Almost one third of US mental health care costs (approximately $50 billion) go toward the treatment of anxiety disorders. Conventional pharmacological treatments for anxiety are often beneficial but have limited efficacy. A meta-analysis of high-quality studies concluded that the efficacy of conventional drug treatments for anxiety disorders varies widely depending on the core symptom being treated. Frequency and severity of panic attacks tend to improve and remain improved in response to benzodiazepines; however, patients who regularly use these drugs are at significant risk for dependence and withdrawal symptoms. Elderly patients who use benzodiazepines are especially at risk for falling.

Phobias, obsessions and compulsions, and symptoms of posttraumatic stress are often poorly responsive to conventional drugs. In the context of efficacy and safety issues associated with conventional treatments for anxiety, psychotropics are the most studied nonpharmacological and integrative treatments for anxiety. In Part 1 of this article, I review research findings on the most substantiated nonpharmacological and integrative treatments for anxiety. In Part 2, I will discuss less substantiated but promising nonconventional approaches.

OVERVIEW
Positive research findings consistently support the use of kava and L-theanine in the treatment of persons with generalized anxiety. Regular relaxation, meditation, and mindfulness practices improve symptoms of generalized anxiety, and these nonpharmacological therapies may be safely combined with conventional drugs. Virtual reality graded exposure therapy (VRGET) will play a significant role in the treatment of many anxiety disorders that respond poorly to currently available treatments, such as drugs and cognitive-behavioral therapy (CBT). Numerous studies show that electroencephalographic (EEG) and electromyographic (EMG) biofeedback are as effective as regular relaxation training or mind-body practices for the treatment of moderately severe symptoms of generalized anxiety. A growing body of evidence supports the use of microcurrent stimulation of the CNS for the management of generalized anxiety.

Less-substantiated treatments for anxiety will be reviewed in Part 2 of this column and include dietary changes, supplementation with L-tryptophan or 5-hydroxytryptophan, regular exercise, massage, acupuncture (including electro-acupuncture), healing touch, and Reiki.

Unlike benzodiazepines and other conventional anti-anxiety treatments, L-theanine does not result in increased drowsiness, slowed reflexes, or impaired concentration.

Kava also interferes with norepinephrine reuptake and has a high binding affinity with y-aminobutyric acid (GABA) and N-methyl-D-aspartate (NMDA) receptors. Kava may also modulate vagal heart tone in patients with generalized anxiety. A systematic review of 11 controlled, double-blind studies that included more than 600 patients concluded that kava was superior to placebo for the short-term management of generalized anxiety. Randomized, controlled, double-blind studies support the use of kava preparations that are standardized to 70% kava lactones in divided doses of 70 to 240 mg/d for the treatment of “stress” and moderate anxiety but not for severe anxiety or agitation. Daily use of standardized kava preparations of 100 to 200 mg was found to effectively reduce anxiety symptoms associated with menopause.

Kava compares favorably with benzodiazepines and other conventional anti-anxiety drugs. The findings of a small, double-blind, controlled trial suggest that patients who have generalized anxiety who gradually increased their daily dose of kava (up to 300 mg) while tapering off a benzodiazepine did not experience worsening anxiety or benzodiazepine withdrawal. A randomized, placebo-controlled, multicenter study of 129 patients concluded that a standardized kava preparation (LI 150) was as effective as 2 commonly prescribed anti-anxiety agents (buspirone [BuSpar] and opioid [Insidon], which is commonly prescribed in Germany) for the treatment of generalized anxiety. Three fourths of patients in both the kava group and the conventional drug group experienced 50% or greater reductions in Hamilton Anxiety Scale scores and were classified as “treatment responders.” Kava is generally well tolerated, even at doses significantly above typical therapeutic doses. Uncommon adverse effects include GI upset, rash, headache, and dizziness. In recent decades, there have been reports of kava inebriation; although this social phenomenon has not been observed in Europe, where kava preparations are used medicinally to treat anxiety, Kava does not potentiate the effects of alcohol consumption in humans. Rare case reports suggest that kava may cross-react with benzodiazepines, increasing their sedating effects. Reports of hepatitis and fulminant liver failure have led to restrictions in the sale of kava products in many European countries and to a warning issued by the FDA. These cases were rare, however, and independent experts have concluded that most reported cases of liver failure were associated with a processing error that resulted in toxic levels of alkaloids in a single batch of kava.
been proposed to explain the anxiety-reducing effects of mind-body practices, including Benson’s relaxation response and Selye’s general adaptation syndrome. One model posits that anxiety is associated with muscle tension and is reduced by behaviors or cognitions that diminish tension and autonomic arousal. The effectiveness of relaxation as a treatment of various anxiety symptoms has been extensively reviewed.27

Guided imagery is widely used as a self-directed treatment of generalized anxiety. Applied relaxation techniques are often practiced together with mental imagery, meditation, or mindfulness training. Imagery can be individualized to the specific anxiety symptoms of each patient and is known to have beneficial effects on the immune system, physiological stress responses, and cognitive-emotional functioning in general.23 The consistent practice of mental imagery effectively reduces many kinds of anxiety symptoms, including generalized anxiety, feelings of panic, and traumatic memories.23,24 Imagery and relaxation techniques are often used together to induce hypnotic trance states, resulting in a dramatic reduction in symptoms of generalized anxiety.25

In a 5-month prospective study, patients with general anxiety randomized to a relaxation group versus a group treated with conventional antidepressants and relaxation experienced equivalent and significant improvements in state anxiety levels by the end of the trial.26 In a small controlled trial, 36 anxious adult outpatients randomized to 12 weekly sessions of applied relaxation or conventional cognitive therapy experienced significant and comparable reductions in anxiety.27

Combining relaxation with guided imagery is probably more effective than either approach alone. In an open trial, 60 women who reported anxiety and postpartum depression experienced significant reductions in both anxiety and depressed mood using a combined relaxation-guided imagery protocol during the first 4 weeks after childbirth.28 In contrast to the largely beneficial effects of relaxation on general anxiety symptoms, panic attacks are sometimes reported during applied relaxation exercises by those who have panic disorder.29

Yoga

Open studies and anecdotal evidence provide a strong argument for the therapeutic benefits of regular yoga practice among persons with generalized anxiety. Virtual reality graded exposure therapy

Controlled studies confirm that VRGET is more effective than conventional imaginal exposure therapy (ie, the use of mental imagery to provoke a feared object or situation) and has comparable efficacy to in vivo exposure therapy.46,47 Anxious or phobic patients are frequently unable to tolerate conventional exposure therapy and remain chronically impaired because they never become desensitized to a feared object or situation. As in imaginal exposure and in vivo therapy, VRGET has the goal of desensitizing the patient to a situation or object that would normally cause anxiety or panic.

Research findings support the use of VRGET as a treatment for many anxiety disorders, including specific phobia, generalized anxiety, panic disorder with agoraphobia, and posttraumatic stress disorder (PTSD).46 In a controlled study, VRGET and conventional CBT were equally effective in the treatment of panic disorder with agoraphobia; however, patients who underwent VRGET required 33% fewer sessions.32

Case reports and controlled studies have demonstrated the efficacy of VRGET for many specific phobias, including fear of flying,51,52 heights, animals, and driving.53-55 In one controlled study (N = 45), 65% of anxious adults who had a specific anxiety disorder according to DSM-IV criteria reported significant reductions in 4 of 5 anxiety measures.55 VRGET is as effective as conventional exposure therapy for fear of flying, and is more cost-effective because both patient and therapist avoid the expense and time commitments required for in vivo desensitization.51,53-55 In a preliminary study, persons who overcame fear of flying using VRGET combined with biofeedback (including respirations, galvanic skin response [GSR], and heart rate) were able to fly without the use of conventional medications or alcohol 3 months posttreatment.52

VRGET is also beneficial in traumatized patients in whom PTSD has been diagnosed. A virtual environment that simulates the devastation following the September 11, 2001, attacks on the World Trade Towers has been successfully used to treat individuals with severe PTSD.53

Emerging evidence suggests that combining VRGET with t-cycloserine, a partial NMDA agonist, results in greater improvement in acrophobic symptoms compared with treatment with VRGET alone. Findings from animal studies and a randomized clinical trial suggest that t-cycloserine functions as a cognitive enhancer by stimulating NMDA receptors, and may facilitate extinction of conditioned fear in patients with phobia.29 Twenty-eight patients with a DSM-IV diagnosis of acrophobia were randomized to receive either 500 mg of t-cycloserine or placebo in combination with 2 sessions of VRGET in a virtual glass elevator environment. Patients receiving t-cycloserine experienced significantly greater improvement in phobic symptoms than matched patients being treated with VRGET alone.46 This difference was noticeable 1 week following treatment and was maintained at 3-month follow-up. VRGET will become more available as technology costs continue to decrease, and it will probably become a widely used and cost-effective approach for outpatient treatment of panic attacks, PTSD, agoraphobia, social phobia, and other specific phobias. Several basic VRGET tools are available over the Internet, permitting mental health professionals to guide patients in the use of these computer-based advanced exposure protocols through real-time videoconferencing anywhere high-speed Internet access is available.46 In the near future, the integrative management of phobias, panic attacks, and other severe anxiety syndromes will combine VRGET, biofeedback, and pharmacological treatment in outpatient settings. Patients with severe phobia will also have the option of gaining access to Web-based VRGET tools via high-speed Internet connections.

Patients who are considering using VRGET should be aware of infrequent but significant safety issues. Fewer than 4% of people experience transient symptoms of dizziness, headache, and blurred vision when in a virtual environment. “Simulator sleepiness” is a feeling of generalized fatigue that occurs infrequently. Intense sensory stimulation during

Open studies and anecdotal evidence provide a strong argument for the therapeutic benefits of regular yoga practice among persons with generalized anxiety.
Anxiety Management

Continued from page 14

VRLG can trigger migraine, seizures, or gait abnormalities in persons who are prone to these medical conditions, and VRLGT is therefore contraindicated in these populations. Anxious patients who are actively abusing alcohol or narcotics should not use VRLGT. Patients who have disorders of the vestibular system should be advised against trying VRLGT. Patients with psychos ish should not use VRLGT because it is a potential virtual reality in a virtual environment can exacerbate depression and potentially worsen reality testing.

EMG, GSR, and EEG biofeedback training has nonspecific beneficial effects on many anxiety symptoms. EMG, GSR, and EEG biofeedback training are effective treatments for generalized anxiety. Patients with chronic anxiety trained in EEG or EMG biofeedback achieve symptom reduction that is similar to those taking conventional anti-anxiety medications.

The long-term benefits of EEG biofeedback for anxious patients have not been clearly established. One study evaluated 2 EEG biofeedback machines on patients complaining of anxiety and “burnout” in an addiction treatment center. Although patients experienced immediate reductions in state anxiety during biofeedback training, long-term effects of burnout were not maintained following discontinuation of treatment.

Microcurrent electrical stimulation

Microcurrent electrical stimulation, also called “cranial-electrotherapy stimulation” (CES), is an effective treatment for generalized anxiety. Quantitative EEG studies have confirmed beneficial changes in brain electrical activity when this approach is used. A meta-analysis of double-blind controlled trials comparing CES with a sham treatment (ie, electrodes applied, but with no current) concluded that measures of generalized anxiety improved in 7 of 8 studies, and the magnitude of improvement reached statistical significance in 4 of these. A larger review encompassing 34 sham-controlled trials conducted between 1963 and 1996 concluded that regular CES treatments resulted in short-term symptomatic relief of generalized anxiety symptoms by direct effect on the brain's electroencephalogram.

In a 10-week open trial of daily self-administered CES therapy in 182 individuals with DSM-III anxiety disorders, 73% of patients reported significant reductions in anxiety that were maintained at 6-month follow-up. Significantly, conventional drugs had failed in 25% of patients in the study, and 58% had received no previous treatment of any kind for their anxiety symptoms. In general, patients who received at least 4 to 6 CES treatments experienced more sustained reductions in anxiety than patients who received fewer treatments. The results of a small, double-blind, sham-controlled study (N = 20) suggest that a single CES treatment in patients who report generalized stress responses lead to beneficial changes in automatic arousal that are sustained at least 1 week following treatment, as measured by decreases in EMG and heat rate. Patients with one or more phobias reported significant reductions in state anxiety when exposure to the anxiety-inducing stimulus was followed by 30 minutes of CES treatment. A comparable reduction was achieved with CES and conventional anti-anxiety medications, suggesting that CES may be an effective approach for patients with phobia who wish to discontinue conventional drugs. Dr Lake is in private practice in Monterey, Calif, and is on the clinical faculty in the department of psychiatry and behavioral sciences at Stanford University Hospital. He chairs the American Psychiatric Association Caucus on Complementary, Alternative, and Integrative Care (www.apacan.org) and is author of the textbook of Integrative Mental Health Care (Thieme, 2006).
LEPSXOP® (escitalopram oxalate) TABLET/CERAL SOLUTION
Lepsxop is indicated for the treatment of depression in adults. 

1. Efficacy: Lepsxop is an efficacious, selective serotonin reuptake inhibitor (SSRI) and is indicated for the treatment of depression in adults. 

2. Duration of Treatment: The recommended duration of treatment for depression is 6-12 months. 

3. Patient Monitoring: Treatment should be initiated with a gradual increase in dosage over several weeks to avoid the risk of adverse events. 

4. Pregabalin: Lepsxop is not recommended as a monotherapy in patients with pre-existing or concurrent use of pregabalin. 

5. Interactions: Lepsxop is contraindicated in patients with a known hypersensitivity to pregabalin or any of its excipients. 

6. Pregnancy: Lepsxop is a SSRI and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. 

7. Lactation: Lepsxop is excreted in human milk. 

References: 


