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Nonpharmacologic Treatment of Generalized Anxiety Disorder: Put Your Mind to It

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Introduction

One of the most common mental health conditions, generalized anxiety disorder (GAD), affects 5 to 12 percent of the United States population.[1] For those in need of treatment, standard options are to pursue antidepressants or psychotherapy, the latter being an appealing choice for many as it aims to confront the foundational issues associated with GAD and involve the sufferer on a more personal level. Ralph Waldo Emerson once said, "Nothing can bring you peace but yourself." This sentiment may be particularly appropriate when considering people who experience GAD.

According to the DSM-V,[2] specific diagnostic criteria are required to make the diagnosis of GAD (see Table 1). As could be expected from examining these diagnostic criteria, GAD can have a profound impact on the lives of people who suffer from it. These negative effects include missed work days, increased sick time, increased consumption of healthcare resources,[3] possible poor health outcomes, the potential for polypharmacy, as well as negatively-impacted social and personal relationships. Given the morbidity associated with GAD, treatment is desirable. Currently available therapy for GAD generally consists of either psychopharmacology, usually with selective serotonin reuptake inhibitors (SSRIs) or other antidepressants or anxiolytics such as benzodiazepines, or nonpharmacologic modalities such as cognitive behavioral therapy (see Table 2).

Table 1: Diagnostic Criteria for Generalized Anxiety Disorder

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 6 symptoms (with at least some symptoms having been present for more days than not for the past 6 months): 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 stress 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 [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).

Source: American Psychiatric Association. *Diagnostic and statistical manual of mental disorders.* 5th ed. Arlington, VA: American Psychiatric Association; 2013:222.

Table 2: Nonpharmacologic Modalities for the Treatment of GAD

Cognitive Behavioral Therapy (CBT)*	Diet and lifestyle modifications
Mindfulness-Cognitive Behavioral Therapy (M-CBT)	Complementary and Alternative Medicines (CAMs)
Yoga	Exercise, moderate

*Most commonly utilized nonpharmacologic modality in GAD treatment
Source: Roseanna Pauli, PA-S

The adoption of nonpharmacologic modalities is an attractive option for many providers and patients alike because it decreases the likelihood of polypharmacy and the potential associated risks and adverse effects of certain medications. SSRIs and benzodiazepines can increase fall and fracture risk, impair cognitive processes, and benzodiazepines may additionally carry the risk of abuse or dependence.[4] Furthermore, the concept of "deprescribing" (lowering the pill burden and optimizing drug regimens) is gaining traction, especially in the elderly. Although not explicitly designated as diagnostic criteria, lack of control is often a feature of GAD that patients complain about, so self-determination of disease management is an important factor to consider when choosing among treatment options. Empowering patients by giving them a breadth of options to choose from may increase compliance and improve treatment outcomes.

Since GAD is usually a life-long disorder, selecting a therapy that is both effective and safe is essential. The relative safety of nonpharmacologic therapies compared to drug therapy, coupled with the preference to avoid medications, are factors favoring nonpharmacologic means for control of GAD. Whether one form of nonpharmacologic therapy is superior in efficacy to another, specifically whether

CBT is better in adult patients, is worth examining. In addition, because this disorder is chronic, the durability of therapeutic actions is important, for which reason evidence confirming symptom control for at least one year's duration is preferable.

Discussion

Medical literature was searched to examine whether CBT was better than other nonpharmacologic therapies. Terms such as "generalized anxiety disorder," "cognitive behavioral therapy," "nonpharmacologic treatment," and "mindfulness" were used. Several studies were discovered, including two relevant randomized trials, a pilot study, and five meta-analyses.

In the randomized controlled trial (RTC) by Wong et al, changes in anxiety levels were compared among 182 adults with GAD randomly assigned to Mindfulness-CBT (M-CBT), CBT-based psychotherapy, and usual care, which was considered unrestricted access to primary care services (no specific intervention).[5] M-CBT was conducted weekly for 8 weeks and included homework such as breathing exercises. The CBT-based psychoeducation group was similarly conducted, however specific teachings that may have enhanced mindfulness were avoided. Active intervention participants were followed for an additional 6 months, with outcome measures assessed at 8- and 11-months post-baseline. Both active treatment arms showed significant reduction in Beck Anxiety Inventory (BAI) scores compared to the usual care group, but no statistical significance between the two active groups was found, which surprised the authors who predicted that M-CBT would be superior. Limitations of this study were its small study size, the lower adherence in the M-CBT group, and the lack of long-term findings for the usual care group in which active treatment was eventually initiated. Additionally, some patients in the MCBT, psychoeducation, and usual care groups were on concurrent medical therapy for anxiety, which could skew results.

In a pilot study, Khalsa et al enrolled 32 adult patients with GAD and employed yoga-enhanced CBT (Y-CBT) in an effort to improve treatment outcomes.[6] Even though the number of patients was small, these patients were all formally diagnosed with GAD and had been treatment-resistant. Participants completed 3 sets of 6 weekly sessions and homework requesting them to practice techniques and rate their effects. Statistically significant improvements in anxiety were observed in these refractory patients, as well as improvements in comorbid symptoms of depression, panic, suicidality, sleep disturbances, sexual dysfunction, and poor quality of life. Important limitations of this study included its lack of ability to discern between the components of Y-CBT (yoga, mindfulness, CBT) and its very small sample size. However, evidence that previously treatment-resistant patients experienced significant improvements with these interventions is very encouraging.

In a second randomized trial, which is ongoing, Brenes et al are performing a two-stage randomized preference trial comparing the effectiveness of CBT with yoga for improving worry in 500 older adults with clinically significant worry, defined as "a chain of thoughts and images, negatively affect laden and relatively uncontrollable."[4(p169)] Participants were randomized to either the preference group or the random group, and then participants of each group were randomized to either to CBT or yoga for 10 weeks with 6 months follow up assessment. CBT is being conducted weekly, while yoga is being performed biweekly. Utilizing the generally conservative intent-to-treat analysis, how patient preference and choice of treatment options affected their efficacy was examined. This study was limited because participants were selected based on clinically significant worry rather than a formal clinical diagnosis of GAD. Although the results of this study are pending, the authors' previous study on late-life GAD found that patients wanted more nonpharmacologic options and preferred to choose which intervention to undergo.[7]

Several meta-analyses examined whether mindfulness-based therapy such as meditation, exercise, and CBT are effective in the treatment of GAD. The table below, Table 3, summarizes the meta-

analyses, their generalized findings, and their strengths and limitations. Some pitfalls to meta-analysis techniques include criteria for study selection, the quality of studies, reactivity effects, and other statistical suppositions. Additionally, some studies have strict diagnostic criteria while others focus on clinical symptom improvement.

Table 3: Meta-Analyses

Title and Author	Findings	Strengths and/or Limitations
The Effect of Mindfulness-Based Therapy on Anxiety and Depression: A Meta-Analytic Review (Hofmann et al)[8]	• Mindfulness-based therapy is moderately effective in improving anxiety and mood symptoms	• Good generalizability
Complementary Medicine, Exercise, Meditation, Diet, and Lifestyle Modification for Anxiety Disorders: A Review of Current Evidence (Sarris et al)[9]	• Strong support exists for lifestyle modifications, including the adoption of moderate exercise • Encouraging preliminary data for dietary improvements, including the avoidance of caffeine, alcohol, and nicotine • Tentative supportive evidence for acupuncture, massage, naturopathy (hampered by overall poor methodology) • Homeopathy is not supported • Kava has supportive evidence to reduce anxiety but risks include hepatotoxicity and lack of herbal standardization • Encouraging evidence to support mindfulness meditation, but insufficient evidence to support yoga and tai chi (scarce current research)	• Nonsystematic approach to data inclusion • Only English language studies were included • Intricate written analysis of the data was not possible due to publication space restrictions
Effect of Cognitive Behavioral Therapy for Anxiety Disorders on Quality of Life: A Meta-Analysis (Hofmann et al)[10]	• Solid evidence for benefit of CBT on improved quality of life (moderate number of rigorous studies) • Face-to-face CBT is significantly better than internet-delivered treatments	• Relatively small sample size • Limited generalizability • Different self-reported instruments used to measure the quality of life

How effective are cognitive behavior therapies for major depression and anxiety disorders? A meta-analytic update of the evidence (Cuijpers et al)[11]	• CBT is probably effective in the treatment of GAD (small number of high-quality studies) • Effects are large when compared to waiting list control groups, but small to moderate when compared to more conservative control groups such as care-as-usual and pill placebo	• Insignificant results could be due to a relatively small number of studies per disorder and the relatively large number of predictors
Exercise as Treatment for Anxiety: Systematic Review and Analysis (Stonerock et al)[12]	• The suggestion that exercise could be a useful, affordable, accessible treatment for anxiety (not many well-designed RTCs) • At present, the existing body of evidence is not of sufficient scientific rigor to recommend exercise as a treatment among individuals with clinically elevated anxiety	• Most studies had significant methodological limitations, including small sample sizes, concurrent therapies, and inadequate assessment of adherence and fitness levels

Source: Roseanna Pauli, PA-S

Most of the evidence in these meta-analyses supports CBT for treating GAD, while exercise, yoga, mindfulness, and lifestyle modifications may work as well. However, more research is needed to confirm the validity of these studies. At this time complementary and alternative medicines (CAMs) have only weak support because generalizability of these studies is limited and actual ingredient identification and potency in CAMs are not standardized. Furthermore, nonpharmacologic modalities for GAD are not often compared against each other, which gap in knowledge could be filled by RTCs designed to make these comparisons directly.

Conclusion

Classic CBT is the most widely accepted, studied, and understood nonpharmacologic modality utilized in the treatment of GAD. It has proven to be effective. Its application is probably best face-to-face, but internet-based approaches are used as well. Versions of CBT augmented with yoga, mindfulness, or other variations are effective as well, but the differentiating and weighting of the value of the individual

components is difficult. Additionally, research into their applications remains limited. Lifestyle modifications, exercise, and CAMs have shown some potential benefits, but clinicians may be hesitant to recommend them because substantial evidence for their efficacy is lacking. Furthermore, the duration of effectiveness has not been well studied in modalities other than CBT, a common shortcoming in the research. Conducting more head-to-head comparisons of CBT versus pharmacotherapies, with or without other modalities, for the treatment of GAD would be of considerable interest and could provide insight into which therapies have more durability.

Besides pharmacotherapy, CBT is the only empirically supported therapy for GAD. CBT's ability to reduce acute anxiety symptoms is well accepted. Furthermore, the effects of CBT have been shown to last up to two years following treatment.[13] Both patient preference and provider comfort play a role in the decision-making process of initiating various forms of therapy. While some patients may be eager to implement pharmacotherapy as a simpler, less demanding remedy, others may desire more self-determination and use of holistic approaches. On the contrary, some providers may not feel comfortable recommending or providing CBT without additional training. Implementing either or both of these approaches is reasonable. Availability and access to care are crucial for the delivery of CBT, as it often requires extra office visits, potential co-pays, dedicated time commitments, and sufficient patient motivation. CBT in its many forms, or even some of the other holistic approaches that do no harm, may be considered in patients with GAD or anxiety symptoms with or without pharmacotherapy.

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