Beyond the Prescription Pad: Approaches to Anxiety

Victoria Maizes MD

Executive Director
University of Arizona Center for Integrative Medicine
Professor of Medicine, Family Medicine and Public Health





Patient case

Anxiety incidence

- Anxiety disorders are extremely common
 - ➤ 40 million American adults per year (18% of our total population)
- Children and adolescents rate ranges from 2-24%
 - most common anxiety disorders in children are Generalized Anxiety Disorder and Social Anxiety Disorder

Anxiety Diagnoses

- Generalized anxiety disorder (GAD)
- Panic attacks
- Phobias
- Obsessive-compulsive disorder
- Post-traumatic stress disorder

Creating an Integrative Treatment Plan

- 1. Screen for medical conditions that mimic anxiety
- 2. Investigate and adjust or remove medications or supplements that could be contributing to anxiety
- 3. Initiate lifestyle changes
- 4. Explore mind-body approaches
- 5. Discuss risks and benefits

Could it be something else?

- Hypo- or hyperthyroidism
- Vestibular dysfunction
- Congestive heart failure
- Cardiac arrhythmia
- Chronic obstructive pulmonary disease
- Pneumonia

- Hyperventilation
- Vitamin B12deficiency
- Porphyria
- Neoplasms
- Pulmonary embolism
- Pheochromocytoma
- Hyperadrenalism
- Overdose?(methamphetamine,

cocaine, stimulant medication)

- Lead toxicity
- Pesticide exposure

Medication or Supplement Side Effects

- Sympathomimetics
- Beta agonists
- Corticosteroids
- > Thyroid hormones
- Estrogen, or oral contraceptives in sensitive patients
- Stimulant or non-stimulant drugs to treat ADHD
- > OTC medications that contain large amounts of caffeine
- Coffee, tea, colas, and energy beverages: Red Bull, 5-Hour Energy, AMP Energy, Full Throttle, Monster, Rockstar, etc.

Conventional Therapy

- Medications
- Benzodiazepine

S

- > SSRIs/SNRIs
- Beta blockers
- Psychotherapy

Limitations of existing medications

- Benzodiazepines
 - Addiction
 - Dependence
 - Hard to wean off
 - > Falls
 - Cognitive changes
 - Long term ineffective

- > Anti-depressants
 - Transient headache and nausea
 - Drowsiness
 - Agitation
 - Weight gain
 - Anorgasmia

Psychotherapy

- Cognitive Behavioral Therapy (CBT)
 - ▶ persons with GAD tend overestimate and catastrophize negative events; show limited confidence in problem solving; and have a low tolerance of uncertainty
 - ➤ CBT: uses cognitive skills that encourage evidencebased thinking, which lessen attentional biases to threat. CBT encourages a problem-coping focus, as well as behavioral skills for enhanced decision making and time management



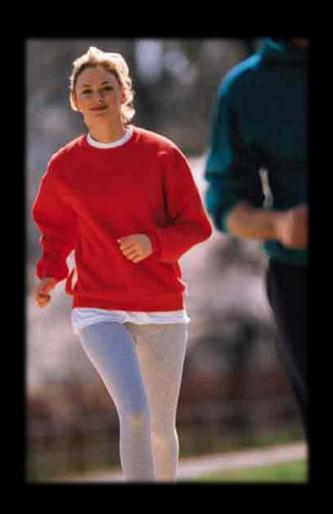
"It's a special hearing aid. It filters out criticism and amplifies compliments."

Non-pharmaceutical approaches

- Physical activity
- Address diet
- Mind Body Approaches
- > Improve sleep
- Consider Supplements and Botanicals
- Consider traditional Chinese medicine or massage

Exercise

- Mechanisms are still under investigation
 - May be mediated through neurobiological adaptations
 - Increased availability of neurotransmitters including serotonin and dopamine
 - Positive effects on HPA axis reactivity to stressors





Aerobic Exercise Training

➤ 242 women with breast cancer randomized to wait list, resistance training, or aerobic exercise training concomitant with chemotherapy

> Results:

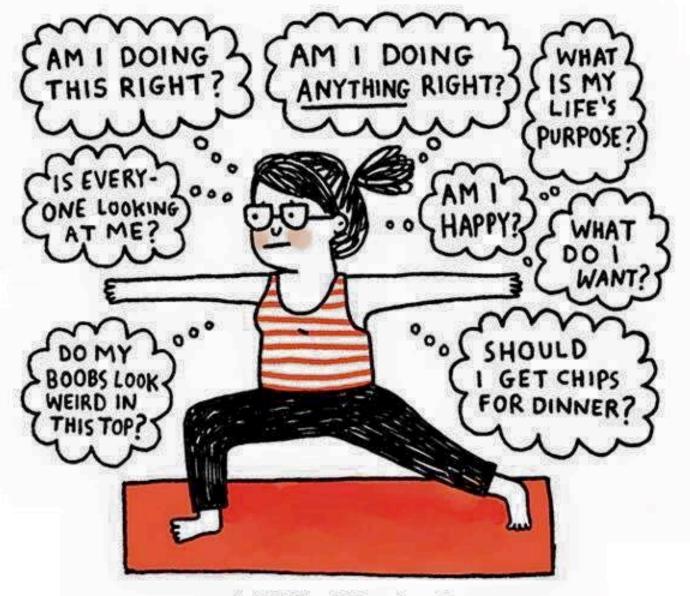
- aerobic group reported significantly lower anxiety
- patients who continued combined resistance/aerobic exercise training program after treatment period experienced continuing improvements in quality of life and reduction in anxiety

Courneya KS et al. Six-month follow-up of patient-rated outcomes in a randomized controlled trial of exercise training during breast cancer chemotherapy. *Cancer Epidemiol Biomarkers Prev.* 2007 Dec;16(12):2572-8.



Yoga for anxiety

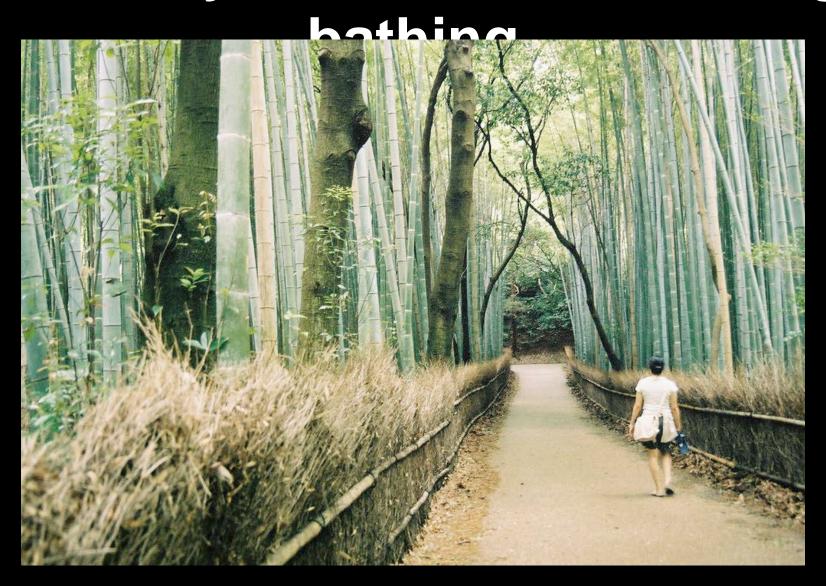
- ➤ 9 women enrolled in an 8-week, 90 min twice weekly lyengar yoga program vs wait list group
 - evaluated diurnal salivary cortisol levels, emotional well-being, and fatigue
 - yoga group had lower cortisol levels, improved emotional well being, and reduced fatigue scores
- 3-month biweekly yoga program with 200 breast cancer survivors:
 - ➤ significant improvements in fatigue, vitality and inflammatory markers (i.e., IL-6, IL-1*B, TNF*~*a*) compared to wait list control



WORRIER POSE

Gemma CORRELL

Shinrin-yoku or Forest Bathing





Tai Chi

- Study of 38 adults -
 - ➤ 20-min Tai chi/yoga class
 - ➤ standing Tai chi movements, balancing poses and a short Tai chi form and 10 min of standing, sitting and lying down yoga poses
 - ➤ State Anxiety Inventory pre/post 20 minute Tai Chi class combined with yoga
 - Overall increase in EEG theta activity
 - Reduction in self reported anxiety symptoms

Tai chi

- Meta-analysis of 40 studies totaling 3,817 subjects
 - 29 psychological measurements
 - ➤ 21 of 33 randomized and nonrandomized trials reported that 1 hour to 1 year of regular Tai Chi significantly increased psychological well-being including reduction of stress (ES, 0.66; CI, 0.23 to 1.09), anxiety (ES, 0.66; CI, 0.29 to 1.03), and depression (ES, 0.56; CI, 0.31 to 0.80), and enhanced mood (ES, 0.45; CI, 0.20 to 0.69)
 - 7 observational studies: beneficial association between tai chi and psychological health



"Mindfulness means paying attention in a particular way; on purpose, in the present moment and nonjudgmentally."

Mindfulness and IBS Relief

- Prospective trial of 93 participants in MBSR
- ➤ Assessed: Rome III IBS status, bowel symptoms (IBS-Severity Scoring System, IBS-SSS), IBS-Quality of Life (IBS-QOL), GI-specific anxiety (Visceral Sensitivity Index, VSI), mindfulness (Five Facet Mindfulness Questionnaire-FFMQ), and functional status (SF-8) at baseline and 2 and 6 months after enrollment
- There was a significant correlation between the change in VSI and the change in FFMQ across the three time

periods (r = 0.33)

Ley DJ Association of participation in a min

Kearney DJ Association of participation in a mindfulness programme with bowel symptoms, gastrointestinal symptom-specific anxiety and quality of life. *Aliment Pharmacol Ther.* 2011 Aug;34(3):363-73.



https://healthy.kaiserpermanente.org/health/care/!ut/p/ao/FchBDo MgEADAt_iAzYZEYfFmhH6hhdsGiZIIGELt99seZ9DjC33hO-3cUy18_uxCLD22md9bqnCnLVZ8okd_Nd4zoysVAocj_o9bT-GM6IzVap2MBamIBCGsgEWPBohoUkKp8UErXjnTZxmGL2IKPpl!/

Guided Imagery

- A directed daydream
- Immersive multi-sensory experience that creates a receptive state
- Targeted goal-directed healing experience

- ➤ 65 breast cancer patients randomly assigned to the experimental (n = 32) or control group (n = 33)
 - Both groups received chemotherapy self-care education
 - > Experimental group also received guided imagery training
- ➤ The training on relaxation with guided imagery was conducted before chemotherapy, and the patients were supplied with a guided imagery CD, to be listened to for 20 minutes daily for 7 days post chemotherapy

- Experimental group showed significant decreases in insomnia (-0.34 ± 0.83, P < 0.05), pain (-0.28 ± 0.58, P < 0.05), anxiety (-3.56 ± 2.94, P < 0.00), and depression (-2.38 ± 2.70, P < 0.00) between the pre and post test</p>
- ➤ Comparing the two groups, statistically significant differences were found in overall symptom distress (B = 0.11, P < 0.05), insomnia (B = 0.50, P < 0.05), depression (B = 0.38, P < 0.05), and physical numbness (B = 0.38, P < 0.05), as well as in anxiety (B = 3.08, P < 0.00) and depression (B = 1.86, P < 0.00) in psychological distress

Relaxing Breath

- 1. Place tip of tongue against ridge on roof of mouth
- 2. Exhale completely through mouth, making a "whoosh" sound
- 3. Inhale deeply through nose to count of 4
- 4. Hold breath for count of 7
- 5. Exhale through mouth to count of 8
- 6. Repeat 3,4, and 5 for a total of 4 breaths

Metta meditation

May I be safe

May I be peaceful

May I be healthy

May I take care of myself easily

May you be safe...

May all beings be safe ...



UNLESS THE MOMENT IS UNPLEASANT, IN WHICH CASE I WILL EAT A COOKIE

Impact of





"I'm going to order a broiled skinless chicken breast, but I want you to bring me lasagna and garlic bread by mistake."

You eat a protein rich meal



Your blood levels of tyrosine rise which leads to a rise in brain levels of tyrosine



You have more energy and feel more alert



dopamine is stored in nerve cells or converted to norepinephrine (with help of vitamin C)

elevated brain tyrosine leads to elevated dopamine levels (in presence of vitamin B6 and magnesium)

You eat a carbohydrate rich meal which leads to release of insulin by the pancreas



blood levels of all amino acids (except tryptophan) drop as the amino acids enter muscle cells



tryptophan levels remain high in your blood and easily enters the brain

high levels of serotonin lead you to feel calm and your mood improves



tryptophan (in presence of vitamins B6,B12 and folic acid) is converted into serotonin



Microbiome and Anxiety

- ➤ 25 healthy women: half ate a cup of commercially available yogurt twice a day for 4 weeks,
 - Yogurt contained strains of four species, bifidobacterium, streptococcus, lactococcus, and lactobacillus
 - ➤ fMRI performed pre and post yogurt exposure to gauge women's response to a series of images of facial expressions
 - ➤ the yogurt eaters reacted significantly more calmly to the images than the control group

"Enjoy the honey heaven dew of slumber" Shakespeare



"Sleep is a criminal waste of time and a heritage from our cave days."

Edison

Sleep deprivation

- Sleep data
 - > 1950s average 8 hours
 - > 2013 average 6.5 hours
- ➤ Teenagers need 9 hours average teen get 5 hours
- > Shift workers -circadian rhythm doesn't adjust







Increases

Mood

Reduces

change

Stress

Attention

Decisionmaking

Creativity

Anger

Impulsivity

Health

Supplements:



Choosing supplements

- > DSHEA
- Evidence
- Quality
- Safety



"Each 8-ounce serving contains the minimum daily requirement of vitamins, minerals and antidepressants."

- ➤ B vitamins 5 RCTs of high dose B vitamins in both healthy and stressed adults all showed reduced stress, anxiety, and depression
- Conclusion: there is sufficient evidence to support the use of high dose B vitamins in the treatment of stress and anxiety in the general population

Rucklidge JJ, Kaplan BK. Broad-spectrum micronutrient formulas for the treatment of psychiatric symptoms: a systematic review. *Expert Rev. Neurother.* 13(1), 49–73;2013.

Schlebusch L, A double-blind, placebo-controlled, double-centre study of the effects of an oral multivitamin-mineral combination on stress. *S. Afr. Med. J.* 90(12),1216–1223 2000.

Inositol

- ➤ Part of the vitamin B-complex
 - ➤ Is required for formation of cell membranes and is important for nerve transmission
 - Small studies for the treatment of anxiety associated with menopause and for benzodiazepine withdrawal
 - Studies used up to 20 g/day. Buy the powder (not 500 mg capsules) mix into water or juice

Kava Kava (Piper methysticum)

- Cochrane Review: kava extracts standardized to 70% kavalactones (approximately twice the concentration usually found in OTC supplements) were superior to placebo for the treatment of anxiety
- Small studies of kava supplements in anxiety associated with menopause and to aid in benzodiazepine withdrawal
- Safety issues: Serious questions regarding kava's safety were raised after case reports suggested that it might cause liver damage. Check LFTs

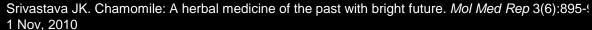
Rhodiola (Rhodiola rosea)

- Herbal supplement widely used to alleviate everyday anxiety, depression, and insomnia
- UCLA pilot study -10 people with GAD
 - > 340 mg rhodiola extract daily for 10 weeks
 - Significant reductions in Hamilton Anxiety
 Scale
 - > Well tolerated (side effects: dizziness and dry mouth)



Chamomile (Matricaria recutita)

- ➤ 57 patients with mild to moderate generalized anxiety disorder (28 treatment group, 29 controls)
 - chamomile capsules containing 220 mg extract from Matricaria recutita, standardized to 1.2 percent apigenin, or placebo
 - ➤ The treatment group showed greater reduction in mean Hamilton Anxiety Rating-A (p=0.047)
 - ➤ Minimal side effects



Amsterdam JD, et al. A randomized, double-blind, placebo-controlled trial of oral Matricaria recutita (chamomile) extract therapy for generalized anxiety disorder. *J Clin Psychopharmacol* 29(4):378-82 Aug, 2009

Other Strategies

Traditional Chinese Medicine



Acupuncture for Anxiety

- ➤ A narrative review of on acupuncture as a treatment of anxiety found consistent improvements following both regular acupuncture and electro-acupuncture
- ➤ A meta-analysis reviewing literature suggests a substantial positive effect for the use of acupuncture in anxiety, although variable study design and needle placement patterns preclude a conclusive endorsement
- RCT of uniform acupuncture treatment for pre-exam anxiety in 60 students showed a strong beneficial effect using a protocol of three 30-minute treatments

Lu W, et al. The value of acupuncture in cancer care. Hematology/oncology clinics of North America 22(4):631-48, viii Aug, 2008

Errington-Evans N. Acupuncture for Anxiety. CNS neuroscience & therapeutics Jun, 2011

Shu S, et al. [Relieving pre-exam anxiety syndrome with wrist-ankle acupuncture: a randomized controlled trial]. [Article in Chinese]. Zhong Xi Yi Jie He Xue Bao. 2011

Massage

- ➤ Massage is one of the oldest of health practices, included in Chinese medical texts written 4,000 years ago.
- Hippocrates advocated massage in the 4th century BC
- Resurgence of interest in the 1970's

- Systematic review of 6 studies of 1,558 patients review using massage for pain and anxiety reduction in oncology patients receiving palliative care
 - Reduction of pain perception statistically significant in massage patients; effect sustained for up to 18 hours
 - Massage significantly associated with reduction in anxiety
 - Full body massage more beneficial than foot massage
- ➤ 68 subjects with GAD randomized to massage (23), thermotherapy (22), or relaxing room therapy (23) for 10 sessions over 12 weeks
 - Measurement of anxiety, depression, and GAD at baseline, post-treatment course, and at 6 months out. All groups experienced symptom improvement
- ➤ 80 post-CABG patients randomized to 4 days of foot reflexology massage for 20 minutes per day versus 1 minute of gentle foot rub with oil
 - significant decreases in anxiety symptoms in the reflexology group

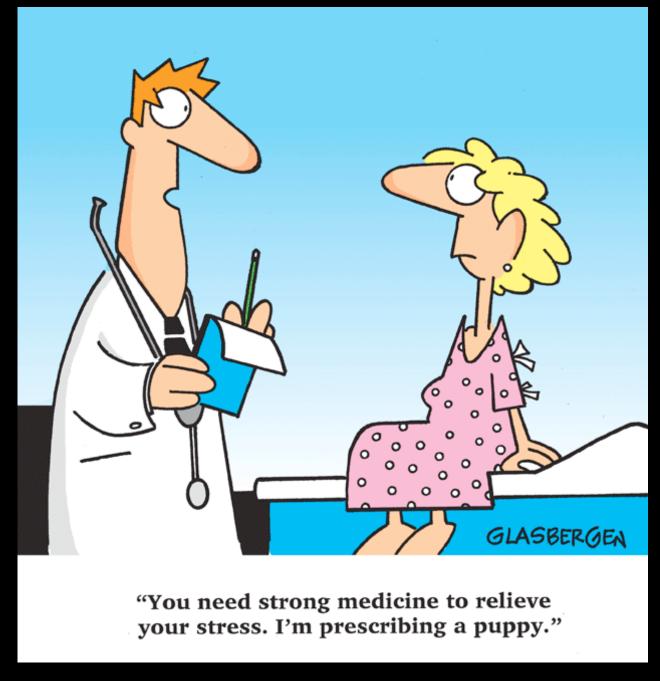
Falkensteiner M The use of massage therapy for reducing pain, anxiety, and depression in oncological palliative care patients: a narrative review of the literature.ISRN Nurs. 2011;2011:929868.

Sherman KJ,et al. Effectiveness of therapeutic massage for generalized anxiety disorder: a randomized controlled trial. *Depress Anxiety.* 2010 May;27(5):441-50. 2010

Bagheri-Nesami M, et al. The effects of foot reflexology massage on anxiety in patients following coronary artery bypass graft surgery: a randomized controlled trial. *Complement Ther Clin Pract* 20(1):42-7 Feb, 2014



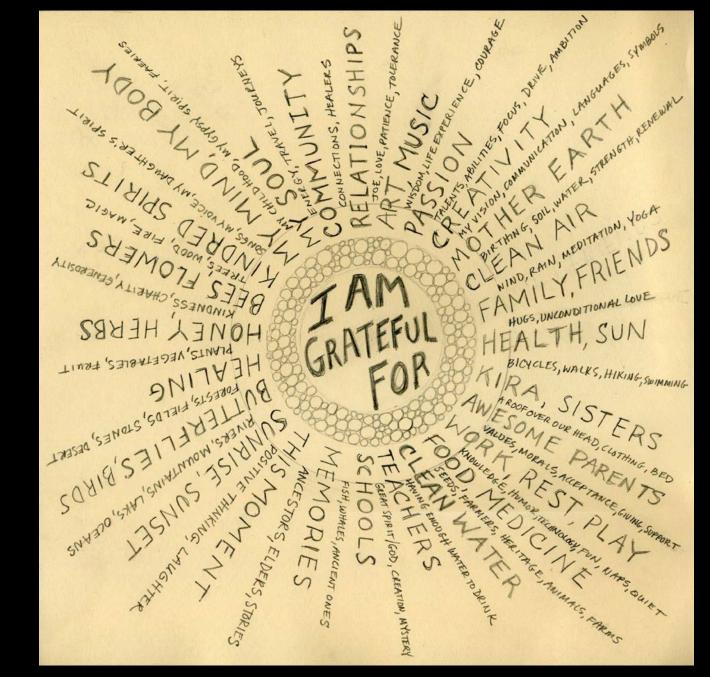
Aromatherapy



Wells DI. The Effects of Animals on Human Health and Well-Being. *The Journal of Social Issues* Vol 65, Issue 3, pages 523–543, September 2009

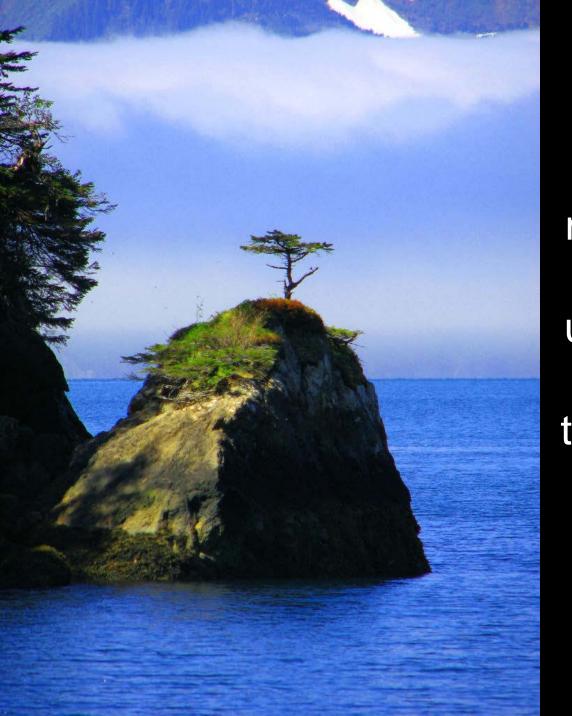
Can you Reframe the Anxiety?

- > Stirred up
- Excited
- Stimulated
- Engaged



Wood, AM, et al. The role of gratitude in the development of social support, stress, and depression: two longitudinal studies. *Journal of Research in Personality*, 42(4);854-871;2008.





"You should sit in meditation for 20 minutes every day

unless you are too busy; then you should sit for an hour."

> Zen proverb