; 29(4): 253–256.
38. Gordon J. An experimental therapeutic approach to psychosocial interventions. *NIMH Director's Message*. 2017. <https://www.nimh.nih.gov/about/director/messages/2017/an-experimental-therapeutic-approach-to-psychosocial-interventions.shtml>
39. Campbell-Sills L, Liverant GI, Brown TA. Psychometric evaluation of the behavioral inhibition/behavioral activation scales in a large sample of outpatients with anxiety and mood disorders. *Psychol Assess*. 2004; 16(3): 244–254.
40. Klenk MM, Strauman TJ, Higgins ET. Regulatory focus and anxiety: a self-regulatory model of GAD-depression comorbidity. *Personal Individual Diff*. 2011; 50(7): 935–243.
41. Woody S, Rachman S. Generalized anxiety disorder (GAD) as an unsuccessful search for safety. *Clin Psychol Rev*. 1994; 14(8): 743–753.
42. Clasen PC, Wells TT, Ellis AJ, Beevers CG. Attentional biases and the persistence of sad mood in major depressive disorder. *J Abnorm Psychol*. 2013; 122(1): 74–85.
43. Botvinick MM, Braver TS, Barch DM, Carter CS, Cohen JD. Conflict monitoring and cognitive control. *Psychol Rev*. 2001; 108(3): 624–652.
44. Mogg K, Bradley BP. Attentional bias in generalized anxiety disorder versus depressive disorder. *Cogn Ther Res*. 2005; 29(1): 29–45.
45. Bernstein A, Hadash Y, Lichtash Y, Tanay G, Shepherd K, Fresco DM. Decentering and related constructs: a critical review and metacognitive processes model. *Perspect Psychol Sci*. 2015; 10(5): 599–617.
46. Fresco DM, Moore MT, van Dulmen MH, Segal ZV, Ma SH, Teasdale JD, et al. Initial psychometric properties of the experiences questionnaire: validation of a self-report measure of decentering. *Behav Ther*. 2007; 38(3): 234–246.
47. King AP, Fresco DM. A neurobehavioral account for decentering as the salve for the distressed mind. *Curr Opin Psychol*. 2019; 28: 285–293.
48. Buhle JT, Silvers JA, Wager TD, Lopez R, Onyemekwu C, Kober H, et al. Cognitive reappraisal of emotion: a meta-analysis of human neuroimaging studies. *Cerebral Cortex*. 2014; 24: 2981–2990.
49. Gohm CL, Clore GL. Affect as information: an individual differences approach. In: Barrett LF & Salovey P, eds. *The Wisdom in Feeling: Psychological Processes in Emotional Intelligence*. New York: Guilford Press; 2002: 89–113.
50. Mennin DS, Fresco DM. Emotion regulation therapy. *Handbook Emot Regul*. 2014; 2: 469–490.
51. Beck AT, Rush AJ, Shaw B, Emery G. *Cognitive Therapy of Depression*. New York, NY: Guilford Press; 1979.
52. Borkovec TD, Alcaine O, Behar E. Avoidance theory of worry and generalized anxiety disorder. In: Heimberg R, Turk C, & Mennin D, eds. *Generalized Anxiety Disorder: Advances in Research and Practice*. New York: Guilford Press; 2004.
53. Hayes SC, Pistorello J, Levin ME. Acceptance and commitment therapy as a unified model of behavior change. *Counsel Psychologist*. 2012; 40(7): 976–1002.
54. Linehan M. *DBT Skills Training Manual*. New York, NY: Guilford Press; 2014.

55. Segal ZV, Teasdale J. *Mindfulness-based cognitive therapy for depression*. 2nd ed. New York, NY: Guilford Press; 2018.
56. Mennin DS, Fresco DM. Advancing emotion regulation perspectives on psychopathology: the challenge of distress disorders. *Psychol Inq*. 2015; 26(1): 80–92.
57. Renna ME, Quintero JM, Soffer A, Pino M, Ader L, Fresco DM, et al. A pilot study of emotion regulation therapy for generalized anxiety and depression: findings from a diverse sample of young adults. *Behav Ther*. 2018; 49: 403–418.
58. Mennin DS, Fresco DM, Ritter M, Heimberg RG. An open trial of emotion regulation therapy for generalized anxiety disorder and cooccurring depression. *Depression Anxiety*. 2015; 32(8): 614–623.
59. Mennin DS, Fresco DM, O'Toole MS, Heimberg RG. A randomized controlled trial of emotion regulation therapy for generalized anxiety disorder with and without co-occurring depression. *J Consult Clin Psychol*. 2018; 86(3): 268.
60. Raab HA, Sandman CF, Seeley S, García E, Liston C, Fresco DM, et al. Greater prefrontal recruitment associated with clinical improvement and regulatory skills in generalized anxiety patients following Emotion Regulation Therapy: a pilot investigation. Under review.
61. DiNardo PA, Brow TA, Barlow DH. *Anxiety Disorders Interview Schedule for DSM-IV: Life Time Version: Client Interview Schedule*. Boulder, CO: Graywind Publications; 1994.
62. Meyer TJ, Miller ML, Metzger RL, Borkovec TD. Development and validation of the Penn State Worry Questionnaire. *Behav Res*. 1990; 28(6): 487–495.
63. Bieling PJ, Antony MM, Swinson RP. The State–Trait Anxiety Inventory, Trait version: structure and content re-examined. *Behav Res Ther*. 1998; 36(7–8): 777–788.
64. Beck AT, Steer RA, Brown GKJSA. Beck depression inventory-II. 1996; 78(2): 490–498.
65. Frisch MB, Cornell J, Villanueva M, Retzlaff PJ. Clinical validation of the quality of life inventory: a measure of life satisfaction for use in treatment planning and outcome assessment. *Psychol Assess*. 1992; 4(1): 92.
66. Leon AC, Olfson M, Portera L, Farber L, Sheehan DV. Assessing psychiatric impairment in primary care with the Sheehan Disability Scale. *The International Journal of Psychiatry in Medicine*. 1997; 27(2):93–105.
67. Nolen-Hoeksema S, Wisco BE, Lyubomirsky S. Rethinking rumination. *Perspect Psychol Sci*. 2008; 3(5): 400–424.
68. Applebaum AJ, Panjwani AA, Buda K, O'Toole MS, Hoyt MA, Garcia A, et al. Emotion regulation therapy for cancer caregivers—an open trial of a mechanism-targeted approach to addressing caregiver distress. *Transl Behav Med*. 2018.
69. O'Toole MS, Mennin DS, Applebaum A, Weber B, Rose H, Fresco DM, et al. A randomized controlled trial of emotion regulation therapy for psychologically distressed caregivers of cancer patients. *JNCI Cancer Spectrum*. 2019.
70. Hagedoorn M, Sanderman R, Bolks HN, Tuinstra J, Coyne JC. Distress in couples coping with cancer: a meta-analysis and critical review of role and gender effects. *Psychol Bull*. 2008; 134(1): 1.
71. Hodges L, Humphris G, Macfarlane G. A meta-analytic investigation of the relationship between the psychological distress of cancer patients and their carers. *Soc Sci Med*. 2005; 60(1): 1–12.
72. Cliff A, MacDonagh R. Psychosocial morbidity in prostate cancer: II. A comparison of patients and partners. *BJU Int*. 2000; 86(7): 834–839.
73. Northouse LL, Katapodi MC, Schafenacker AM, Weiss D, eds. The impact of caregiving on the psychological well-being of family caregivers and cancer patients. *Seminars Oncol Nurs*. 2012; 28(4): 236–245.
74. Kim Y, Shaffer KM, Carver CS, Cannady RS. Prevalence and predictors of depressive symptoms among cancer caregivers 5 years after the relative's cancer diagnosis. *J Consult Clin Psychol*. 2014; 82(1): 1.
75. O'Toole MS, Zachariae R, Renna ME, Mennin DS, Applebaum A. Cognitive behavioral therapies for informal caregivers of patients with cancer and cancer survivors: a systematic review and meta-analysis. *Psycho-Oncol*. 2017; 26(4): 428–437.
76. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983; 67(6): 361–370.
77. Etkin A, Prater KE, Hoelt F, Menon V, Schatzberg AF. Failure of anterior cingulate activation and connectivity with the amygdala during implicit regulation of emotional processing in generalized anxiety disorder. *Am J Psychiatry*. 2010; 167(5): 545–554.
78. Etkin A, Schatzberg AF. Common abnormalities and disorder-specific compensation during implicit regulation of emotional processing in generalized anxiety and major depressive disorders. *Am J Psychiatry*. 2011; 168(9): 968–978.
79. Renna ME, Seeley SH, Heimberg RG, Etkin A, Fresco DM, Mennin DS. Increased attention regulation from emotion regulation therapy for generalized anxiety disorder. *Cogn Ther Res*. 2017; 42(2): 121–134.
80. Buodo G, Sarlo M, Palomba D. Attentional resources measured by reaction times highlight differences within pleasant and unpleasant, high arousing stimuli. *Motiv Emot*. 2002; 26(2): 123–138.
81. Lang PJ, Bradley MM, Cuthbert BN. International Affective Picture System (IAPS): Technical manual and affective ratings. *NIMH Center Study Emot Attent*. 1997; 1: 39–58.
82. O'Toole MS, Renna ME, Mennin DS, Fresco DM. Changes in decentering and reappraisal temporally precede symptom reduction during emotion regulation therapy for generalized anxiety disorder with and without co-occurring depression. *Behav Ther*. 2019; 50(6): 1042–1052.
83. Ochsner KN, Ray RD, Cooper JC, Robertson ER, Chopra S, Gabrieli JD, et al. For better or for worse: neural systems supporting the cognitive down-and up-regulation of negative emotion. *Neuroimage*. 2004; 23(2): 483–499.
84. Menon V, Uddin LQ. Saliency, switching, attention and control: a network model of insula function. *Brain Struct Funct*. 2010; 214(5-6): 655–667.

85. Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. *Proc Natl Acad Sci*. 2001; 98(2): 676–682.
86. Fresco DM, Roy AK, Adelsberg S, Seeley S, García-Lesy E, Liston C, et al. Distinct functional connectivities predict clinical response with emotion regulation therapy. *Front Human Neurosci*. 2017; 11: 87.
87. Scult MA, Fresco DM, Gunning FM, Liston C, Seeley SH, García E, et al. Changes in functional connectivity following treatment with emotion regulation therapy. *Front Behav Neurosci*. 2019; 13: 1–14.
88. American Psychological Association. *Diagnostic and Statistical Manual of Mental Disorders*. Washington, DC: American Psychological Association. 2013: 133–137.
89. Krueger RF, Watson D, Barlow DH. Introduction to the special section: toward a dimensionally based taxonomy of psychopathology. *J Abnorm Psychol*. 2005; 114(4): 491–493.