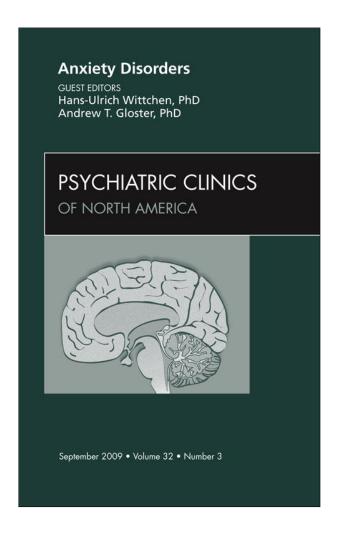
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Psychotherapy for Generalized **Anxiety Disorder:** Don't Worry, It Works!

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KEYWORDS

• GAD • Worry • Psychotherapy • CBT • Exposure

As described by Allgulander in this issue and by others. 1 generalized anxiety disorder (GAD) differs from other anxiety disorders. Patients do not fear a specific external object or situation, as in the phobias. There is no distinct symptomatic reaction pattern, as in panic disorder. The feared scenarios are not bizarre, improbable, or inflexible, as they often are in obsessive compulsive disorder. Avoidance, although central, is less obvious and often is prominent only on the cognitive-emotional level.^{2,3} Furthermore, the key component of GAD, uncontrollable and persistent worrying, is easily confused with the lay concept of worry.⁴ and the frequently occurring comorbid disorders often make the recognition of GAD difficult.⁵ These specifics highlight the challenge in treating patients suffering from GAD effectively with psychotherapy. On the other, research in the treatment of GAD has led to innovative, promising, and specific developments, such as massed worry exposure, 6 meta-cognitive therapy, 7,8 well-being therapy,9 and combination treatments based on a cognitive behavioral therapy (CBT) platform, 10,11 all of which deserve specific attention.

EVIDENCE FOR THE EFFICACY AND EFFECTIVENESS OF PSYCHOTHERAPY IN GENERALIZED **ANXIETY DISORDER**

As mirrored by recent comprehensive meta-analyses, 12,13 the majority of psychotherapeutic treatment studies for GAD compared CBT with a wait-list or a treatmentas-usual control group. CBT was usually effective, with a mean between-group effect size (Hedges's g) of 0.82 for anxiety measures across all studies. 13 On the basis of 12 studies with 162 patients, Hunot and colleagues¹² found a standardized mean difference (SMD) between CBT and wait-list/treatment-as-usual of -1.00 (95%)

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confidence interval [CI], -1.24 to -0.77). The standardized mean difference was large, ranging between 0.08 and 2.00, indicating that it is possible to achieve very favorable results but that such a response is not standard. Results for worry only, the core symptom of GAD, are similar, with an average SMD of -0.90 (see also¹⁴). Withingroup effect sizes are clearly higher (> 2),¹⁵ and it must be emphasized that, when GAD was the primary disorder, the majority of studies included comorbid mental disorders.

Hunot and colleagues¹² and Westen and Bradley¹⁶ summarize that about 50% of the GAD treatment completers and about 40% of the intend-to-treat samples achieve high end-state functioning after CBT for GAD. Psychopharmacological treatment was similarly effective. 12,13 In sum, CBT has clearly proven effective in GAD, but its effects nevertheless have been characterized as lower than in other anxiety disorders (eg, 10,16,17). It is unclear whether these skeptical evaluations are correct, because they do not take into account that the anxiety disorders differ in natural persistence and that GAD has been characterized as especially persistent. 18 Thus, the better improvement rates reported in other anxiety disorders may be attributable in part to a higher a priori probability of the disordered system to change (eg, in panic disorder). This possibility is also likely because everyone worries (ie, nonpathological worry is part of every person's psychological constellation), whereas this universality is not the case with panic attacks. As a result, typical outcome indices used in GAD studies may be less malleable than in other anxiety disorders. That said, a number of recently published randomized, controlled trials (RCTs) using CBT^{10,11,15,19,20} reach clearly higher within-group effect sizes than reported in the cited meta-analyses, with within-group effect sizes greater than 2 for the main outcome measures.

Another problem in evaluating previous findings is that many older studies fail to describe which specific CBT interventions and techniques were used. Instead, they often simply refer to a classic overarching book on the treatment of anxiety.²¹ In other trials, techniques were stipulated but were combined (eg, the trial by Borkovec and Costello²² combined applied relaxation, self-control desensitization, and brief cognitive therapy). Other common elements encompass self-monitoring of worrying, stimulus control, cognitive restructuring, and different forms of anxiety management.^{15,23} The finding of a global effect of such treatment mixtures makes it hard to understand which of the treatment elements contribute effectively to treatment success and should be optimized – and which do not.²⁴ Newer CBT approaches specifically designed for GAD are reviewed in more detail later in this article.

One specific CBT intervention, applied relaxation, ²⁵ also reached favorable results without being combined with other CBT techniques. ^{6,25–28} In applied relaxation, patients learn relaxation procedures that reduce autonomic arousal and are taught to use these procedures to cope better with situations in which they previously experienced excessive tension or worrying. The importance of this finding is that the effects are achieved without the exposure techniques usually applied in CBT for anxiety, and no element from cognitive therapy is integrated. ⁶

Only a few studies have systematically examined the efficacy of interventions for GAD from therapeutic orientations other than CBT (see ¹² for a comprehensive review). Until recently, there was only one controlled study for psychodynamic treatment in GAD. ²⁹ A new study by Leichsenring and colleagues ¹⁹ compared manualized short-term psychodynamic psychotherapy (STPP) and CBT for GAD. Both CBT and STPP yielded significant, large, and stable improvements in symptoms of anxiety and depression. Although no significant differences in outcome were found between treatments with respect to the primary outcome measure (anxiety symptoms as measured

by the Hamilton Anxiety Rating Scale;³⁰ effect size = 2.62 for CBT, effect size = 2.14 for STPP), CBT was superior to STPP on measures of trait anxiety, worry, and depression. Additionally, a third RCT testing STPP demonstrated the efficacy of a modified version of STPP, affect-focused body therapy.³¹

To summarize, there is clear evidence that the collection of interventions consistent with CBT theory is efficacious for adult patients who have GAD. Nevertheless, only some adult studies achieved extensive rates of improvement or remission. Further, preliminary evidence suggests that STPP can be effective, although it currently seems to be inferior to CBT in its ability to reduce trait anxiety, worry, and depression.

The results presented in the previous paragraphs come from RTCs that used structured diagnostic interviews with independent assessors and explicit treatment manuals and incorporated fidelity checks of treatment (eg, 12). The extent to which positive results derived under such conditions transfer to practitioners who may service a different patient population and have different supervision intensity remains to be investigated. Kehle³² demonstrated that CBT for GAD was effective for completers of a treatment delivered in a "frontline service setting," with favorable effect size for the reduction of worrying and depression. Only 28% (n = 8) of those originally intending to receive treatment (n = 29) actually completed treatment, however. In this study, treatment consisted of only eight manualized, highly structured sessions. For noncompleters (n = 21), CBT was not or was only marginally effective. On the other hand, CBT for GAD was highly effective in the private practitioner setting when 15 to 25 sessions were used. 19,20 These trials yielded effect sizes at the upper bound of those published to date, thereby demonstrating that CBT also can work in the natural setting, at least when quality monitoring is implemented at the level used in a RCT and treatment is not too short.

GAD typically develops during childhood and adolescence, often reaching clinical levels of symptom expression during early adulthood. Effective treatment for GAD in younger samples is therefore desirable, but RCTs are lacking in this specific age group. Two case series demonstrate that CBT might also be effective in youth and point to the need to enhance efforts to investigate more intensely early treatment approaches to GAD.

GAD is also the anxiety disorder with the highest incidence in older age.¹⁸ Six RCTs have examined CBT for GAD in elderly participants.^{12,36} The trials showed that anxiety symptoms, worry, and depression could also be effectively reduced in the elderly, and also in a primary care setting,³⁶ but the magnitude of effects on anxiety and depression symptoms was smaller in the elderly than in adult participants. Accordingly, the attrition rate was higher in elderly participants.

Furthermore, it has been demonstrated that four sessions of CBT combined with four sessions specifically designed to maintain well-being (well-being therapy) successfully prevented relapse in patients who had GAD and who had undergone pharmacological treatment. Finally, all trials that included follow-up assessments (of up to 1 year) indicated that treatment gains were maintained. Although maintenance of treatment gains thus has been better documented than in pharmacotherapy, longer follow-up intervals are desirable, given the "waxing and waning" nature of GAD. 18

Although all this evidence indicates that psychotherapy for GAD is efficacious in various forms, subgroups, and settings, major limitations in the present knowledge must be emphasized. First, long-term follow-up studies (with a follow-up interval of more than 1 year) are largely lacking (see²⁹ or¹⁵ for exceptions), leaving the duration of treatment gains unclear. Second, it is unclear which treatment elements are most effective and what changes in current treatments could further improve response

rates, treatment success, and transfer to specific populations and routine practice. Finally, because extant treatments based on different or even contradictory rationales achieve nearly equivalent outcomes, the mechanism(s) through which psychotherapy works remain unclear. This uncertainty signals the need for more theory-driven research.

NEW TREATMENT DEVELOPMENTS

Numerous efforts have been made in recent years to enhance symptom reduction and response rates in CBT. Efforts have centered either on targeting more directly the putative underlying core mechanisms of disorder^{6,8} or on broadening the range of interventions toward dysfunctional aspects of the patients' lives that previously were ignored or at least not explicitly targeted.^{10,11}

Massed Worry Exposure

Systematic exposure to worrisome thoughts operates on the assumption that worry functions as avoidant behavior. That is, worry is believed to prevent deeper, and often more aversive, emotional processing of thoughts and images, thus perpetuating worry via negative reinforcement.² To the extent that this assumption is correct, excessive worrisome thinking can be reduced by exposing the patient to the emotions and cognitions that are avoided during worrying episodes. This exposure traditionally is accomplished by first generating a fear hierarchy of worrisome thoughts, then having the client expose him-or herself to purposeful worry and corresponding images for an extended period (ie, 20-30 minutes). Gradually, the worry and images are increased in intensity. Conceptually, this procedure makes a great deal of sense, especially in light of the generally strong effects generated by exposure therapies in other disorders.³⁷ Recently, Hoyer and colleagues⁶ refined worry exposure and applied it as a massed exposure in sensu. In other words, patients were motivated to confront their worst worry imagery right away and to try to experience the accompanying anxiety as intensely as possible until habituation occurred rather than proceeding gradually through the stimulus hierarchy. It was demonstrated that this treatment, which directly targets the avoidance described in the avoidance theory of worry, 2 could be deployed successfully as a stand-alone treatment of GAD (ie, without the additional use of cognitive or relaxation interventions). Patients treated with massed worry exposure achieved stable improvement equal to applied relaxation.⁶ Furthermore, negative meta-cognitions about worry (ie, fearful cognitions that worrying could be debilitating) were reduced successfully. Although worry exposure was used as a singular treatment component to demonstrate that it is an active treatment ingredient, treatment efficacy might be increased by adding other empirically validated treatments components. It also is of theoretical importance that this treatment focused solely on worry and yet proved efficacious. This finding can be seen as strong evidence that clinical worry should continue to be regarded the core syndrome of GAD.

Meta-Cognitive Therapy

The psychological understanding of the clinically relevant forms of worrying is of vital importance for an adequate treatment planning in GAD.⁷ The meta-cognitive model of GAD⁷ asserts that individuals who have GAD, like most people, hold positive beliefs about worrying as an effective means to prevent negative things from happening (positive meta-cognitions). When worrying becomes inflexible and persistent, however, patients also begin to develop negative assumptions about worrying, most importantly beliefs and appraisals about the uncontrollability of worrying and about the

dangerousness of its consequences for personal functioning (negative meta-cognitions). According to the self-regulatory executive function theory, meta-cognitions guide cognition, emotion, and behavior.³⁸ The negative meta-cognitions about worrying both lead to an elevation in distress and worry and motivate counterproductive efforts to control, stop, or prevent worrying. As a consequence, interventions aiming at cognitive restructuring in meta-cognitive therapy do not target the multiple fearful beliefs and assumptions that patients who have GAD may have; instead, these interventions focus on the negative meta-cognitions about worrying. Short episodes of worry exposure are among the behavior experiments suitable for challenging dysfunctional meta-cognitive beliefs about worrying.⁷ In these episodes, patients learn that worrying is not harmful and that efforts to suppress worrying are superfluous. Because meta-cognitive therapy of GAD is based directly on a theory of disorder, this approach seems particularly elegant and promising, although independent validation is needed. Currently no controlled trials of meta-cognitive therapy in GAD exist, but an open trial with 10 patients achieved guite favorable results, including recovery rates of 87.5% at posttreatment and 75% at 6 and 12 months' follow-up.8

Interpersonal Aspects

Both applied relaxation and cognitive therapy, or a combination of both, led to significant changes in symptoms of anxiety and depression, but both procedures failed to improve interpersonal functioning.¹⁵ Because of this finding and the need to improve the moderate rates of high end-state functioning following treatment, CBT has begun to target interpersonal problems in addition to GAD symptoms. The additive interpersonal features concentrate on four areas: (1) current relationships, (2) origins of current interpersonal problems, (3) the therapeutic relationship, and (4) avoidance of emotion.² The authors suggest that these areas should be targeted strategically based on a functional analysis of the contingencies that shape and maintain the client's interpersonal problems. The theoretical rationale for targeting these factors is based on the assumption that a client's worry is associated with the tendency to avoid negative emotions and reactions from others. This avoidance, in turn, leads to protective behaviors that have the effect of shutting others out and keeping the patients from expressing their feelings and opinions. Recent data from an open trial 10 demonstrate the overall efficacy of the approach of integrating CBT with elements from interpersonal therapy and emotional processing and the incremental contribution of interpersonal emotional processing therapy (see also³⁹).

Acceptance and Mindfulness Techniques

Because worry is primarily verbal behavior, Roemer and Orsillo⁴⁰ hypothesize that procedures derived from theories of verbal behavior and stimulus equivalence (ie, mindfulness and acceptance and commitment therapy [ACT]),⁴¹ might increase the efficacy of treatment targeting chronic worriers. Some of the procedures used are found also in other CBT packages, including early cue detection, self-monitoring, and reduction of avoidance behaviors. ACT differs in its promotion of mindfulness and personal values and in the acceptance of problems rather than striving for direct change, which itself is conceptualized as a form of emotional avoidance. Mindfulness may be effective precisely because it brings worriers into the present as opposed to the future, where they spend so much time and where refutable evidence is not obtainable.⁴² Current data using ACT and mindfulness is preliminary but encouraging. Beyond a series of case studies⁴⁰ and a small open trial (n = 11),⁴³ an RCT¹¹ demonstrated very favorable effect sizes even in the intent-to-treat analyses: 86.7% of the

completers reached high end-state functioning at 9-month follow-up, and 76.5% no longer met diagnostic criteria for GAD.

Although these newer developments seem promising, direct comparison of these treatments and their effects is not possible because of differences in inclusion criteria, experience of therapists, and other differences that make it hard to identify which treatment is the best for a particular patient.⁴⁴ The active or even the indispensable ingredients in the treatment packages remain unknown—a quagmire addressed in the next section.

EVIDENCE FOR ACTIVE INGREDIENTS AND MECHANISMS

Given that GAD is a condition that involves interacting cognitive, emotional, and somatic components,³ a comprehensive package of CBT interventions can be expected to yield the highest therapeutic impact; however, comparison between a full CBT package and some if its components (ie, cognitive therapy alone; applied relaxation with self-control desensitization) failed to find clear superiority of the complex program and found no differences between the components. 15 Until additional methodologically rigorous component-control studies are funded and conducted that allow clear delineation of which techniques are active components and which are inactive or even iatrogenic,²⁴ the search for the most potent specific ingredients of CBT therapy will remain a matter of theorizing. Clear understanding of the mechanisms of therapeutic action is further frustrated by the different levels of abstraction and constructs that are used across studies. The different levels of target variables range from neurotransmitters and neurons to thoughts and meta-cognitions. When different terms are used to describe the same phenomenon, nonproductive debates can develop. In addition to more precise definitions, research is charged with the task of providing a clearer understanding of how each level of analysis adds explanatory and predictive value, thereby providing practitioners concrete information on which to base clinical decisions.

At the phenomenological level, patients who have GAD behave as if negative events should never happen in their lives unless they know ahead of time exactly what will occur. This attitude has been referred to as an intolerance of uncertainty, which has proven to be an important vulnerability factor for GAD. 45,46 But how can what these patients fear be better understood? What is at the core of their avoidance? Why do they find it necessary to avoid strong negative emotions and resort to using the subtle strategy of worrying? The answer to these questions is seldom clear for patients when they begin treatment, 6,47 as evidenced by patients' common description that they "fear something indescribable." When therapy begins, patients often state that they believe that they are incapable of coping with or even imagining their feared outcomes (eg, imagining the death of a loved one) and that such situations exceed their limits. They fear they might go insane when imagining these scenes. Such statements suggest that the apprehension centers around the anxiety about feeling "overwhelmed" in surprising situations characterized by negative outcomes with the likelihood of strong emotions. Because negative surprises are always possible, a state referred to as "anxious apprehension" ensues and can be present most of the time (more than 6 hours a day^{4,48}). It follows, then, that treatments work by counteracting anxious apprehension, be it by developing familiarity and tolerance of the feared emotions (eg, worry exposure), by restructuring assumptions about their feared consequences (eq. meta-cognitive therapy), by combinations of these mechanisms (eq, ACT; interpersonal and emotional processing therapy), or by teaching the patient skills to manage upcoming unintended apprehension directly (eg, applied relaxation).

Direct comparisons of these diverse efficacious techniques are needed to optimize future offers of treatment not only in terms of effect sizes but also in terms of attrition and applicability in practice.

Clues for understanding the mechanism of action can also be derived at the procedural level of analysis (eg, what a therapist does) and at the process level (eg, what interventions are thought to change). Procedures include nonspecific factors, such as talking, listening, and encouraging, that cut across treatment approaches and very specific factors, including the application of techniques previously described (eg, worry exposure, counteracting the tendency to avoid emotionally aversive, cognitive reframing, relaxation, and other techniques). Arguably, however, process analysis generates the most interesting debates, the resolution of which offers the greatest promise for improving current therapies. For instance, one theory of verbal behavior posits that therapeutic change occurs because the relational networks that exist between verbal stimuli have been altered so that the patient is more flexible to engage in value-laden behaviors while simultaneously abandoning inflexible value-inconsistent behaviors (eg, uncontrollable worry is replaced by the ability to stop and start worrying when doing so serves the patient's chosen values).⁴⁹ Testing these assumptions, however, requires complex mediational analyses: it must be demonstrated that the relational frameworks change first and that other positive changes follow. Similarly, in meta-cognitive theory it is assumed that the change of meta-cognition is the central element that precedes further change (eg, in the tendency to worry), an assumption that awaits empirical confirmation.⁵⁰

In summary, based on the present empirical evidence, it can be argued only that patients' subjective deficit—anxious apprehension surrounding a perceived inability to cope with ambiguous and catastrophized outcomes and the emotions associated with them—can be reduced by diverse strategies and that multiple pathways seem to reach the same end point.¹⁷ Or, as Borkovec and colleagues¹⁵ put it (p. 296): "targeting some response processes in therapy for a sufficiently long period of time might ... affect all the other processes involved in the therapy of anxiety." At the same time, there is no psychological therapy of GAD, including the STPP approach, that does not include an element which makes patients (at least subjectively) more competent to cope with strong emotions and feared negative outcomes.

SIMILARITY TO OTHER ANXIETY DISORDERS

The phenomenological characteristics of GAD may mislead researchers and clinicians alike. Among the factors that differentiate GAD from other anxiety disorders is the fact that observable avoidant behavior is less frequent and, when present, is more difficult to detect (eg, not reading the newspaper, not opening letters). As such, the status of GAD as an independent anxiety disorder has been questioned. Evidence for this position has included the fact that the diagnostic category of GAD is less reliable than other anxiety disorders, largely because of the difficulty of rating "uncontrollable" (as opposed to everyday) worry. Worry also is mistaken as simply a symptom of depression because its topographical characteristic of repetitive negative thinking is combined with the absence of clearly observable avoidance, it is easy to assume erroneously that GAD is simply a prodromal stage of depression, especially because patients who have GAD often develop subsequent depression. Sa

In contrast to these assumptions, evidence has accumulated that worrying can well be distinguished from depressive rumination.^{54,55} Furthermore, the fact that GAD often precedes depression is similar to other anxiety disorders⁵⁶ and can be explained

by the high and persistent impairment that is associated with GAD even when no other comorbid mental disorders exist.⁵⁷ Longitudinal epidemiological studies also show that the pattern of symptom development in GAD is more similar to other anxiety disorders than to depressive disorders.⁵⁸ Based on current evidence, the authors believe that GAD should be characterized primarily as a disorder of dysfunctional avoidance and remain subsumed under the category of anxiety disorders.

The categorization of GAD as an anxiety disorder is supported further by the approaches used to treat it. Although the effectiveness of a treatment alone cannot logically be used to understand the etiology of a disorder, it is clear that all treatments reviewed earlier in this article are basically treatments for anxiety (and not, for example, for negative mood). The targeted fear in GAD is less concrete than that seen in other anxiety disorders, but the experience or notion that this fear is not justified is part of all treatments described earlier.

WHAT NEEDS TO BE DONE TO MAKE IT BETTER?

It is generally agreed that therapy works better in some patients than in others. To find out which variables determine these different responses to treatment is more than complicated, however. To improve the treatment of GAD outcomes, prediction research needs to test hypotheses about the underlying mechanisms of change and the factors that influence these processes. This knowledge could directly inform treatment planning and increase the responder rates for those who complete treatment. But what are the moderators and mediators of change? Ideally, an examination of interventions for GAD would examine which intervention works best for a particular level of worry (eg, high versus medium versus low), with which comorbidities (either with other diagnoses or common dimensions), in which cluster of symptoms (eg, full-fledged GAD, subclinical GAD, or another primary diagnosis), in which situations and time frames (eg, proximal or distant threat), and with which therapeutic goals (eg, interpersonal conflicts, indecision, or poor performance). Furthermore, therapy time, format, and setting also must be taken into account. This list of response-modifying factors could easily be continued (see 50).

Unfortunately, little information exists at this level of analysis, and only a few studies have systematically analyzed the predictors of change in GAD. In his review, Durham⁵⁰ summarized that beyond the possible exception of symptom severity (which may predict not only treatment responsiveness but also the natural course), no other predictor of treatment change could be confirmed across studies. Only very few studies on the prediction of treatment success in GAD exist, and those that do indicate that homework adherence was associated positively with outcome as well as, contradictory to expectations, symptom severity and number of comorbid diagnoses.⁵⁹ Although based on pooled data from three trials of older adults, the results from this study nevertheless may not be robust as defined by consistent replication across multiple independent studies. Therefore one possibility for improving knowledge about treatment is increased coordination in prediction research across studies. Unfortunately, in the present research practice of psychotherapy for GAD, such coordinated research efforts do not exist.

One final critical consideration is that outcome prediction research often focuses primarily on outcome defined as the reduction of symptoms in those who complete therapy. Because efficacious treatments exist, such research should focus more on what is necessary to attract patients to treatment and to keep them in treatment and on whether the treatment is acceptable to therapists and patients.

ROUTINE CARE AND OBSTACLES FOR DISSEMINATION

Although GAD is common, patients who have GAD are less often seen in specialty anxiety clinics. ⁶⁰ Instead, patients who have GAD regularly seek help from general practitioners; their complaints may focus on the bodily symptoms associated with disorder, and the disorder itself may easily go undetected. ⁵ Few patients are diagnosed correctly, and even fewer are referred to psychiatric or psychotherapeutic treatment. This failure in diagnosis and referral is especially common in older adults who have GAD. ⁶¹ One necessary improvement, therefore, is to get more patients into the ideally suited treatment, and optimized screening tools may be part of this avenue. ⁵

As outlined in this article, the problems with the reliability of the diagnosis of GAD⁵¹ may result in part from the less pronounced and less discernible nature of the disorder. Nevertheless, the forthcoming revision of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM), the DSM-V, may help make GAD criteria more reliable and less complicated and make the use of this diagnosis easier in practice. Once the patient is referred to a psychotherapist, it still is not clear whether a modern and efficacious psychotherapeutic treatment will be offered. The data by Kehle³² indicate that patients in routine practice do not necessarily adhere to a CBT treatment, at least not when it is highly structured and condensed. The most efficacious treatments have been published only recently, and it makes sense to increase efforts to transfer them into practice as soon as possible.

SUMMARY

Although room for improvement exists, the psychological treatment of GAD should not be viewed pessimistically. Especially more recent innovative refinements of CBT methods^{8,11} yielded highly favorable recovery rates of up to 70% or 80% (depending on point of assessment). Treatment effects achieved using extant treatments therefore are no longer substantially worse than those for most other anxiety disorders. Nevertheless, future research is strongly encouraged to investigate assumed underlying mechanisms of action, mediators of change, and the length of therapy necessary to achieve change. Along this road, GAD, previously also described as "the basic anxiety disorder" (eg,⁶²), may serve as a paradigm for the intriguing study of what really makes "the worried mind" more calm.

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