

CHAPTER 19

Generalized Anxiety Disorder

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Generalized anxiety disorder (GAD) is a chronic and highly comorbid illness characterized by excessive and uncontrollable worry (Box 19–1). It is marked by a later onset than other anxiety disorders (Kessler et al. 2005) and is associated with fluctuations in symptom severity and impairment (e.g., Wittchen et al. 2000). It demonstrates both a low probability of recovery (32%–58%) and a high likelihood of recurrence (45%–52%)

(Rodriguez et al. 2006) over a 2- to 12-year period. GAD is associated with significant disability and impairment comparable to pure major depressive disorder (Hoffman et al. 2008) and can be more debilitating than pure substance use disorders, some anxiety disorders, and personality disorders, even after controlling for sociodemographic variables and comorbid conditions (Grant et al. 2005).

Box 19–1. DSM-5 Diagnostic Criteria for Generalized Anxiety Disorder

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- A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).
- B. The individual finds it difficult to control the worry.
- C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months):

Note: Only one item is required in children.

1. Restlessness or feeling keyed up or on edge.
 2. Being easily fatigued.
 3. Difficulty concentrating or mind going blank.
 4. Irritability.
 5. Muscle tension.
 6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).
- D. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism).
- F. The disturbance is not better explained by another mental disorder (e.g., anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder [social phobia], contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).

Individuals with GAD attempt to enhance their sense of control or preparedness through anticipation of negative outcomes or worst-case scenarios. They scan their environment for potential danger and negatively interpret neutral or ambiguous stimuli as threatening (Mathews and MacLeod 1994). Because of their lack of present moment focus, these individuals tend to ignore information in their immediate surroundings that could potentially challenge their distorted views (Borkovec and Newman 1998), which triggers emotional distress. This emotional distress is associated with many somatic features, including restlessness, fatigue, irritability, concentration difficulties, muscle tension, and sleep disturbance. Overall, GAD is a serious and costly mental illness with regard to degree of distress, disability and subsequent loss of work productivity, and quality of life (Newman 2000). Thus, targeted interventions are necessary to effectively address core symptoms and associated features.

In this chapter we discuss several empirically established approaches to treatment for GAD, including conventional

cognitive-behavioral therapy (CBT), pharmacotherapy, psychodynamic psychotherapy, and integrative psychotherapy.

A Cognitive-Behavioral Approach to Treating GAD

Because maladaptive patterns of thoughts and behaviors can be viewed as central to GAD, CBT has been extensively tested and has demonstrated efficacy; it is currently the best-established psychotherapeutic treatment. Within a CBT framework, change is promoted through identifying early anxiety triggers, challenging and disrupting individuals' misconceptions and factors maintaining worry, actively testing the validity of erroneous beliefs, using modified desensitization methods, reducing avoidance behaviors, improving skills to manage worry and anxiety, and developing more adaptive ways of responding to neutral and ambiguous situations (e.g., Newman et al. 2006).

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The initial steps in treatment involve educating patients about their symptoms and treatment goals in order to promote positive expectations and thereby enhance outcomes (Newman and Fisher 2010). Patients are then asked to engage in self-monitoring to recognize shifts in internal state and triggers for that state and to identify maladaptive patterns when reacting to perceived threats. Through this process, patients draw connections between their worries and their somatic states (e.g., muscle tension), distorted thoughts, and external triggers.

Once responses to perceived threats are identified, patients are asked to maintain a present focus and develop and implement cognitive, imagery, relaxation, and behavioral interventions to combat their habitual responses (Newman and Borkovec 2002). Cognitive restructuring involves learning the association between thoughts and emotions, identifying cognitive errors, and replacing these distortions with more accurate thoughts. Therapists then ask patients to practice challenging these cognitive distortions in their daily lives.

In addition to cognitive restructuring, relaxation techniques are used to address elevated anxiety. Patients are typically instructed to relax a series of muscle groups and engage in breathing exercises during and between sessions (Newman and Borkovec 2002). Coupling their thoughts with their autonomic state, patients are asked to simultaneously “let go” of their worries while they relax. Once patients have mastered relaxation, those techniques are combined with aversive imagery using self-

control desensitization (SCD). In SCD, patients imagine themselves encountering a worry trigger, and when they become anxious, they focus on relaxing away their stress response.

Borkovec and Ruscio (2001) evaluated the efficacy of CBT via a meta-analysis of 13 randomized controlled trials (RCTs) of CBT for GAD and found consistent outcomes across the studies. Although meta-analyses are limited by the quality of studies included, they generally adhere to uniformly applied criteria when selecting studies in attempts to reduce bias. Moreover, the validity of Borkovec and Ruscio’s findings was strengthened by incorporating studies that selected participants whose symptoms met the diagnostic criteria for GAD, included follow-up assessments 6–24 months posttreatment, and reported low attrition rates. Additionally, most studies used treatment protocols ($k=9$), conducted adherence checks ($k=8$), and measured nonspecific factors such as therapy expectancy and credibility ($k=8$). CBT significantly reduced anxiety symptoms by posttreatment (mean $d=2.48$), and gains were maintained for up to 2 years (mean $d=2.44$). CBT was also superior both to a wait list and no treatment ($d=1.09$) and to placebo psychotherapy at posttreatment ($d=0.71$) and follow-up ($d=0.30$). CBT was also superior to both cognitive therapy and behavior therapy alone at posttreatment ($d=0.26$) and follow-up ($d=0.54$).

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is d Cohen’s d ? 

Two more recent meta-analyses (Covin et al. 2008; Hanrahan et al. 2013) also examined the efficacy of CBT and yielded findings similar to those of

Borkovec and Ruscio. Covin et al. (2008) found that individual CBT ($d=1.72$) was more effective than group CBT ($d=0.91$), and the effect of CBT on worry was larger for young adults ($d=1.69$) than for older adults ($d=0.82$). CBT is also effective for children with anxiety disorders. For example, In-Albon and Schneider (2007) compared CBT for childhood anxiety disorders (excluding posttraumatic stress disorder and obsessive-compulsive disorder) with alternative therapies and control conditions. However, these investigators included studies ($k=24$) in which participants met diagnostic criteria for a variety of anxiety disorders, and they did not differentiate between anxiety disorders. They found that active CBT ($d=0.86$) was superior to a wait-list control condition ($d=0.13$). Individual and group therapy were also equally effective in children at posttreatment and follow-up, but results were mixed regarding the incremental efficacy of a parent-focused treatment component.

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Interpersonal and Emotional Processing Deficits in GAD

Dyadic relationships form a centerpiece to development, and disturbances in relationships commonly underlie anxiety and mood disorders. Interpersonal processes have been implicated in the development and maintenance of anxiety disorders. Individuals with GAD exhibit a heterogeneous variety of interpersonal problems marked by intrusive, exploitable, cold, and nonassertive characteristics (Przeworski et al. 2011). They are

more likely to have enmeshed relationships or engage in role reversal, such as the child or adolescent assuming parental responsibility (e.g., Cassidy and Shaver 1999), and they report a predominance of worry about interpersonal concerns and conflicts (Breitholtz et al. 1999). GAD is also more commonly associated with marital discord or dissatisfaction than any other anxiety disorder (Whisman 1999). These interpersonal areas of concern predict negative CBT outcomes, higher dropout rates, and reduced probability of remission (Borkovec et al. 2002). Furthermore, individuals with GAD report greater sensitivity to negative emotion (Llera and Newman 2010), increased emotional intensity (Mennin et al. 2005), and increased reactivity to negative emotional expression in others (Erickson and Newman 2007) when compared with individuals without anxiety.

Integrative Therapies

Several therapies have addressed these interpersonal and emotional processing deficits by adding interpersonal and emotional techniques to conventional CBT. Newman and colleagues (2004) developed an integrated treatment protocol that incorporates cognitive-behavioral, interpersonal, and emotion-based interventions with the aims of identifying dysfunctional relationship patterns and enhancing emotional processing (Newman et al. 2004). Findings from a randomized controlled trial comparing CBT plus supportive listening ($n=40$) with CBT plus interpersonal/emotional processing therapy (I/EP; $n=43$), using an additive design, indicated that both treatments were effective in reducing symptoms and that this symptom reduction was maintained at 2-year follow-up. In

addition, 69% of patients in the integrative treatment and 53% of patients receiving CBT achieved high end-state functioning at 2-year follow-up (Newman et al. 2011). The efficacy of I/EP might be improved by recent conceptualizations that individuals with GAD may use worry not to avoid emotion but rather to brace themselves for a potential negative outcome (see Newman and Llera 2011; Newman et al. 2013 for a complete review). This provides conceptual support for an additional exposure-based treatment for GAD, such that individuals with GAD can be exposed to negative emotional contrasts by eliciting a relaxed state prior to emotional exposure.

AUTHOR: 1) The in-text citation "Newman et al. 2013" is not in the reference list. Please correct the citation, add the reference to the list, or delete the citation. 

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The conceptualization of worry as a cognitive avoidance strategy (Borkovec et al. 2004) helped to motivate the development of other therapies. Targeting the heightened emotional intensity and maladaptive emotion regulation strategies characteristic of GAD, emotion regulation therapy proposes to address emotional avoidance through the integration of emotional components into a cognitive-behavioral framework (Mennin et al. 2006). Acceptance and commitment therapy (ACT) also aims to reduce reliance on emotional avoidance strategies, as well as decrease individuals' negative interpretations of their thoughts and increase their ability to en-

act behavioral change that conforms to their values and to focus on the here and now (Roemer et al. 2008). In a controlled examination of the efficacy of acceptance-based therapy for GAD, patients were randomly assigned to receive immediate ($n=15$) or delayed ($n=16$) treatment. ACT significantly reduced clinician-rated and self-reported GAD symptoms. ~~This improvement was maintained at 3 and 6 month follow-up.~~ Seventy-eight percent of participants no longer had symptoms that met criteria for GAD, and 77% achieved high end-state functioning at posttreatment (Roemer et al. 2008).

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Psychodynamic Psychotherapy

Ambivalence and difficulties with early attachments are theorized to play a role in the development and maintenance of GAD. In the absence of secure attachment during early developmental periods, individuals may view the world as threatening, uncontrollable, and unpredictable and underestimate their ability to cope with perceived stressors (Bowlby 1982). To enhance their sense of control, they may develop perfectionistic tendencies, seek excessive approval from others, and require constant reassurance regarding their worries. They may also present as self-conscious and overly conformist. Psychodynamic treatments for GAD have focused on patients' inability to tolerate letting their guard down and the insecure relational dynamics characteristic of GAD.

Crits-Cristoph and colleagues (1995) developed a short-term dynamic treatment for GAD based on supportive-expressive therapy (SET; Luborsky 2000). The SET model of GAD suggests that early traumatic events can influence the development of *schemas*, or mental representations of self, others, and the world, especially schemas about others' ability to successfully meet their interpersonal needs. Accordingly, individuals with GAD may exhibit uncertainty regarding the attainment of love, stability, security, and protection. Worry serves a defensive function for individuals with GAD, who are fearful of potential negative outcomes, leading them to avoid thinking about more emotionally salient issues (Borkovec et al. 2004). This avoidance perpetuates worry and maladaptive relational patterns.

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- 1) Please check the sentence beginning "Worry serves a defensive function...." Correct as edited? 
 - 2) Re: "especially schemas about others' ability to successfully meet their interpersonal needs": By their, do you mean the individual's? 
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Founded on a modified form of psychoanalytic principles, SET is guided by delineation of a core conflictual relationship theme (CCRT), which comprises 1) the wishes and needs of the GAD patient, 2) responses of the other, and 3) subsequent responses of the patient. The CCRT is not equivalent to the psychoanalytic concept of transference. In fact, the emphasis on CCRT distinguishes SET from traditional psychodynamic psychotherapy. SET works by helping patients to identify the CCRT across various areas of their lives and to understand how it relates to the anxiety

they experience. In SET, both supportive and expressive (insight-oriented) techniques are used to help deepen patients' understanding of their relationships and their connection to their anxiety. Patients also learn improved ways of coping with their feelings, expressing their needs, and responding to others. SET also emphasizes development of a positive therapeutic alliance to address emotional sequelae of an insecure attachment style.

In an open trial of brief SET (i.e., 16 weeks) for GAD, Crits-Cristoph and colleagues (1996) found that treatment significantly reduced participants' anxiety, worry, and interpersonal problems, thereby providing preliminary support for this brief psychodynamic psychotherapy for GAD. Leichsenring et al. (2009) further validated these results in an RCT, in which SET was found to result in significant improvement in GAD symptoms and interpersonal problems.

Pharmacotherapy for GAD

Among the first medications with demonstrated efficacy were the γ -aminobutyric acid (GABA) agonist benzodiazepines, such as alprazolam, diazepam, and lorazepam. Response rates in placebo-controlled trials have ranged from 45% to 66% (Baldwin et al. 2011a; Lydiard and Monnier 2004) with effect sizes across studies of 0.38 (Hidalgo et al. 2007). Although these medications are rapidly effective in short-term use, long-term use of these medications is controversial because of the potential for tolerance, dependence, withdrawal symptoms, sedation, and motor and cognitive abnormalities (Lydiard and Monnier 2004). Accordingly, benzodiazepines are

mostly recommended for treatment of acute anxiety symptoms.

Given safety concerns related to benzodiazepines, selective serotonin reuptake inhibitors (SSRIs) have been considered first-line pharmacological treatment (Katzman et al. 2011). Earlier studies indicated that buspirone (e.g., Rickels et al. 1982), a 5-HT_{1A} partial agonist, and imipramine (e.g., Rickels et al. 1993), a tricyclic antidepressant, demonstrated efficacy in treating GAD. Subsequently, the SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) have been shown to be efficacious for GAD on the basis of more than 20 randomized placebo-controlled trials. The SNRIs venlafaxine XR and duloxetine were demonstrated efficacious, with 60%–80% response rates for venlafaxine and 52%–65% response rates for duloxetine (e.g., Baldwin et al. 2011a). In controlled trials of SSRIs, response rates were between 62% and 81% for paroxetine and 52% and 78% for escitalopram, with a mean response rate of 63% in adult studies overall (Baldwin et al. 2011a; Lydiard and Monnier 2004). Overall effect size was 0.36 for the SSRI treatments (Hidalgo et al. 2007). The relative efficacy of different medications for GAD is not well established; however, in a recent meta-analysis fluoxetine was ranked first for response and remission and sertraline was ranked first for tolerability, which was higher than that of the SNRI treatments (Baldwin et al. 2011b).

AUTHOR: Paragraph above: Last sentence: Were rates for both fluoxetine and sertraline higher than for SNRIs (“both of which were higher . . .”)? Or just sertraline? 

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Pregabalin, a GABA analogue that depresses the release of excitatory neurotransmitters, has demonstrated efficacy for GAD in randomized placebo-controlled trials. It has been approved by the U.S. Food and Drug Administration for the treatment of seizures and fibromyalgia in the United States and was recently approved for the treatment of GAD in the European Union. Across studies, response rates for pregabalin ranged from 44% to 61%, although some studies did not find significant differences from placebo (Baldwin et al. 2011a; Lydiard and Monnier 2004). A recent meta-analysis found an overall effect size of 0.36 across seven placebo-controlled trials (Boschen 2011).

Comparative Efficacy of Treatments for GAD

Controlled investigations have compared CBT, psychodynamic therapy, and pharmacotherapy in the treatment of GAD. For example, Durham et al. (1994) and Leichsenring et al. (2009) tested forms of psychodynamic treatment against CBT for GAD. Durham and colleagues (1994) compared a non-manualized analytic therapy with manualized cognitive therapy (CT) and anxiety management training. Although CT appeared to be more effective than analytic psychotherapy, the lack of a manualized psychoanalytic treatment, lack of training of analytic therapists prior to the trial, and lack of evaluation of therapist adherence critically limited this study.

To help correct for nonequal comparisons, Leichsenring and colleagues (2009) compared manualized supportive-expressive therapy (SET) with CBT in the treatment of GAD. The treatments did not differ on the primary anxiety outcome measure, two additional measures of anxiety, and a measure of interpersonal dysfunction, although effect sizes at posttreatment and 6-month follow-up favored CBT over SET for GAD. However, CBT was superior to SET on measures of trait anxiety, worry, and depression. The latter findings may highlight CBT's core targeting of maladaptive thought processes such as worry. Nevertheless, given the very limited scientific literature evaluating efficacy of any form of dynamic therapy for GAD and the narrow range of the SET intervention for GAD in comparison with the wider range of dynamic therapy, it is premature to make definitive claims about differential efficacy.

In a comparison of the effectiveness of CBT versus pharmacotherapy for GAD, a meta-analysis that incorporated 65 controlled studies and used random effects modeling (Mitte 2005) revealed no significant differences in the effect sizes for anxiety reduction in CBT trials versus pharmacotherapy, suggesting no differences in efficacy between these two treatment types. However, attrition rates were higher in pharmacotherapy, indicating that CBT may be better tolerated. Notably, most of the pharmacotherapy studies in this comparison used benzodiazepines, which have demonstrated rapid short-term effects but less usefulness over time. There are only two small controlled studies directly examining combined pharmacotherapy plus CBT for GAD (Bond et al. 2002; Power et al. 1990), with mixed results. Specifically, Power and colleagues found that all CBT conditions (i.e., CBT alone, CBT

plus placebo, and CBT plus diazepam) were superior to diazepam and placebo conditions in reducing GAD symptoms. Conversely, Bond and colleagues examined brief psychotherapy (i.e., anxiety management training or nondirective therapy) combined with buspirone or placebo in the treatment of GAD. They reported no significant differences between treatment groups, with all groups demonstrating significant improvement in symptoms. Neither of these studies examined SSRI or SNRI medications. For GAD in adults, unlike for other anxiety disorders, there have been no collaborative trials of CBT and pharmacotherapy comparing the efficacy of the best-established forms of each treatment. However, the Child/Adolescent Anxiety Multimodal Study (CAMS; Ginsburg et al. 2011), a multisite clinical trial, examined the effect of sertraline alone, CBT alone, CBT plus sertraline, and clinical management with pill placebo in children and adolescents with separation, social, and/or generalized anxiety disorder. Participants in the CBT plus sertraline condition had significantly higher rates of remission than other conditions. This study incorporated a generalized treatment protocol and aggregated across anxiety disorders. Furthermore, one recent study offered individuals seeking SNRI treatment the option of additional CBT and found no additive effect beyond those treated with SNRIs alone who had refused CBT treatment (Crits-Christoph et al. 2011).

When a decision is being made regarding a course of treatment for GAD, it is important to consider the benefits and limitations of various treatment approaches. CBT is typically delivered over a relatively short period of time (e.g., 16 weeks), exhibits long-term effects, and teaches skills that can be used in every-

day life, but it does not typically focus on interpersonal issues. Accordingly, treatment providers may opt to conduct integrative treatments or brief dynamic therapy to focus on relational dynamics. However, psychotherapeutic approaches in general require more of a time commitment on the part of the patient. In CBT, for example, a patient must not only attend weekly sessions for at least several months but also participate in between-session homework. Conversely, pharmacotherapy is fast acting and effective in reducing acute anxiety. However, evidence suggests that the magnitude of these benefits may be lower for GAD than for other anxiety disorders (Hidalgo et al. 2007). While taking medication such as SSRIs, patients may experience significant side effects, which can include nervousness, sexual dysfunction, weight gain, drowsiness, and sleep problems (Baldwin et al. 2011a). Also, patients may require ongoing treatment to maintain benefits of medication. Therefore, it is important to consider and discuss all treatment options.

Comorbidity is an important issue in the treatment of GAD. Little is known about how CBT, psychodynamic psychotherapy, and pharmacotherapy compare in their effects on comorbidity as it relates to outcomes for GAD. However, CBT for GAD led to decreased rates of comorbid anxiety disorders and dysthymia (Borkovec et al. 1995; Newman et al. 2010). Also, presence of personality disorders predicted better outcome from nonmanualized brief psychodynamic psychotherapy than from SSRIs or SNRIs (Ferrero et al. 2007). Antidepressants are preferred over anxiolytics in part because of their broader efficacy in treating frequently comorbid mood disorders. Further research is needed to clarify how each of the therapies is affected by comorbidity.

Although randomized controlled trials have demonstrated the utility of many therapies in reducing GAD symptoms through clinically significant change, they are not effective for everybody (Newman and Borkovec 2002). Therefore, it is important not only to determine the most efficacious and long-lasting treatments for GAD and to consider maintenance treatment to enhance response and remission rates, but also to improve short-term treatments to boost acute-phase functioning and increase compliance.

Conclusion

The severity and pervasiveness of GAD, its fluctuating course, and the degree of associated functional impairment underscore the need for effective treatments. Various psychological and pharmacological treatments for GAD target specific cognitive, behavioral, affective, interpersonal, and physiological processes that have been implicated in the development and maintenance of this disorder. CBT, the most well established psychotherapy for GAD, generally includes such interventions as self-monitoring, relaxation training, and cognitive therapy directed toward negative appraisals. The efficacy of CBT in reducing core and related symptoms of GAD has been extensively documented in a series of randomized controlled trials. Investigations into the efficacy of CBT typically reveal average high-end-state functioning (i.e., no longer meeting criteria for GAD) in about 50% of participants. Therefore, conventional CBT models have been enhanced through incorporation of interpersonal, mindfulness, and emotional techniques to address additional areas of dysfunction not typically targeted in CBT protocols. To date, inte-

grative psychotherapy for GAD has been more successful in reducing anxiety symptoms and associated features, as demonstrated by increased rates of remission.

Likewise, brief psychodynamic psychotherapy for GAD (e.g., SET) has centered on elucidating patients' recurrent maladaptive relationship patterns and their relationship to their worry and anxiety. Although the one extant comparative efficacy study favored CBT over SET, empirical investigation of various models of psychodynamic treatment for GAD is still in its infancy.

Pharmacotherapy is another empirically established form of treatment for GAD. It can be used alone or in combination with psychotherapy and is effective in addressing acute worry and anxiety. The preferred pharmacotherapies of SSRIs or SNRIs are broadly effective for treating frequently comorbid depression.

Despite short- and long-term gains following various therapeutic interventions for GAD, treatments are being further developed and refined by conducting additive and dismantling designs that examine incremental validity of individual treatment components, exploring moderators and mediators of treatment, and investigating mechanisms of change across treatment approaches.

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