

Always Leading & Inspiring

## Complimentary Medicine in Mental Health:

### What's the evidence?

Randy Swingen, FNP-c

# Objectives

- 1. Define complementary medicine.
- 2. Identify herbs and supplements that alter neurotransmitters.
- 3. Describe mental health benefits of fish oil.

#### Complementary & Alternative Medicine

 Complementary medicine is treatments that are used along with standard medical treatments but are not considered to be standard treatments. One example is using dietary changes to treat diabetes along with diabetes medications.

- Alternative medicine is treatments that are used instead of standard medical treatments.
- Any practice that is put forward as having the healing effects of medicine, but is not founded on evidence gathered using the scientific method.
- One examples is chiropractic treatment.

 Integrative medicine is a total approach to medical care that combines standard medicine with the CAM practices that have been shown to be safe and effective. They treat the patient's mind, body, and spirit. It focuses on patient self healing and empowerment, and aims for a collaborative approach through a partnership model.

### Examples of Complementary & Alternative Medicine

• Traditional Chinese **medicine**, homeopathy, and naturopathy.

• Mind and body practices like acupuncture, massage therapy, and tai chi.

Natural health products like herbs, dietary supplements, and probiotics.



 Albizia is an herb that was originally grown in southern and eastern Asia. The flowers and stem bark are used to make medicine. Albizia is taken for anxiety, depression, and sleep problems (insomnia); to improve mood; and to reduce swelling associated with trauma.  Albizia has an influence on the neurotransmitters GABA, serotonin, and dopamine.

 Different fractions within the herb exert slightly different effects on neurotransmitters.





 Baikal Skullcap is an herb used in Chinese medicine that has antibacterial, antiviral, anti-inflammatory, hepatoprotective, anxiolytic, hypocholesterolemic, neuroprotective, and antimetastatic actions.  Baikal skullcap has been shown in vivo to produce an anxiolytic effect mediated through activation of the benzodiazepinebinding sites of GABA-A receptors.

 In a rodent study, baicalin exerted a biphasic effect on the sleep-wake cycle and exerted a somnogenic effect (hypnotic).



- **Bergamot** is a fragrant citrus fruit common throughout the Mediterranean. It is chiefly cultivated to produce essential oils.
- It has mainly been used for its fragrant properties in perfumes. It is the citrus aroma associated with Earl Grey tea.
- Taken orally, can improve cardiovascular health.

- An open-label study of 54 elementary school teachers evaluated two 10-minute sprays of bergamot oil aromatherapy for effects on stress. Exposure resulted in a significant decrease in blood pressure and heart rate when measured 5 minutes after exposure compared to 5 minutes before.
- Found to be most effective for groups with moderate to high anxiety, but not for groups with mild anxiety.



 Chromium is a mineral. It is called an "essential trace element" because very small amounts of chromium are necessary for human health.

 The best sources of chromium are broccoli, liver, and brewer's yeast. Other sources include potatoes, whole grains, seafood, and meats. • Chromium is taken to improve blood sugar control in people with diabetes.

 It is also taken for depression, schizophrenia, bipolar disorder, and binge eating disorder.

 Chromium influences serotonergic pathways and affects amino acids (5-HTP and 5-HT1A) used to produce serotonin.





- Ginkgo biloba is one of the world's oldest living trees, dating back more than 200 million years.
- Ginkgo has been used medicinally for decades and is the most popular therapeutic agents prescribed in Europe by medical doctors.

 Studies report that Ginkgo biloba leaf extract can stabilize or improve several measures of cognitive function and social functioning in people with Alzheimer's vascular or mixed dementia.

 An in vitro study found that ginkgo significantly increased the uptake of serotonin but not dopamine. • There are clinical studies showing that ginkgo exerts significant neuroprotective effects after acute ischemic stroke.

 Gingko has demonstrated stress-alleviating and anxiolytic-like activity in preclinical studies.

 Gingko may reduce the sexual dysfunction side effects of antidepressants and improve sleep continuity however, results are mixed.  Taking ginkgo with certain antidepressants, such as fluoxetine (Prozac) and imipramine (Tofranil), as well as with Xanax might decrease their effectiveness.



 Kava Kava is an herbal remedy that's made from the roots of *Piper methysticum* -- a type of plant found in the islands of the Pacific Ocean. Its name means "intoxicating pepper." People on Pacific islands like Fiji have used it for hundreds of years in social gatherings and traditional medicine. They dry out the roots or crush them into a powder, add water and drink the mixture.

 Kava kava ("kava" for short) contains substances called kavapyrones. They act much like alcohol on your brain, making you feel calm, relaxed, and happy. The plant is also thought to relieve pain, prevent seizures, and relax muscles.

 The kava lactones interact with dopaminergic, serotonergic, GABAergic, and glutamatergic neurotransmission.  Several meta-analysis and systematic reviews have been published over the last two decades evaluating the results of randomized trials investigating kava extract in anxiety.

• ALL have concluded that kava is an effective treatment for anxiety.

 The effect is not apparent after a single dose but requires treatment for at least 1 week to establish benefits.  The hypnotic activity of kava extract was confirmed in a randomized controlled trial to improve the quality of sleep significantly.

 Oral kava tablets made with a liquid extract significantly increased female libido compared to placebo.

• Effective for depression in cases where anxiety was accompanied by depression.

- Long term, high doses have been shown to cause reversible elevations in liver enzymes.
- Caution is advised when combining kava with alcohol due to the CNS sedative effects.

 May cause headaches, dizziness, fatigue, diarrhea, and skin problems.



• **Magnesium** comes from the name of the ancient Greek city of Magnesia, where large deposits of magnesium were found.

 Has long been used as a laxative and as a foot soak to ease aches and pains.

 More recently, it is taken orally to alleviate musculoskeletal pain.  Magnesium has an effect on serotonin receptors and a variety of other migrainerelated receptors and neurotransmitters. The evidence of magnesium for migraine prevention is "probable".

 Studies have shown oral magnesium supplementation to decrease fluid retention and mood swings of PMS.  Several studies have demonstrated a positive correlation between magnesium status and ADHD pathology.

- There have been three magnesium supplementation studies in combination with vitamin B6 producing significant behavioral improvement.
- Preliminary reports of a recent study with magnesium alone are promising.



- St. John's Wort has been used medicinally since ancient Greek times to rid the body of evil spirits. Since as early as 1500, it has been used to treat neuralgia, anxiety, neurosis, and depression.
- St. John's Wort comprises 25% of all antidepressant prescriptions in Germany.

- SJW inhibits the synaptic reuptake system for serotonin, noradrenaline, and dopamine.
- Has been shown to bind at GABA-A and B receptors to inhibit GABA reuptake, to evoke GABA release from synaptosomes, and to exert an anxiolytic effect.
- SJW significantly upregulates both 5-HT<sub>1A</sub> and 5-HT<sub>2A</sub> receptors and has a significant affinity for opiate sigma receptors, contributing to the antidepressant effect.

- Several studies confirm the anxiolytic effects of SJW extract. Activity at the GABA receptors and an increase in circulating GABA levels are likely involved.
- SJW significantly improves the hippocampus-dependent spatial working memory and alleviates some other negative effects of stress on cognitive function.

 37 double-blind, randomized studies using SJW over 4 weeks concluded that SJW extracts were superior to placebo for improving symptoms and SJW produced effects similar to synthetic antidepressants in adults with <u>mild to moderate depression</u>.

 A systematic review concluded that SJW was superior to placebo, similarly effective as antidepressants, and had fewer side effects in patients with <u>major depression</u>.



- Tyrosine is an amino acid that is naturally produced in the body from another amino acid called phenylalanine. It's found in many foods, especially in cheese, where it was first discovered. In fact, "tyros" means "cheese" in Greek.
- Also found in soy products, chicken, fish, almonds, avocados, bananas, dairy, eggs, nuts, beans, etc.

- Many of the pharmacological actions of tyrosine relate to its role as a precursor for a number of neurotransmitters and hormones.
- Tyrosine forms DOPA, which is converted to dopamine and, in turn, forms noradrenaline and adrenaline.
- Has been used in the military in the US and the Netherlands to counter stressful effects of cold and prolonged physical activity. Also improves cognition in soldiers under psychological stress.

- Tyrosine is a popular supplement in mild depression due to its role as a precursor to dopamine and noradrenaline.
- A pilot study of 85 pediatric patients demonstrated improvements in ADHD symptoms when tyrosine was mixed with tryptophan, vitamin C, B vitamins, and selenium.
- Tyrosine has been a useful aid in the withdrawal of cocaine, caffeine, and nicotine although larger studies are needed.

- Tyrosine appears to enhance the release of catecholamines when neurons are firing at an increased rate due to stress.
- Studies indicate high dose tyrosine may also improve some aspects of performance and help sustain working memory when multitasking in stressful situations.
- Some studies have suggested tyrosine could potentially suppress appetite and stimulate brown adipose tissue.



- **Thiamine**, also known as vitamin B1, is one of eight essential B vitamins that has many important functions throughout the body.
- It's used by nearly all your cells and responsible for helping convert food into energy.
- Since the human body is unable to produce thiamine, it must be consumed through foods, such as meat, nuts and whole grains.

- Thiamin is involved in the biosynthesis of a number of neurotransmitters including acetylcholine and gamma-aminobutyric acid. It may also be involved in nerve impulse transmission.
- A deficiency of thiamin impedes the brain's ability to utilize glucose for energy leading to mental depression, anxiety, irritability, apathy, poor concentration, forgetfulness, and demntia.



• Vitamin B5, also called pantothenic acid, is one of the most important vitamins for human life. It's necessary for making blood cells, and it helps you convert the food you eat into energy. Vitamin B5 is one of eight B vitamins. All B vitamins help you convert the protein, carbohydrates, and fats you eat into energy.

- Pantothenic acid is essential in controlling stress and the ability to cope with stressful events due to its involvement in the synthesis of the neurotransmitter acetylcholine.
- It is essential for the adrenal cortex function and the synthesis of steroid hormones, and is often used together with other B vitamins during times of stress in order to improve the body's response and restore nutrient levels.



- Vitamin B12 is a nutrient that helps keep the body's nerve and blood cells healthy and helps make DNA, the genetic material in all cells.
- Studies have found as many as 30% of patients hospitalized for depression to be deficient in vitamin B12.

- A study of 700 community-living, physically disabled women over the age of 65 found that vitamin B-12 deficient women were twice as likely to be severely depressed.
- A study of 225 hospitalized, acutely ill older patents receiving oral nutritional supplements showed significant increases in plasma B-12 levels and a decrease in depression scores.





- Vitamin D is a fat-soluble vitamin responsible for increasing intestinal absorption of calcium, magnesium, and phosphate, and multiple other biological effects.
- Your body makes vitamin D when direct sunlight converts a chemical in your skin into an active form of the vitamin (calciferol).

- The Neurodevelopmental Theory of Schizophrenia suggests that low prenatal vitamin D interferes with brain development by interacting with D-responsive/susceptible genes.
- The evidence to date supports the hypothesis of a developmental basis of vitamin D deficiency and its association with schizophrenia.
- The hypothesis has a consistent positive relationship appearing for males and strong evidence in dark-skinned populations.



- Melatonin is a hormone in your body that plays a role in sleep. The production and release of melatonin in the brain is connected to time of day, increasing when it's dark and decreasing when it's light. Melatonin production declines with age.
- It is derived from the amino acid tryptophan. Within the pineal gland, serotonin is acetylated and then methylated to yield melatonin.

# There are a few excellent sources of naturally-occuring melatonin in foods:

 Fruits and vegetables (tart cherries, corn, asparagus, tomatoes, pomegranate, olives, grapes, broccoli, cucumber)

• Grains (rice, barley, rolled oats)

 Nuts and Seeds (walnuts, peanuts, sunflower seeds, mustard seeds, flaxseed) Research on melatonin use for specific conditions shows efficacy for:

- Circadian rhythm sleep disorders in the blind.
- Delayed sleep phase (delayed sleep-wake phase sleep disorder).
- Insomnia.
- Jet lag.
- Shift work disorder.
- Sleep-wake cycle disturbances.

 Melatonin is thought to be safe when taken long term, though most sources recommend short-term use.

• Nonaddictive – can be taken nightly.

 Too much melatonin can disrupt your sleep cycle, so start with the smallest dose (1-3 mg).



- Valerian is a perennial plant native to Europe and Asia and naturalized in North America.
- Numerous clinical studies confirm sedative or hypnotic activity for valerian.
- Anxiolytic activity has been demonstrated.
- Antidepressant activity has been seen.

- Valerian stimulates the release of GABA, inhibits GABA reuptake, and may modulate GABA activity at the receptors.
- Three randomized studies compared valerian with benzodiazepines used for sleep and showed no statistically significant differences between the treatments.
- A randomized study showed low-dose valerian reduced situational anxiety without causing sedation.



- Fish oil is a dietary source of omega-3 fatty acids — substances your body needs for many functions, from muscle activity to cell growth.
- Omega-3 fatty acids are derived from food. They can't be manufactured in the body. Fish oil contains two omega-3s called docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).

- Dietary sources of DHA and EPA are fatty fish, such as salmon, mackerel and trout, and shellfish, such as mussels, oysters and crabs. Some nuts, seeds and vegetable oils contain another omega-3 called alpha-linolenic acid (ALA).
- Because fatty acids are major components of the brain, they influence neurotransmitter synthesis, degradation, release, reuptake, and binding.

- Several epidemiological studies have reported low plasma fatty acid (DHA) levels in individuals with schizophrenia, ADHD, dyslexia, personality disorders, depression, and bipolar disorder.
- Low DHA level is considered a significant risk factor for the development of Alzheimer's dementia.
- Two studies have found evidence of low levels of EPA and DHA in autistic patients.

- Depression rates are 10 times higher in countries with limited seafood intake (and postpartum depression is 10-50 times higher), suggesting fish oil plays a role in depression *prevention*.
- Fish oil has **not** been found to be effective in *treating* postpartum depression.
- Some studies in adults suggest that omega-3 fatty acids may be beneficial in the treatment of mild to moderate depression, but more research is needed.

 Fish oil has been used to reduce aggressive behavior in children and adolescents.

• More research is needed to study the efficacy of fish oil in ADHD.

 Four out of five trials of fish oil in the adjunctive treatment of schizophrenia have produced positive results.



- Cannabidiol is a phytocannabinoid discovered in 1940. It is one of some 113 identified cannabinoids in cannabis plants and accounts for up to 40% of the plant's extract.
- In 2018, clinical research on cannabidiol included preliminary studies of anxiety, cognition, movement disorders, and pain.

 While CBD is an essential component of medical marijuana, it is derived directly from the hemp plant, which is a cousin of the marijuana plant.

 CBD is commonly used to address anxiety, and for patients who suffer through the misery of insomnia, studies suggest that CBD may help with both falling asleep and staying asleep.

- For generalized anxiety disorder (GAD), the National Institute on Drug Abuse (NIDA) says that CBD has been shown to reduce stress in animals such as rats.
- Study subjects were observed as having lower behavioral signs of anxiety. Their physiological symptoms of anxiety, such as increased heart rate, also improved.
- More research needs to be done, specifically on humans and GAD.

- CBD may also benefit people with other forms of anxiety, such as social anxiety disorder and post traumatic stress disorder (PTSD). It may help treat anxiety-induced insomnia as well.
- In 2011, a study researched CBD's effects on people with SAD. Participants were given an oral dose of 400 milligrams (mg) of CBD or a placebo. Those who received CBD experienced overall reduced anxiety levels.

- Multiple recent studies have shown that CBD can help with PTSD symptoms, such as having nightmares and replaying negative memories. These studies have looked at CBD as both a standalone PTSD treatment as well as a supplement to traditional treatments like medication and cognitive behavioral therapy (CBT).
- A 2017 literature review on CBD and psychiatric disorders concluded that there isn't enough evidence to tout CBD as an effective treatment for depression.

 "In humans, CBD exhibits no effects indicative of any abuse or dependence potential.... To date, there is no evidence of public health related problems associated with the use of pure CBD." -(World Health Organization)

 Side effects of CBD include nausea, fatigue and irritability.



 Cannibis is widely used to self-medicate by people with chronic pain, neurological diseases, PTSD, and schizophrenia.

 The two major constituents of cannabis are THC (the psychoactive component) and CBD (cannabidiol).  High CBD content medical cannabis may provide an alternative for the one-third of people who do not respond to conventional antipsychotic medication and the many others who experience intolerable side effects.

(Robson, Guy, &Di Marzo, 2014).

 The psychoactive components of cannabis THC may be beneficial in Alzheimer's disease because it inhibits the enzyme acetylcholinesterase (AChE).

(Eubanks et al., 2006)

- Significant evidence supports its use as an antidepressant and anxiolytic.
- Cannabis increases serotonin and dopamine levels.
- Some research suggests that low doses of cannabis decreases depression but at high doses, increases it.

(Babmico, Katz, Debonnel, & Gobbi, 2007)

#### References

- Braun, Lesley, and Cohen, Mark; Herbs & natural supplements an evidence-based guide, Volume 2, 2017, Elsevier.
- National Cancer Institute at the National Institutes of Health; Complementary and Alternative Medicine; retrieved July 30, 2019 from <a href="https://www.cancer.gov/about-cancer/treatment/cam">https://www.cancer.gov/about-cancer/treatment/cam</a>.
- National Center for Complementary and Integrative Health, Complementary, Alternative, or Integrative Health: What's In a Name? retrieved July 30, 2019 from <a href="https://nccih.nih.gov/health/integrative-health">https://nccih.nih.gov/health/integrative-health</a>.
- Web MD; Vitamins and supplements; 5-HTP. Retrieved August 7, 2019, from <a href="https://www.webmd.com/vitamins/ai/ingredientmono-794/5-htp">http</a>
- Healthline; 7 benefits and uses of CBD oil (plus side effects); retrieved August 28, 2019, from <a href="https://www.healthline.com/nutrition/cbd-oil-benefits#section7">https://www.healthline.com/nutrition/cbd-oil-benefits#section7</a>
- Grinspoon, Peter, M.D. Harvard Health Publishing, Harvard Medical School; Cannabidiol (CBD) what we know and what we don't; retrieved August 28, 2019 from <a href="https://www.health.harvard.edu/blog/cannabidiol-cbd-what-we-know-and-what-we-dont-2018082414476">https://www.health.harvard.edu/blog/cannabidiol-cbd-what-we-know-and-what-we-dont-2018082414476</a>
- Shannon, Scott, M.D., Lewis, Nicole, N.D., Lee, Heather, PA-C, & Hughes, Shannon, PhD (2019); Cannabidiol in anxiety and sleep: A large case series; retrieved August 29, 2019 from <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6326553/</u>
- Mayo Clinic Staff, Mayo Clinic (March 30, 2018), Melatonin. Retrieved August 29, 2019 from <a href="https://www.mayoclinic.org/drugs-supplements-melatonin/art-20363071">https://www.mayoclinic.org/drugs-supplements-melatonin/art-20363071</a>
- National Institutes of Health, Office of Dietary Supplements, Valerian (March 15, 2013). Retrieved September 4, 2019 from <a href="https://ods.od.nih.gov/factsheets/Valerian-HealthProfessional/">https://ods.od.nih.gov/factsheets/Valerian-HealthProfessional/</a>
- Mayo Clinic Staff, Mayo Clinic; Fish oil (2019); retrieved September 4, 2019 from <a href="https://www.mayoclinic.org/drugs-supplements-fish-oil/art-20364810">https://www.mayoclinic.org/drugs-supplements-fish-oil/art-20364810</a>
- Healthline (2019); Using CBD oil for anxiety: Does it work? Retrieved September 5, 2019, from <a href="https://www.healthline.com/health/cbd-for-anxiety#how-to-buy-cbd-oil">https://www.healthline.com/health/cbd-for-anxiety#how-to-buy-cbd-oil</a>
- Korn, Leslie. Nutrition essentials for mental health, a complete guide to the food-mood connection; 2016, W.W. Norton & Company