Integrative Management of Anxiety

Program in Integrative Medicine
Tucson
January, 2007

James Lake M.D.
www.IntegrativeMentalHealth.net

Private practice, Monterey
Adjunct faculty, Stanford
Substantiated Non-conventional treatments of anxiety

- Most work done on non-conventional treatments addressing generalized anxiety, but relatively little research done on panic attacks, phobias, obsessions or compulsions.
- Kava-kava and L-theanine substantiated for generalized anxiety substantiated by research.
- Regular relaxation, meditation and mindfulness practice improve many symptoms of generalized anxiety, and may be safely combined with biological or energy-information therapies.
Virtual reality graded exposure therapy (VRGET) is a rapidly evolving modality will play a significant future role in the treatment of many anxiety symptoms that are poorly responsive to conventional psychological and pharmacological approaches.

VRGET is an effective and cost-effective treatment of generalized anxiety, social phobia, specific phobias and panic attacks.
Substantiated Rx (3)

- EEG and EMG biofeedback are probably as effective as regular relaxation training or mind-body practices for moderate symptoms of generalized anxiety.

- Use of micro-current stimulation for generalized anxiety supported by consistent research findings.
Provisional and possibly effective non-conventional Rx

- **Provisional** non-conventional treatments of anxiety include dietary changes, supplementation with L-tryptophan or 5-HTP, regular exercise, massage, EEG biofeedback training, acupuncture (including electro-acupuncture) and Reiki.

- **Limited research findings, anecdotal reports and inconsistent evidence** suggest that Passion flower extract, Ashwagandha, certain vitamins and minerals, the essential oils of Lavender and Rosemary, DHEA, certain Bach flower remedies, Healing Touch, QiGong, certain homeopathic remedies, paraspinal electrical stimulation, thought field therapy, and intercessory prayer are possibly effective treatments in some cases of anxiety.
Substantiated non-conventional Rx

- Kava kava
- L-theanine
- Meditation and mindfulness training
- Virtual reality graded exposure therapy
- EEG biofeedback
- Micro-current stimulation
Kava kava for generalized anxiety

- Used in traditional Polynesian culture for ceremonial purposes and as an inebriant.

  *In contrast to benzodiazepines*, when Kava is used at recommended doses (typically between 60 and 300mg/day) patients do not experience mental slowing or impaired cognitive functioning (Russell 1987).
Kava

- Animal studies suggest putative mechanism of action involves serotonin blockade in the amygdala by alpha-pyrone, a principle bioactive constituent.

- Interferes with norepinephrine reuptake and binds with GABA and NMDA receptors, both of which modulate anxiety.

Kava kava

- A Cochrane systematic review of 11 controlled double-blind studies including 600 patients concluded that Kava was superior to placebo for the short-term management of generalized anxiety (Pittler 2004).

- Double-blind studies and one meta-analysis (Singh and Blumenthal, 1996; Hansel 1996) support standardized Kava preparations (70% kava lactones) at doses between 70mg to 240mg/day for the treatment of “stress” and moderate anxiety, but not severe anxiety or agitation.
Early systematic review of 7 quality studies involving a total of 377 patients concluded that Kava 300mg/day is more effective than placebo in reducing non-psychotic anxiety states (Pittler 1998).

Daily use of standardized kava preparations 100-200mg/day effectively reduces anxiety symptoms associated with menopause (De Leo 2000).
Kava for generalized anxiety compares favorably to benzodiazepines and other conventional anti-anxiety drugs.

The findings of a small double-blind controlled trial suggest that generally anxious patients who gradually increase their daily dose of kava (up to 300mg/day) while tapering off of a benzodiazepine do not experience worsening anxiety or benzodiazepine withdrawal (Malsch 2001).
Kava

Multi-center DBRCT (N=129) concluded that a standardized Kava preparation (LI 150) was as effective as two commonly prescribed anti-anxiety agents (Buspirone™ and Opipramol™) in the treatment of generalized anxiety in outpatients (Boerner 2003).

75% of patients in both the Kava group and the conventional drug group were classified as “treatment responders,” and experienced 50% or greater reductions in HAM-A scores.
Kava—safety issues

- Kava is generally well tolerated even at doses significantly above usual therapeutic doses. Uncommon adverse effects include gastrointestinal upset, rash, headaches and dizziness (Schulz 2001).
- In recent decades there have been reports of Kava inebriation (Matthews 1988), although this social phenomenon has not been observed in Europe where Kava preparations are used medicinally to treat anxiety.
- Rare case reports suggest that Kava may cross-react with benzodiazepines increasing their sedating effects (Almeida 1996), but Kava does not potentiate the effects of alcohol consumption in humans.
Kava—safety

- Rare case reports of hepatitis (Escher 2001) and fulminant liver failure (Kraft 2002) have led to restrictions in the sale of Kava products in many European countries and a warning by the FDA.
- However, independent experts have concluded that most reported cases of liver failure were associated with a processing mistake resulting in toxic levels of alkaloids in a single batch of Kava (Waller 2002; Dragull 2003).
- Nevertheless, it is judicious to advise patients against taking Kava (Bone 1993) when there is a question of alcohol abuse or concurrent use of conventional sedative-hypnotics.
- One case report suggests that Kava may interfere with anti-Parkinsonian drugs (Izzo 2001).
L-theanine

- L-theanine is a constituent of Green tea which is widely used as a restorative in traditional Chinese medicine.
- Purified L-theanine extracted from Green tea is widely used to treat anxiety symptoms and depressed mood in China, Japan and other Asian countries.
- The calming effects believed to compensate for the stimulating effects of caffeine in Green tea (Kakuda 2000).
The anti-anxiety effect of L-theanine is achieved through enhanced alpha brain wave activity and increased synthesis of GABA (Juneja 1999; Kakuda 2000).

Increased GABA, in turn, increases brain levels of dopamine and reduces serotonin, resulting in general feelings of calm and well-being (Mason 2001).
L-theanine

- Changes in brain electrical activity are dose-dependent, and similar to EEG changes in meditation, including increased alpha waves in the occipital and parietal regions (Ito 1998).
- Calming effect usually noticed within 30 to 40 minutes after L-theanine is taken at a dose of 50 to 200mg, and typically lasts 8 to 10 hours.
- **Moderate anxiety** often improves with 200mg once or twice daily. **Severe anxiety** may require doses up to 600mg to 800mg daily taken in increments of 100mg to 200mg spaced over the day.
L-theanine—safety

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

There is *no risk of developing tolerance or dependence*, and there have been no reports of serious adverse side effects or interactions with other natural products or conventional synthetic drugs.
Applied relaxation

- Applied relaxation is a generic term for **somatic or mind-body exercises used to diminish generalized anxiety**.
- Relaxation techniques include sustained deep breathing, progressive muscle relaxation, guided imagery, and systematic desensitization (Davis 1982).
- Applied relaxation techniques often practiced together with mental imagery, meditation or mindfulness training.
Guided imagery

- Guided imagery is a commonly used self-directed treatment of anxiety.
- Imagery can be individualized to the specific anxiety symptoms of each patient.
- Guided imagery has beneficial effects on the immune system, physiological stress responses, and cognitive-emotional functioning in general (Achterberg 1985).
Mental imagery and relaxation

- Consistent practice of mental imagery reduces many kinds of anxiety symptoms, including generalized anxiety, panic and traumatic memories (Zahourek 1998; Achterberg 1994).

- Imagery and relaxation techniques often used together to induce hypnotic trance states resulting in a dramatic reduction in symptoms of generalized anxiety (Spiegel 1978).
Relaxation

- 5-month randomized prospective study anxious patients randomized to a relaxation group versus conventional antidepressants and relaxation reported *equivalent and significant improvements in state anxiety* levels by the end of the trial (Bernal 1995).

- Small RCT 36 anxious adult outpatients enrolled in 12 weekly sessions of applied relaxation vs conventional cognitive therapy experienced *significant and comparable reductions in anxiety* (Ost 2000).
Relaxation and guided imagery

- In an open trial 60 women with anxiety and post-partum depression reported significant reductions in both anxiety and depressed mood using a combined relaxation-guided imagery protocol during the first four weeks after childbirth (Rees 1995).

- Caution—in contrast to beneficial effects on generalized anxiety, panic attacks have been reported during applied relaxation by individuals diagnosed with Panic Disorder (Knott 1997).
Yoga (1)

- The **regular and skillful practice of specific yogic postures or breathing methods** results in sustained changes in brain activation, and possibly beneficial changes in neurotransmitter activity that manifest as a subjective state of alert calmness.

- Training in a particular style of yoga called *Sudarshan kriya yoga* involves a specialized breathing technique that decreases serum cortisol (Gangadhar et al 2000).
Yoga (2)

- Patients diagnosed with any anxiety disorder improve significantly when they combine a daily yoga practice with relaxation and mindfulness training (Miller 1995).

- Yoga reduces anxiety in patients with hypertension and epilepsy (Panjwani 1995; Chaudhary 1988), and probably reduces test anxiety (Malathi 1999).
Yoga (3)

- Preliminary evidence suggests that regular yoga practice reduces need for conventional drugs in generally anxious patients (Chaudhary 1988).

- Findings of a small controlled study showed that the regular practice of a specific Kundalini yoga left-nostril breathing technique significantly reduced symptom severity in patients diagnosed with obsessive-compulsive disorder (Shannahoff-Khalsa 1999).
Yoga—safety

- No absolute contra-indications to the practice of yogic postures or yogic breathing exercises.
- Rare case reports of fatal air embolism and basilar artery occlusion following vigorous Yogic practices.
- Patients with cardiovascular disease, chronic pain syndromes or other physical impairments should consult with their physician before undertaking Yoga or any mind-body training program that can potentially affect autonomic activity.
Meditation and mindfulness training

- Beneficial physiological effects of meditation include decreased oxygen consumption, respiratory rate and blood pressure, and decreased autonomic arousal (Delmonte 1985).

- Mindfulness-based stress reduction (MBSR) pioneered by Kabat-Zinn has been validated as effective for reducing the physical, emotional and cognitive consequences of chronic stress (Kabat-Zinn 1990).

- MBSR incorporates elements of different Eastern meditation practices and western psychology.
Meditation and mindfulness training


- 93% of patients (N=322) who started a 10-week MBSR program successfully completed it.

- The majority of those reported significantly decreased physical and emotional distress, improved quality of life, a greater sense of general well-being and increased optimism (Abbey 2004).
Meditation and mindfulness training

- Patients diagnosed with Irritable Bowel Syndrome (IBS) experienced significantly fewer symptoms of both IBS and anxiety when they engaged in two brief (15 min) daily sessions of mindfulness meditation (Keefer 2001).

- Increased self-awareness in the present moment through mindfulness training helps the anxious patient to make choices that permit avoidance of potentially stressful situations or engage in more effective coping when stress is unavoidable (Epstein 1999).
Virtual reality graded exposure therapy (VRGET)

- Anxious or phobic patients are frequently unable to tolerate conventional kinds of exposure therapy, and remain chronically impaired because they never become desensitized to a feared object or situation.
- VRGET is more effective than conventional imaginal exposure therapy and has comparable efficacy to in vivo exposure therapy (Pertaub 2001; Emmelkamp 2001).
- VRGET has the goal of desensitizing the patient to a situation or object that would normally cause anxiety or panic.
VRGET

- VRGET is an effective treatment of many anxiety symptoms including specific phobias, generalized anxiety, panic disorder with agoraphobia (Vincelli 2000) and post-traumatic stress disorder (Riva 2001).

- VRGET and conventional cognitive-behavioral therapy were equally effective in the treatment of panic disorder with agoraphobia, however patients who underwent VRGET required 33% fewer sessions (Vincelli 2003).

- Case reports and controlled studies have demonstrated the effectiveness of VRGET in many specific phobias including fear of flying (Rothbaum 2000; Wiederhold 2002), fear of heights, fear of small animals, fear of driving, and others (Rothbaum 1999; Glantz 1996).
VGRET

- 65% of anxious adults (N=45) diagnosed with a specific anxiety disorder reported significant reductions in 4 of 5 anxiety measures (Maltby 2002).

- VRGET is as effective as conventional exposure therapy for fear of flying, and is more cost-effective because both patient and therapist avoid significant time commitments and the need to use airplanes (Rothbaum 1999; Rothbaum 2000).

- Individuals who overcame fear of flying using VRGET combined with biofeedback were able to fly without the use of conventional medications or alcohol 3 months after treatment ended (Wiederhold 2002).
VRGET

- VRGET is beneficial for traumatized patients diagnosed with PTSD.

- A virtual environment that simulates the September 11, 2001 attacks of the World Trade Towers has been successfully used to treat individuals who suffered from severe PTSD following the attacks (Difede 2002).

- Combining VRGET with D-cycloserine, a partial NMDA agonist, results in greater improvement in acrophobia symptoms compared to VRGET alone.

- VRGET will soon become a widely used and cost-effective approach for the outpatient treatment of panic attacks, post-traumatic stress disorder, agoraphobia, social phobia and specific phobias.
VRGET

- VRGET tools are available on-line so that patients can use advanced exposure protocols at home through real-time videoconferencing where high-speed internet access is available (Botella 2000).

- Future integrative approaches to phobias, panic attacks, and other severe anxiety syndromes will combine VRGET with biofeedback in outpatient settings or in the patient’s home via broadband internet connections, with conventional CBT, mind-body practices, and conventional medications.
VGRET—safety

- Approx. 4% of individuals experience transient disorientation, nausea, 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 VRGET can trigger migraines, seizures or gait abnormalities in individuals who have these medical problems, and is contra-indicated in these populations.
VGRET—safety

- Anxious patients who abuse alcohol or narcotics should not use VRGET.
- Psychotic patients should not use VRGET because immersion in a virtual environment can exacerbate delusions and potentially worsen reality-testing (Wiederhold 2005).
Biofeedback

- EMG, thermal and EEG biofeedback training are effective treatments of generalized anxiety (Hurley 1992; Wenck 1996; Vanathy 1998).

- Clinical effectiveness of biofeedback training is probably equivalent to conventional relaxation techniques (Scandrett 1986; Roome 1985) for the management of generalized anxiety in both adults and children.

- Chronically anxious patients trained in EEG or EMG biofeedback achieve symptom reduction similar to those taking conventional anti-anxiety medications (Rice 1993; Sarkar 1999).
Biofeedback

- GSR biofeedback in combination with a relaxation technique improves anxiety more than relaxation alone (Fehring 1983).

- The *long-term benefits of EEG biofeedback for anxious patients have not been clearly established.*

- Addicts using EEG biofeedback in a residential treatment facility reported immediate reductions in state anxiety during biofeedback training, but *long-term effects on “burnout” were not maintained following discontinuation* (Ossebaard 2000).
Microcurrent electrical stimulation

- Micro-current electrical stimulation is an effective treatment of generalized anxiety.
- A meta-analysis of double-blind sham-controlled trials concluded that measures of generalized anxiety improved in 7 of 8 studies, and the magnitude of improvement reached statistical significance in 4 of these (Klawansky 1995).
- 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 mediated by direct effects on autonomic brain centers (DeFelice 1997).
10-week open trial of daily self-administered CES therapy in 182 individuals diagnosed with DSM-III anxiety disorders

73% of patients reported significant reductions in anxiety maintained at 6 month follow-up (Overcash 1999).

One fourth of patients had failed trials on conventional drugs, and 58% had received no previous treatment of any kind for anxiety.
CES

- Patients who receive at least 4 to 6 CES treatments experience more sustained reductions in anxiety compared to patients who receive fewer treatments.

- In a small double-blind sham-controlled study (N=20) a single CES treatment of patients with generalized stress results diminished autonomic arousal (EMG and heart rate) sustained at least one week following treatment (Heffernan 1995).
Patients diagnosed with one or more phobias reported significant reductions in state anxiety when exposure was followed by 30 minutes of CES treatment (Smith 1992).

Comparable anxiety reduction was achieved with CES and conventional anti-anxiety medications suggesting that CES may be an effective approach for phobic patients who wish to discontinue conventional drugs.

Hospitalized patients with histories of drug or alcohol abuse reported significant reductions in anxiety compared to matched patients who received sham CES (Schmitt 1986).
Provisional Rx

- Dietary modifications
- Ayurvedic herbs
- Amino acids
- Inositol
- Exercise
- Massage
- Music and binaural sound
- Acupuncture
- Reiki
Dietary modifications

- Individuals with anxiety related to reactive hypoglycemia report reduced anxiety with low carbohydrate intake, high protein, and avoidance of caffeine (Bell 1999).

- Caffeine consumption increases serum epinephrine, norepinephrine and cortisol levels, and can result in “nervousness” in healthy adults, or increased feelings of generalized anxiety or panic attacks in predisposed individuals (Uhde 1984; Charney 1985).

- Dietary deficiency in tryptophan leads to reductions in brain serotonin levels and more severe symptoms in individuals who report general anxiety or panic attacks (Klaassen 1998).
Ayurvedic herbs

- Ayurvedic herbal preparations containing *Bacopa monniera* and *Centella asiatica* have been traditionally used for millennia to treat symptoms that resemble generalized anxiety.

- Findings of DBRCTs suggest both herbs effectively reduce general anxiety symptoms (Stough 2001; Bradwejn 2000).

- Ayurvedic compound herbal formula called Geriforte™ may alleviate symptoms of generalized anxiety (Shah 1993).

- Adverse effects have not been reported when the above Ayurvedic herbals are used at recommended doses.
Amino acids—L-tryptophan and 5-HTP

- L-tryptophan and 5-HTP are widely used to treat generalized anxiety but few double-blind studies have examined efficacy.
- Both amino acids are essential precursors for serotonin synthesis.
- More extensive research literature on 5-HTP for anxiety than L-tryptophan.
- DBRCT (N=79) 58% of generally anxious patients randomized to L-tryptophan 3g/day reported significantly greater reductions in baseline anxiety compared to placebo (Zang 1991).
Amino acids—5-HTP

- Animal studies and human clinical trials show that 5-HTP has consistent anti-anxiety effects (Soderpalm 1990; Kahn et al. 1987).
- 5-HTP may inhibit panic attacks induced by carbon dioxide (Schruers 2000).
- Generally anxious patients randomized to 5-HTP and carbidoba reported significant reductions in anxiety comparable to clomipramine. No change in placebo group (Kahn 1987).
Amino acids—5-HTP

5-HTP may be safely combined with conventional anti-anxiety drugs with monitoring for serotonin syndrome.

- Adverse effect risk minimized when 5-HTP is started at 25mg/day and slowly increased over several weeks.

- Gradually increasing bedtime dose to 200mg-400mg reduces daytime anxiety and improves sleep quality in chronically anxious patients with insomnia.

- Greater research evidence, smaller effective doses and increased CNS availability make 5-HTP the preferred choice over L-tryptophan.
Inositol is a precursor of a second messenger, phosphatidyl-inositol, which is an integral part of receptors for serotonin, norepinephrine and other neurotransmitters.

DBRCTs suggest that high doses of inositol improve anxiety symptoms that respond to SSRI's, including panic attacks, agoraphobia, obsessions and compulsions (Belmaker 1998).

Conventional drugs are effective in only two thirds of patients who report panic attacks (Palatnik 2001).

Inositol in doses up to 20g/day reduces the severity and frequency of panic attacks by interfering with one of the physiological causes of panic (m-CPP) (Benjamin 1997).
Inositol

- 4 week DB crossover study (inositol 12 g/day) and imipramine, showed *equal efficacy in reducing frequency and severity of panic attacks and agoraphobia* (Benjamin 1995).

- A one month DBRCT (N=20) concluded that inositol (up to 18g/day) and fluvoxamine (up to 150mg/day) had *similar efficacy in reducing the frequency of panic attacks* (Palatnik 2001).

- The average weekly panic attacks in inositol group decreased by 4 vs decrease by 2 in fluvoxamine group.

- *Adverse effects not reported with recommended doses of inositol.*
Exercise

- Open studies *suggest* that regular aerobic exercise or strength training improves anxiety (Paluska 2000).
- 20 to 30 minutes of daily exercise significantly reduces symptoms of generalized anxiety (Osei-Tutu 1998).
- Prospective 10 week study of exercise in panic-prone individuals *suggests* that regular walking or jogging (4 miles three times a week) reduces severity and frequency of panic attacks (Stevinson 1999).
- *Caution* if heart disease or chronic pain.
Massage

- Anxiety reducing effects of massage probably mediated by decreased cortisol and increased parasympathetic tone (Acolet 1993; Serepca 1996).
- Anecdotal evidence, a established history of widespread use for stress reduction, and positive findings of many open trials support use of regular massage therapy for Rx of chronic moderate anxiety, and anxiety related to test-taking, work stress or the anticipation of invasive medical procedures (McKechnie 1983; Shulman 1996; Field 1996; Okvat 2002; Kim 2002).
Music and binaural sound

- Music and sound are used in many cultures and healing traditions for their anxiety-reducing benefits.
- In a randomized study anxious adults assigned to music-assisted reframing vs cognitive therapy experienced greater reductions in overall anxiety (Kerr 2001).
- Binaural listening routes slightly different sound frequencies to the right and left hemispheres. The brainstem “constructs” binaural beats on the basis of inter-hemispheric frequency difference.
- Some binaural beats induce a calm, relaxed state (Atwater 1999).
- The therapeutic use of sound frequency patterns to achieve different therapeutic goals is analogous to the use of different EEG biofeedback protocols.
Acupuncture and acupressure are widely used in Asia and Western countries to treat anxiety. Extensive case reports suggest that different acupuncture protocols are beneficial for symptoms that resemble generalized anxiety and panic attacks (Flaws 2001). To date few small prospective DBRCTs are positive. Most studies on the anxiety-reducing effects of acupuncture examine general benefits of acupuncture on diverse cognitive, affective and behavioral symptoms, including anxiety.
Acupuncture

- Narrative review of controlled studies, outcomes studies and published case reports on acupuncture for anxiety and depressed mood (British Acupuncture Council 2002).
- Sham-controlled studies yielded consistent improvements in anxiety using both regular acupuncture and electro-acupuncture.
- Significant differences between protocols in both regular and electro-acupuncture pointing to general beneficial effect or possibly a placebo effect.
Positive findings of most controlled studies *suggest* general anxiety-reducing effect, but inconclusive because of design flaws: absence of standardized symptom rating scales, limited follow-up, and poorly defined differences between protocols used in different studies.
Acupuncture

DBRCT (N= 36) mildly depressed or anxious patients randomized to an acupuncture protocol for anxiety vs sham protocol. HRV and mean heart rate measured at 5 and 15 minutes after treatment.

- Resting heart rate significantly lower in the treatment group but not the sham group, HRV changes suggested modulated autonomic activity and reduced overall anxiety. (Agelink et al. 2003).
Acupuncture

- DBRCT (N=55) adults (not diagnosed with an anxiety disorder) randomized to bilateral auricular acupuncture protocol based on “shenmen” point (the “relaxation” point)—vs sham point. Acupuncture needles remained in place for 48 hours.

- The “relaxation” group was significantly less anxious at 30 minutes, 24 and 48 hours, but no significant inter-group differences in blood pressure, heart rate or electro-dermal activity (Wang 2001).
Acupuncture

- Small DBR sham-controlled trial 85% adults with anxiety and moderate depression reported significant anxiety reduction following 10 sessions using specific acupuncture points (Du.20, Ex.6, He.7, PC.6, Bl.62) (Eich 2000).

- Rare transient adverse effects of acupuncture include bruising, fatigue and nausea.

- Very rare cases of pneumothorax have been reported.
Reiki

- Two studies *suggest* that regular Reiki treatments reduce severity of anxiety in chronically stressed individuals (Heidt 1981; Kramer 1990).

- Patients with mixed anxious depressed mood reported significant relief following weekly treatments with contact or non-contact Reiki (Shore 2004).
Reiki

- 120 chronic pain patients randomized to Reiki, sham Reiki, progressive muscle relaxation and no treatment (Dressen 1998).

- Improvements in state anxiety (and pain) in patients receiving Reiki were significantly greater than the other three groups.

- Findings limited because of possible unreported differences in the use of anti-anxiety medications between Reiki treatment groups and control groups.