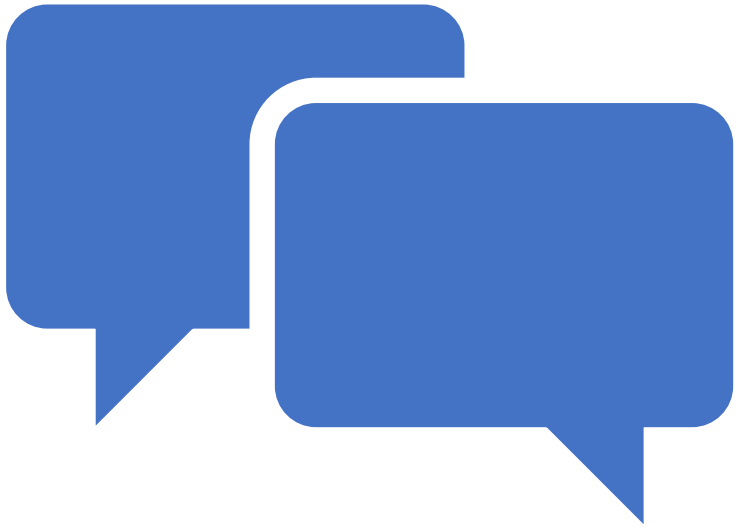
Think Again

Fall Term 2021

Class 9

Email and Website



mattepstein7@gmail.com

http://olli-think-again.weebly.com

On Tap for Today

- Review
- Science Behind Brain Health
- Microbiome
- Psychedelics

Review

- Keeping the brain healthy is consistent with what it takes to keep the rest of our bodies healthy.
- Sleep
- Exercise
- Relaxation
- Eat the right foods
- Avoid the wrong foods
- Avoid toxins

New Study

- Published yesterday Abstract
- Shows genetic basis for mental health problems related to air pollution
- Includes depression, anxiety, cognitive impairment, and learning difficulties, among others
- Differs in effect based on genetic predisposition
- See microbiome forest study in later slides

Review

- Stevia
- Glyphosate and Toxins
- Sleep

So Let's Use Stevia Instead of Chemicals

- Not so fast. Sure it comes from the leaves of a plant and is 'natural'.
- So is anthrax.
- The FDA has recognized a highly sophisticated stevia extract as GRAS (Generally Recognized as Safe), not the leaves or crude extracts.
- The research is very preliminary but indicates while it does not kill beneficial bacteria, it appears to interfere with their communication networks. Article Abstract
- That may explain why some people experience gastric distress.

Extent of Exposure Debatable
Not That it Exists

- Discussions about exposure to toxins often leads to political discussions.
- The extent of exposure and how toxic individual plastics and chemicals may be raises ideological issues.
- Data is data.
- Special interest involvement in writing regulatory statutes, billions spent on lobbying, and political appointments making up the top levels of regulatory agencies are not debatable.
- Whether through failure to regulate or lack of knowledge, it is up to us to protect our brains and bodies.

Glyphosate in Children's Foods

- Study measured glyphosate in 28 conventionally grown oat-based foods marketed to or for children.
- All 28 had dangerous levels. Article
- The number of products with glyphosate and the levels were even worse than studies. Report
- While most were clean and those that had glyphosate were at lower levels, they were even found in organic foods.

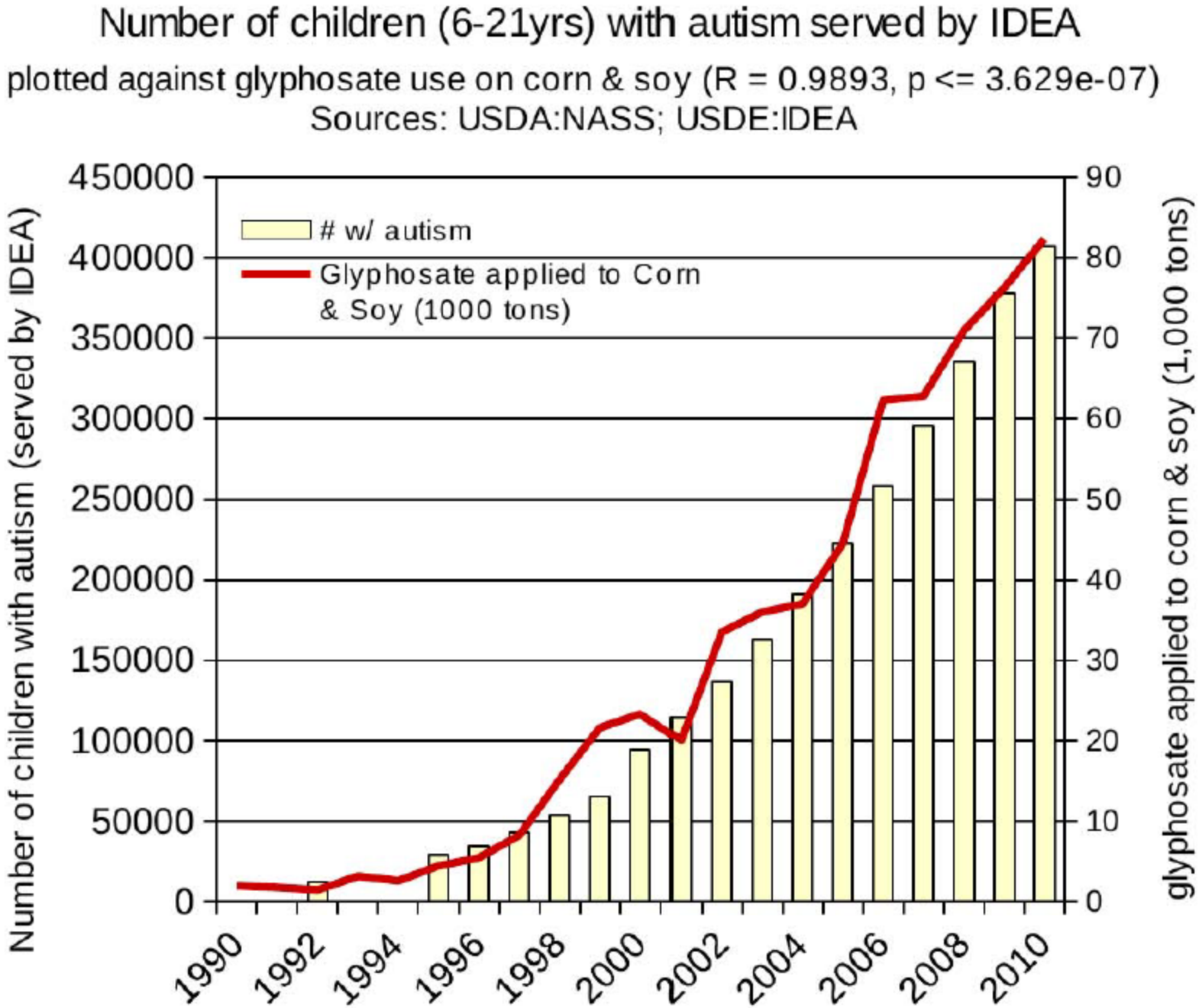


Figure 23. Correlation between children with autism and glyphosate applications.

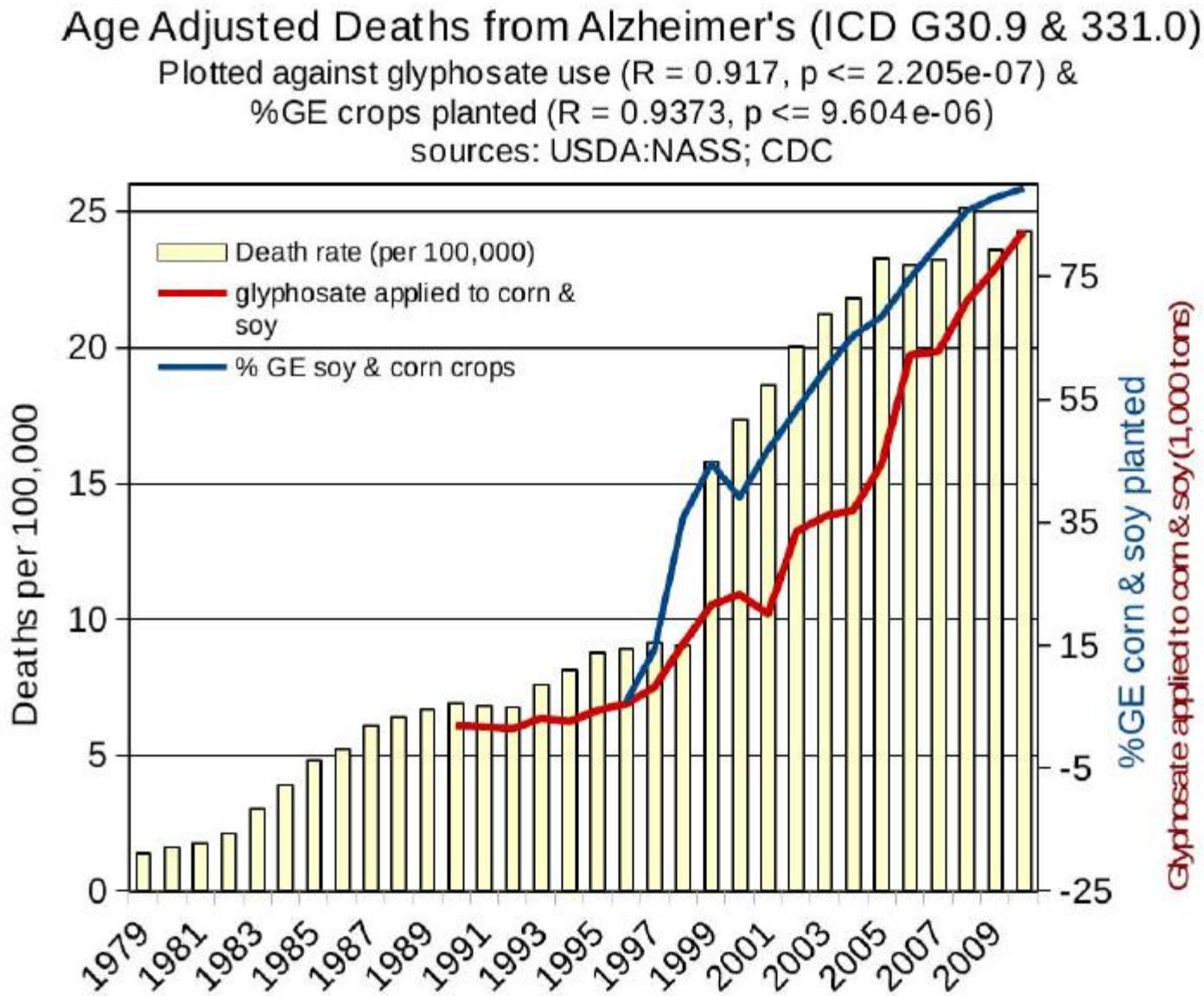


Figure 25. Correlation between age-adjusted Alzheimer's disease deaths and glyphosate applications and percentage of US corn and soy crops that are GE.

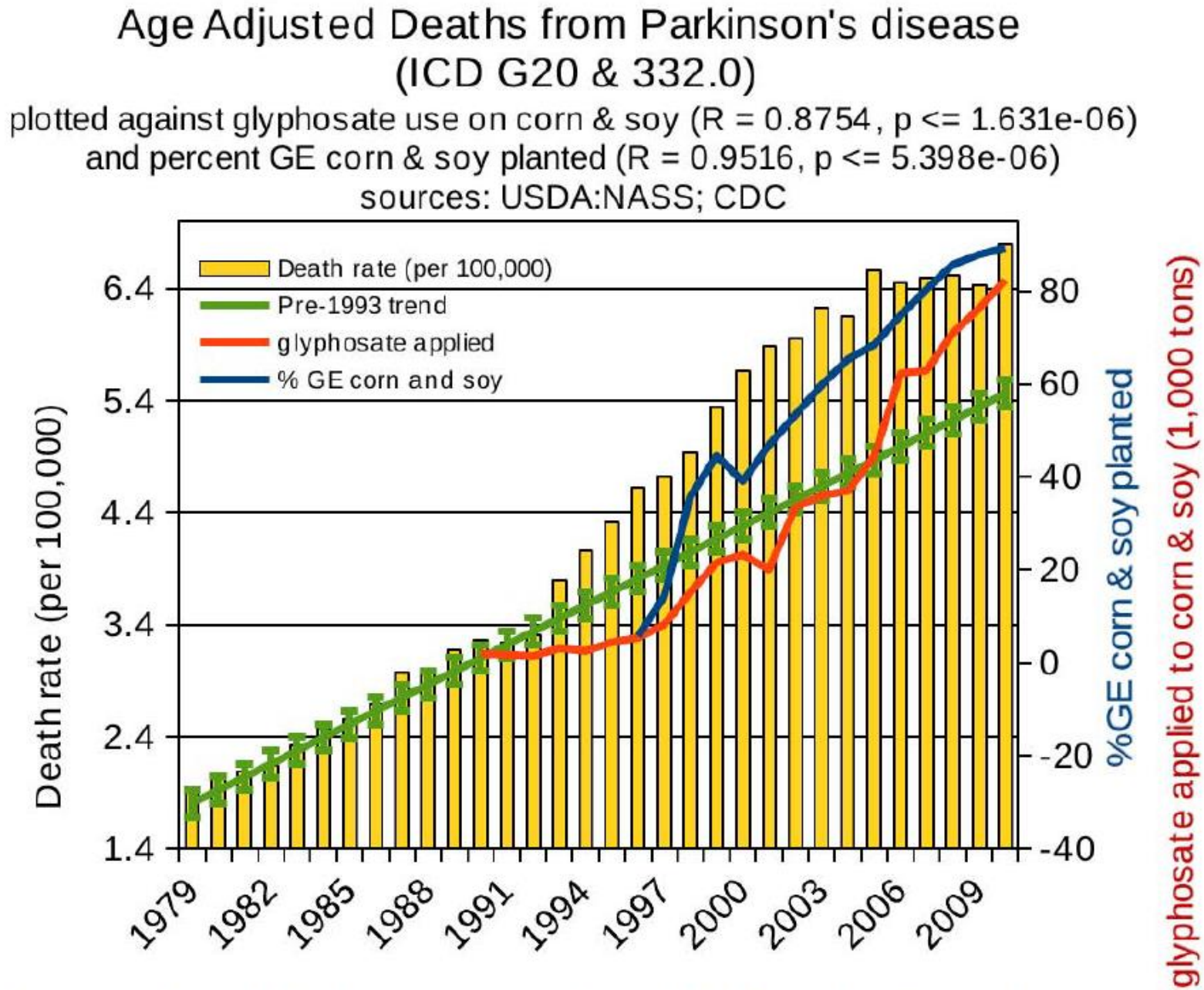


Figure 26. Correlation between age-adjusted Parkinson's disease deaths and glyphosate applications and percentage of US corn and soy crops that are GE.

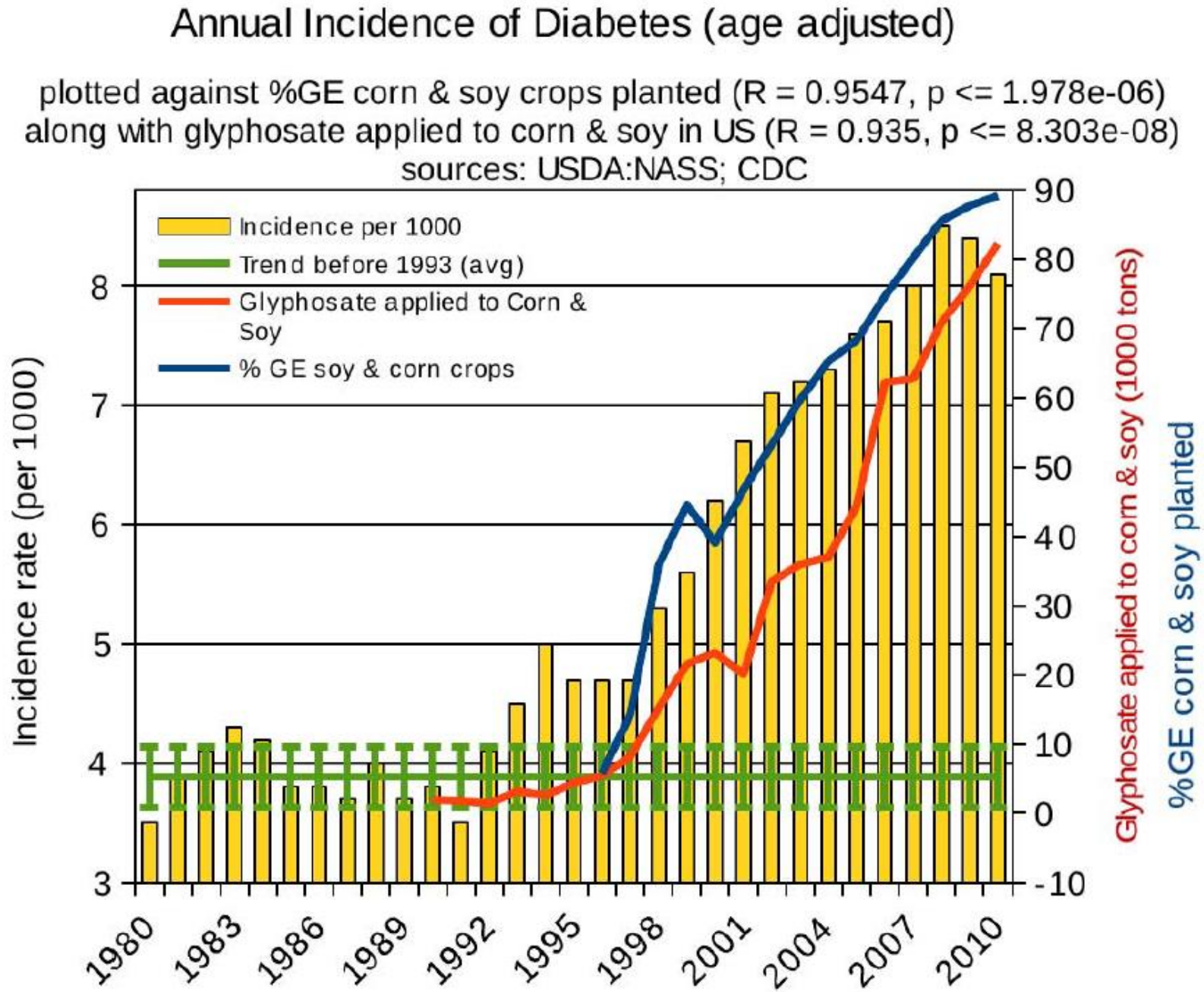


Figure 14. Correlation between age-adjusted diabetes incidence and glyphosate applications and percentage of US corn and soy crops that are GE.

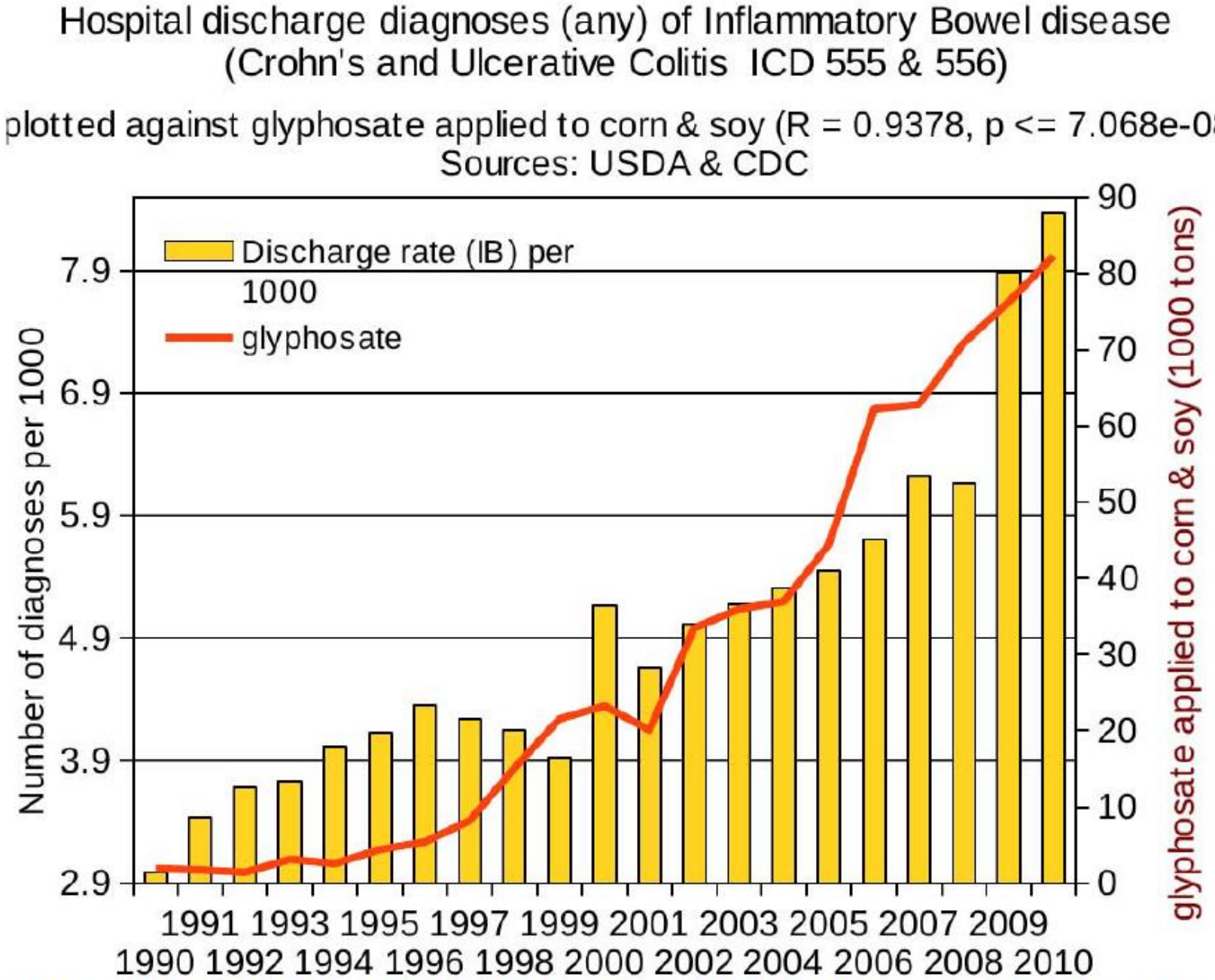


Figure 20. Correlation between inflammatory bowel disease and glyphosate applications to US corn and soy crops.

Virtually Identical Graphs

Intestinal infection deaths	Senile dementia	Liver cancer	Kidney cancer	Bladder cancer
Thyroid cancer	Hypertension related deaths	Deaths related to obesity	Deaths from hemorrhagic stroke	End stage renal disease
	Acute renal failure death	Inflammatory bowel disease (Crohn's and ulcerative colitis)	Study	

Sample Glyphosate Microbiome Studies

- Major alteration of female rat microbiome – Study
- Glyphosate may have an impact on half of the species in the core human gut microbiome – Study
- Epigenetic transfer to multiple generations - Study

Sleep and Cognitive Decline

- Last week we talked about the importance of sleep in keeping the brain healthy.
- Researchers conducted longitudinal studies comparing self-reported hours of sleep to later cognitive decline.
- Studies showed 7-9 hours to be optimal with correlations with cognitive decline appearing above and below that range.
- Two problems with that approach
  - Sleep Times are self-reported
  - Hours of sleep may not reflect quality of sleep

New Sleep Study

- This study attached tiny EEG's to foreheads of subjects for 4-6 nights to measure both sleep and quality of sleep.
- Conducted follow up cognitive testing for an average of 4.5 years.
- Found best results between 4.5-6.5 hours of sleep with cognitive decline occurring above and below those numbers.
- EEG measured sleep of 4.5-6.5 hours is equivalent to 5.5-7.5 hours of self-reported sleep.
- Many more measurements taken and more studies needed but a major step in refining prior studies. Abstract Article

Restoring Sleep

- This is the first study I have seen that measured whether restoring sleep impacts amyloid plaques, a common symptom of Alzheimer's Disease.
- Sleep was restored through stimulation of the thalamic reticular nucleus (TRN).
- Not only prevented further accumulation of plaques but started cleaning away existing ones.
- Nothing is better than allowing our bodies to do what only they know how to do.

Digging Deeper Into the Science

- We know the activities that correlate with improved brain health and generally why it works that way.
- Scientists continue to discover knew and exciting processes that underlie those correlations.
- Books are written on each process, or even components of the processm, obviously beyond our capacity in this course.
- But a few examples should give us a better picture.
- The brain is complicated with multiple activities and processes occurring simultaneously.

Recurring Themes

Immune Response

Inflammation

- We will see these words in relation to virtually every condition that impacts the brain, and more so with aging.
- We want our immune systems to target the right pathogens, leave healthy cells alone, and then go back to the barracks.
- We want only the inflammation needed to support the immune action and no more.
- Inflammation and immune response are primarily regulated by our microbiome that we will discuss later.

Brain Derived Neurotrophic Factor (BDNF)

- Neurotrophic factors are proteins responsible for growth and survival of nerve cells during development.
- BDFN are neurotrophic factors created in our brains.
- Article about BDNF (focused on Huntington's Disease) Article
- Physical exercise improves BDNF; adding cognitive training no improvement Study Article
- Dr. John Ratey refers to exercise as Miracle Gro for the brain. That phrase is now often used to apply to BDNF. Article
- Frontiers in Neuroscience Article

Dr. Perlmutter and BDNF

Video

Other Neurotropic Factors

- We discussed BDNF's earlier – neurotropic factors, peptides created by the brain itself, released by exercise and intermittent fasting.
- Neurotropic factors (neurotrophins) can also come from food and supplements.
- It has become a hot issue with lots of money made with little clinical evidence.
- But that does not mean the concept is not valid.

Nerve Growth Factor (NGF)

- NGF was the originally identified neurotrophin.
- Like BDNF's, responsible for growth, survival, and plasticity of neurons, and can be released in similar ways.
- Can also be increased by foods, including certain mushrooms (maybe all) and green tea, among others.
- Examples of apparently healthy mushrooms on following slides.
- Limited research with small sample sizes.

Magic Mushrooms

- No, not those, just ordinary mushrooms.
- Population survey study based on data from the US National Health and Nutrition Examination Survey (NHANES), 2005–2016 found lower levels of depression in those who ate mushrooms. Study
- While numbers were large, this type of research has limited reliability.
- Logic is that mushrooms are the highest dietary source of the amino acid ergothioneine—an anti-inflammatory which cannot be synthesized by humans. High levels may lower the risk of oxidative stress, which could also reduce the symptoms of depression."

Lion’s Mane

- Small, random assignment to condition, showed measurable cognitive improvement compared to control.
- Condition reverted to baseline after mushroom intake stopped.
- Improvement increased throughout active period [Abstract]

Cordyceps

- Used for many conditions in traditional Chinese and Tibetan medicine
- Similar chemical makeup as Lion’s Mane
- Appears to work on Neurotrophic Growth Factor.

Reishi

- Favorite of Chinese herbalists
- Chinese call it the “Mushroom or Immortality” because of its reputation for extending life.
- Rat study Study
- Over 3 days, modulated cytokines, limiting brain inflammation
- Far from conclusive on any issue but promising

Chaga

- Chaga is a fungus that grows on trees, not a true mushroom.
- Has been used in traditional folk medicine in many cultures.
- One of many claims is stress reduction.
- Considered to be an adaptogen.
- Very limited research.
- Sample Article

Mushrooms and Alzheimer's Disease

- Studies are beginning to come out showing mushrooms can prevent AD.
- Small sample sizes and limited controls.
- Dr. Andrew Weil article and references to studies. Article
- Mechanism appears to be NGF and and anti-inflammatory properties

Intermittent Fasting and Brain Health

- Multiple alternatives including hour restricted and full day (usually limit to 8 hours a day of eating or fast 2 days per week)
- Dr. Mark Mattson, Johns Hopkins – Tedx Talk Video Article
- Harvard Study – worms and mitochondria Article Study
- Review of Research (#8 Brain) Article
- Molecule produced during fasting has anti-aging effect on vascular system – Article Study
- Other health benefits but small study – Article

How Intermittent Fasting May Work

- When our bodies lack sufficient glucose, as when we fast, the body looks to the liver for a supply of fatty acids to provide an energy source. The resulting state is referred to as ketosis.
- β-hydroxybutyrate (BHB), a ketone body synthesized in the liver, becomes a primary source of energy. Scientific Article
- Three benefits may result. First, it may reduce accumulations of liver fat that are not otherwise reached.
- Second, BHB may have senolytic effects, preventing or addressing senescence. Study
- Third, produces Brain Derived Neurotropic Factors (BDNF's), similar to exercise.

Dr. Mark Mattson (excerpt, full video link above)

Video

Alzheimer's Disease (AD)

- When you talk about brain health, the discussion inevitably turns to AD.
- The build-up of amyloid plaques and tau tangles appears to correlate with symptoms of AD.
- Yet many with those plaques and tangles show no AD symptoms and those without them often do not.
- Treatment has focused on drugs to eliminate the plaque and tangles but even doing so fails to ameliorate the disease.

Amyloid Plaques and Tau Tangles

- The plaques and tangles are harmful but may be symptomatic as opposed to causative.
- The processes that create the plaques and tangles are both normal and healthful, but something went wrong allowing those processes to get out of control or morph into something harmful.
- More and more the focus is shifting to why that process occurs and how cognitive decline may be prevented even when they do.

Transcription Factor (TF)

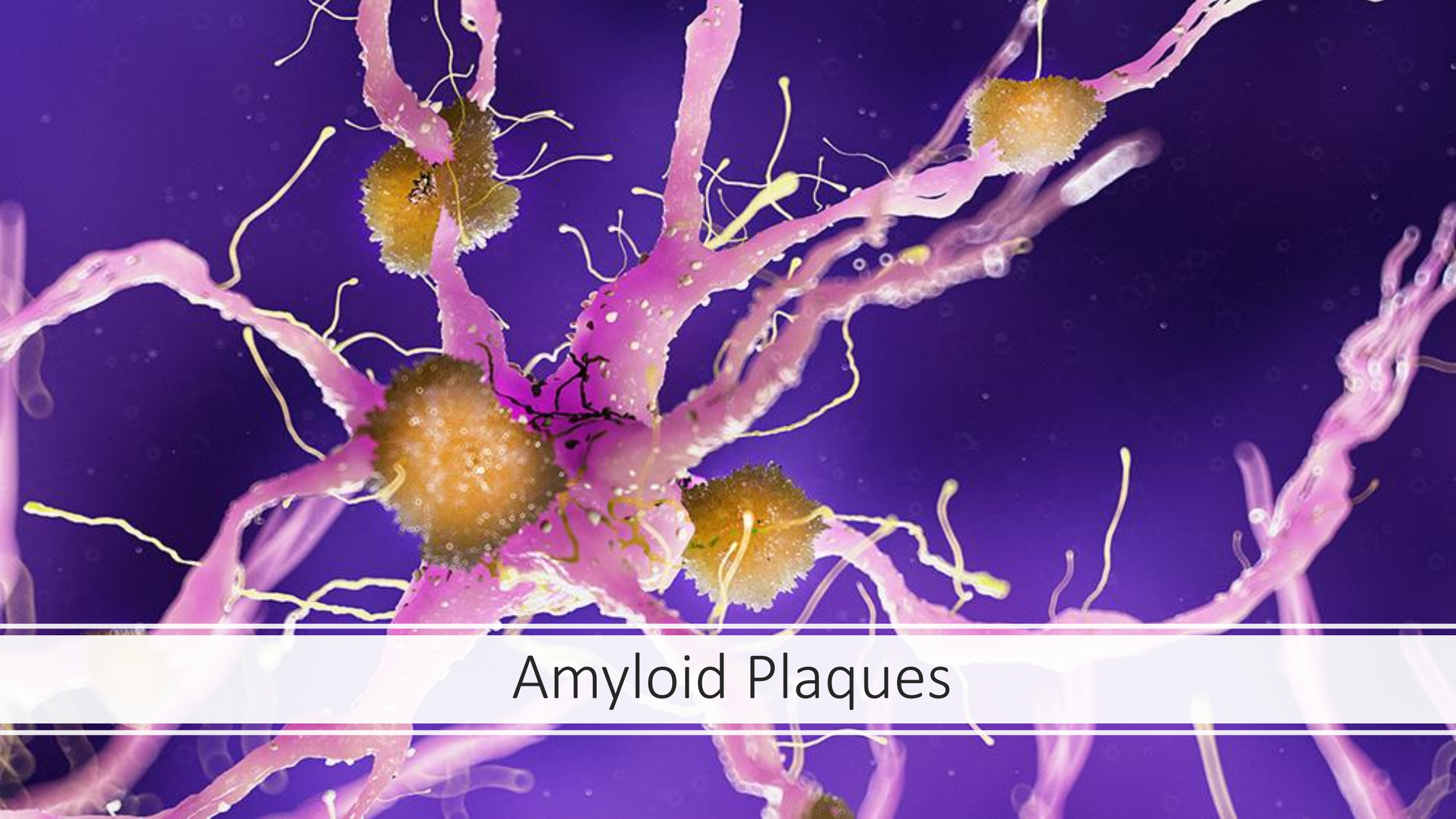
- Also called sequence-specific DNA-binding factor.
- Protein that regulates the transcription of genetic information from DNA to messenger RNA.
- (Think of mRNA COVID vaccines.)
- Turns genes on and off to make sure they are expressed in the right cell at the right time in the right amount.
- One of the epigenetic mechanisms.

Myocyte Enhancer Factor-2 (Mef2)

- Mef2 is a transcription factor found in all eukaryotes (organisms whose cells have a nucleus enclosed in a nuclear envelope).
- Mef2 plays a critical role in embryonic development, muscle and cardiac development, and regulating the cardiac stress response.
- Newborn mice with Mef2 knocked out die within 10 days with major cardiac defects.

New Study Focusing on Mef2

- An MIT study published yesterday in Science Translational Medicine looked at Mef2 production.
- In both mice and humans, high levels of Mef2 correlate with maintaining cognitive functioning despite neurological symptoms of disease.
- It is also known that physical and mental enrichment correlates with cognitive resilience and reduced symptoms of AD.
- The study showed that those types of enrichment increase the expression of Mef2, possibly identifying the mechanism involved. Study Article



Amyloid Plaques

Tau Tangles Video

Flavonoids

Plant Bioactive Compounds

- Plants produce multiple bioactive compounds, historically broken down into three classes.
- Primary metabolites related directly to plant growth.
- Secondary metabolites relate to the plant's interaction with its environment.
- Hormones regulate internal processes including the creation of metabolites.
- Recent research blurs many of those lines.

Flavonoids (or Bioflavonoids)

- Flavonoids are considered secondary plant metabolites.
- They are of the polyphenol class and have long been associated with anti-oxidative, anti-inflammatory, anti-mutagenic, and anti-carcinogenic properties among many other healthy effects.
- There are many different subcategories of flavonoids.
- Flavonoids are found in a wide variety of plants and plant-based beverages.
- Blueberries are a particularly good source of flavonoids, containing at least 9 different subcategories, including anthocyanins that give them their color.

Video

Blueberry Study

- There have been numerous studies showing the benefits of flavonoids generally and blueberries specifically.
- The most reliable are human studies, with random assignment to condition, that add a single variable to the experimental group.
- This study had 26 subjects, but the small numbers enabled extensive testing of biological, particularly neurological impacts.
- The experimental group were given blueberry concentrate for 12 weeks, placebos for the control group. Study

Results

- The experimental group showed some improvement on cognitive tasks but the number of subjects was too small to show statistical significance.
- What was interesting was the increased cerebral perfusion found in multiple areas of the brain of the experimental group.
- Brain areas included, among other regions, the anterior cingulate cortex, insula, thalamus, as well as the occipital and parietal lobes.
- Areas associated with maintenance of cognitive function in older adults.
- The study suggests the benefits of flavonoids may result, at least in part, from increased blood flow, explaining both the neurological and cardiovascular impacts.

Senescence

- Major area of recent focus in studying and addressing age related diseases and conditions of the brain.
- Historically, senescence indicated that cells had stopped dividing.
- When that happens, they give off secretions that promote an inflammatory or immune response intended to eliminate them.
- In recent years, researchers have found that non-dividing cells, such as neurons, can also become senescent. In other words, they stop working but do not go away.
- As we age, we produce more senescent cells. Scientific Article
- They are often referred to as zombie cells since they are neither dead nor alive. If they simply died, they would not pose a threat.

Removing Senescent Cells

- Autophagy is the process the brain uses to remove senescent cells.
- As we age, that process can become less effective.
- If natural processes fail, there are limited options to eliminate senescent cells to stop the secretions that induce inflammation.
- One option is strengthening the immune system generally so that it is able to destroy and remove senescent cells.
- Alternatively, senolytic drugs or supplements are a class of chemicals that kill senescent cells, allowing the immune system to remove them. Scientific Article
- Many of those are currently undergoing various stages of trials, including one using the flavonoid quercetin.

Adaptogens

- Theory is that they help body adjust to physical, chemical, and biological stress.
- Purpose is to return body to balanced state referred to as homeostasis.
- Not great research but limited research is promising. WebMD article
- Ayurvedic Medicine relies heavily on adaptogens.

Ayurvedic Medicine

- Ancient Indian medical system, one of the world's oldest
- Still practiced in India and elsewhere
- Relies heavily on herbs and plants but also includes such things as diet, exercise and lifestyle
- Heavy use of adaptogens such as ginseng, ashwagandha, astragalus, and many others
- Ginseng is also an important herb in Chinese traditional medicine, another system with thousands of years of practice that continues to this date.
- NCCIH Article

How Can We Be Sure?

- Simple answer – we cannot.
- Western medicine looks to well designed, double blind, controlled research with sufficient subjects.
- Many limitations but significant strengths.
- Alternatively, many look to traditional remedies that have been used for up to thousands of years in other cultures. Time tested rather than laboratory tested.
- It too has many limitations but also significant strengths.
- Unlikely meaningful research dollars will be invested in substances that cannot be patented but many patented drugs are based on traditional substances.

Peanut Brain

Peanuts, Stress, and Cognition

- Study published September 20, 2021 evaluated affect of peanut product consumption on cognitive functions and stress response in healthy young adults.
- Three groups consumed skin roasted peanuts, peanut butter, and butter from peanut oil for six months.
- Peanut oil lacks phenolic compounds and fiber and was used as the control.
- Evaluated polyphenol intake, cognitive functions, anxiety, depression, Short Chain Fatty Acids (SCFAs), very long chain saturated fatty acids (VLCSFAs), and cortisol.

Results for Experimental Groups

- Improved immediate memory
- Lower anxiety scores
- Lower depression scores
- Skin roasted peanut scores exceeded those of peanut butter but both were statistically significant in all areas.
- Cortisol levels reduced significantly in all three groups.
- Significant correlation between improvements and polyphenol intake, SCFAs, and VLCSFAs) Study

Green Tea Benefits

- Beneficial effect of green tea on brain health has been assessed through numerous studies. Systemic Review
- They tend to show reduced anxiety, greater cognition, and improvements to working memory.
- Some studies show potential for protection against dementia.
- Benefits for other conditions and illnesses, including cancer.
- The assumption has generally been the the active agents are polyphenols that serve as anti-oxidants.

Reactive Oxygen Species (ROS)

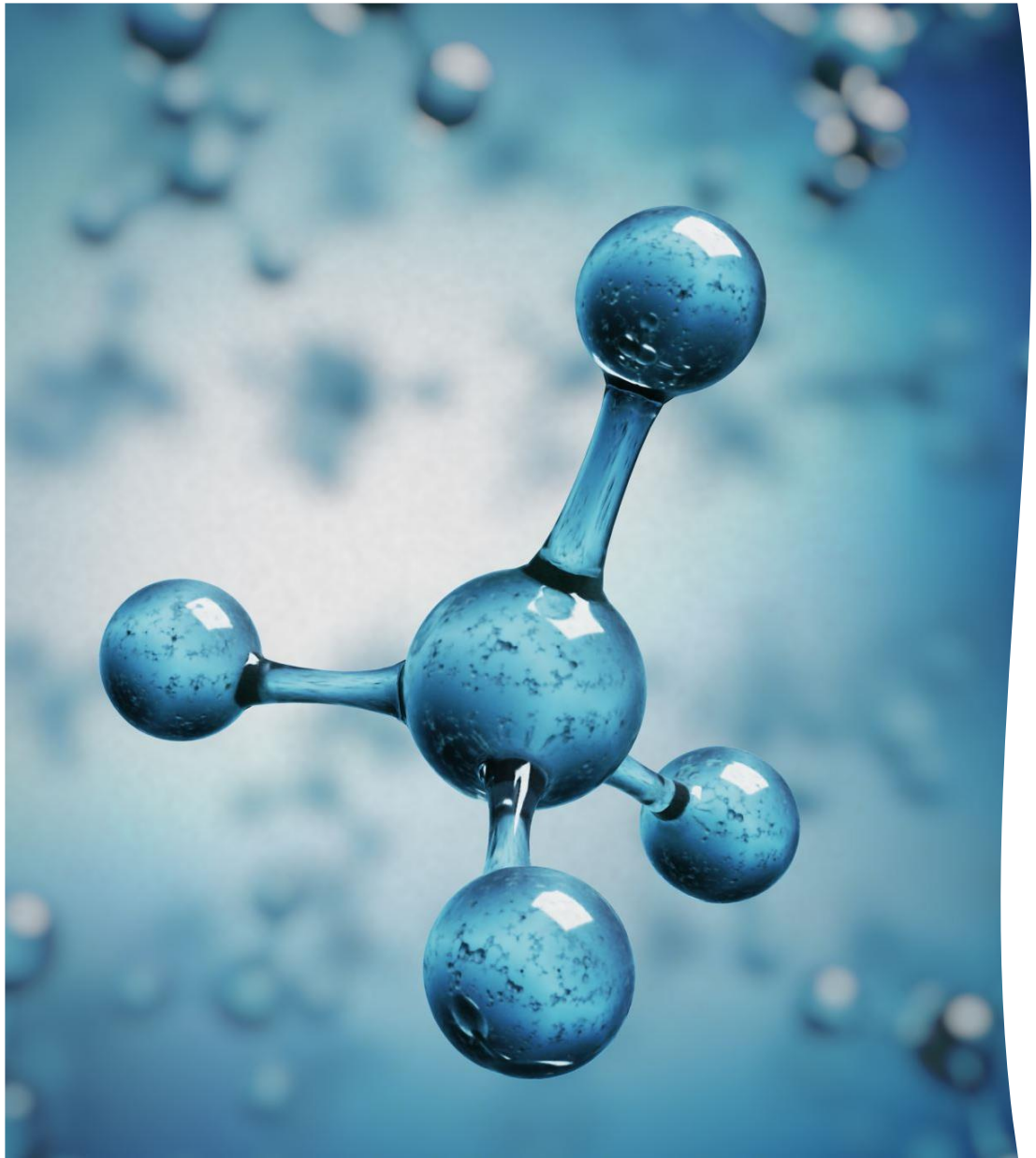
- When cells use oxygen, there is a natural release of chemically unstable molecules called ROS that contain oxygen and react with other molecules.
- They are also called free radicals with superoxide being the most significant.
- ROS support many healthy functions but can also cause oxidative stress when not controlled as designed.
- Oxidative stress can lead to senescence and other cell damage that can cause dementia, cognitive impairment, and other illnesses.

Video

Bring in the Cleanup Crew

- Superoxide dismutases (SOD) are a class of enzymes that catalyze the dismutation of superoxide into oxygen and hydrogen peroxide. As such, they are an important antioxidant defense in nearly all cells exposed to oxygen.
- Catalase (CTL) is a protective enzyme present in nearly all animal cells responsible for the degradation of hydrogen peroxide.
- Problems occur when the cleaning crew are not up to the job.
- As we age, we create more free radicals and have more difficulty clearing them out.

Polyphenols



- Polyphenols are compounds found in virtually all plant foods.
- Following ingestion of polyphenols, animals show reduction in oxidants, leading to the conclusion that they acted as antioxidants.
- In fact they appear to be both pro and anti oxidants.
- The primary polyphenols in green tea are catechins with EGCG being the most abundant (approximately 59%) and most widely studied.
- Epigallocatechin Gallate (EGCG) is most active in nature and appears to have the highest number of therapeutic benefits.

Green Tea Study

- Study published October 4, 2021 used nematodes as subjects.
- EGCG and the second most common catechin epicatechin gallate (ECG) were fed to the subjects.
- Consistent with other studies, resulted in reductions in oxidants.
- This time they looked at immediate and intermediate effects and found that the catechins actually served as pro-oxidants.
- The animals responded by producing their own antioxidants, SOD and CTL, that resulted in the oxidant reduction. Study
- Supporting rather than supplanting natural mechanisms work better.
- Compare SSRIs and MAOIs to psychedelics for depression.

Brewing Green Tea for Maximum Effect

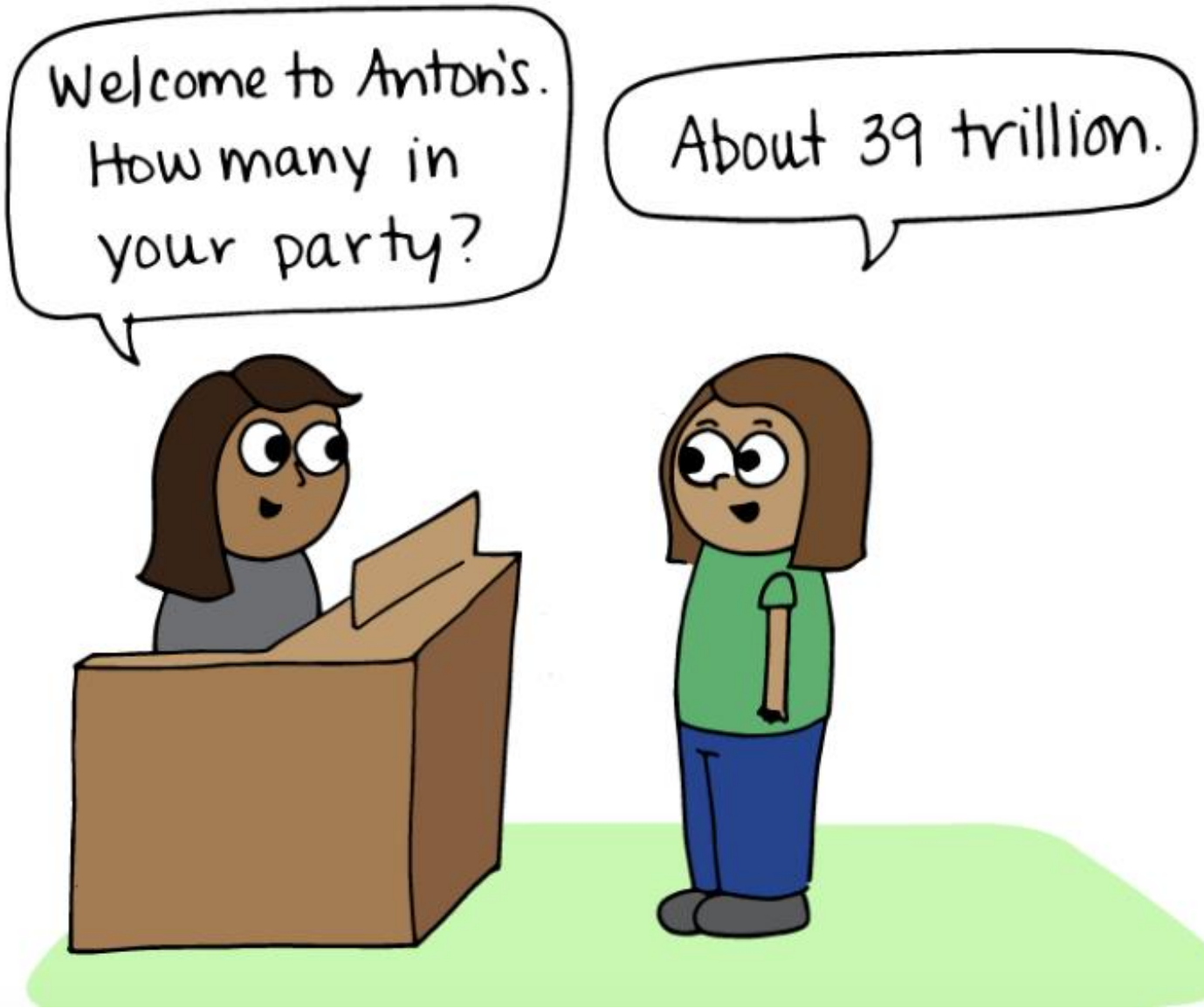
- Chemicals in green tea soaked in hot water release at different times.
- Flavor and aroma compounds release in 60-90 seconds.
- Polyphenols start releasing in significant amounts in approximately 3 minutes but it takes 5 minutes to release most of them and 20 minutes to release almost all.
- Over 3 minutes, tannins release and while they are beneficial, they may also have a bitter taste.
- For most green teas, best results occur at about 175^{o} F.
- Loose tea releases compounds more quickly than tea bags.
- White tea is similar to green tea but the fermentation and processing of black tea and oolong tea destroy most of the polyphenols.

Use Extracts and Supplements with Caution

- A number of studies has found green tea extract supplements to be ineffective compared to green tea itself.
- There are always questions about supplements, including quality control and how the body processes the content.
- The body is designed to process foods, not supplements.
- Probiotics supplements do not appear to produce the benefits of probiotic and prebiotic foods but the research is not definitive.
- The authors of this study worry that if green tea polyphenols are pro vs. anti oxidants, extracts could contain too much and reverse the desired effect.

Microbiome

"They were my mother's microbes...
and now they're yours!"


Welcome to Anton's. How many in your party?
About 39 trillion.

What is the Human Microbiome?

- Hundreds of trillions of microbes living on or within the human body.
- There are multiple types but we will focus mainly on bacteria.
- The majority live in the gut, primarily the intestines, but they are virtually everywhere including the skin and nose.
- Some are beneficial, some pathogenic, and others commensal (symbiotic relationship where one benefits and no effect on the other). But life is not that simple and there can be a combination of beneficial and pathogenic or the benefits or risks may not yet have been discovered.
- Every person has a unique microbiome that will vary over time.

Numbers

- The counts are sophisticated estimates that have been refined over time.
- The human body probably contains about 37.2 trillion cells.
- Estimates of bacteria vary widely but most fall between 37-49 trillion.
- Over 4,000 distinct bacteria have been identified to date.
- It is estimated that we host approximately 370 trillion viruses.
- While the human genome contains 20,000 to 25,000 different genes, human microbiome estimates up to 232,000,000 different genes.

Why Should We Care?

- The human microbiome plays an integral role in the functioning of the human body. We could not live without them.
- Bacteria feed on what we eat and produce byproducts, metabolites, that may be harmful or beneficial.
- Problems arise when we have too few of some bacteria and metabolites, too many of others, an imbalance, or lack of diversity.
- Adjusting the balance can help maintain, restore, or improve health.
- By measuring the impact on the microbiome, we can judge which elements and products may be toxic, beneficial, or neutral in ways that are beyond our capacity through other means.

Roles of Gut Bacteria

- They are critical to digestion, immune reactions, and protection from other pathogens.
- Nutrient and mineral absorption
- Synthesis of enzymes, vitamins and amino acids
- Production of short-chain fatty acids (SCFAs) through fermentation that provide energy for epithelial cells, enhance epithelial barrier integrity, and provide immunomodulation and protection against pathogens

Immune Cells

- Immunity allows us to survive in a world of pathogens, some of which would be harmful or fatal if unchecked.
- When balanced, our immune systems attack things that threaten us and ignore things that are healthy or necessary.
- Problems arise when one of six things occur (much simplified)
  - Our immune system is overwhelmed – too much to handle
  - Our immune system fails to recognize or respond
  - We lack immunity to the specific pathogen
  - Our immune system is too weak
  - Our immune system attacks something it should not – autoimmune diseases
  - Our immune system overreacts, creating harm.

Microbiome and the Immune System

- Animal studies have long shown a positive correlation between a healthy microbiome and and healthy immune system.
- Recent human study is the first to show concentration of different types of immune cells in the blood changes in relation to the presence of different bacterial strains in the gut. Article - Abstract
- Used bone marrow transplant patients, with effectively eliminated immune systems who were treated with antibiotics to prevent infection. Basically, immune system and gut bacteria were eliminated allowing them to measure both as they gradually returned.

Inflammation and the Microbiome

- The bacteria in the microbiome are an intricate component of the immune and inflammatory response systems.
- They can be implicated in both causing and failing to control unhealthy inflammation.
- A healthy microbiome can prevent unhealthy inflammation.
- An unhealthy microbiome can cause unhealthy inflammation.
- As we review illnesses, conditions, and research studies, you will see how often we refer to increases and decreases in bacteria that control or exacerbate inflammation.

Inflammation – Dr. Jekyll or Mr. Hyde

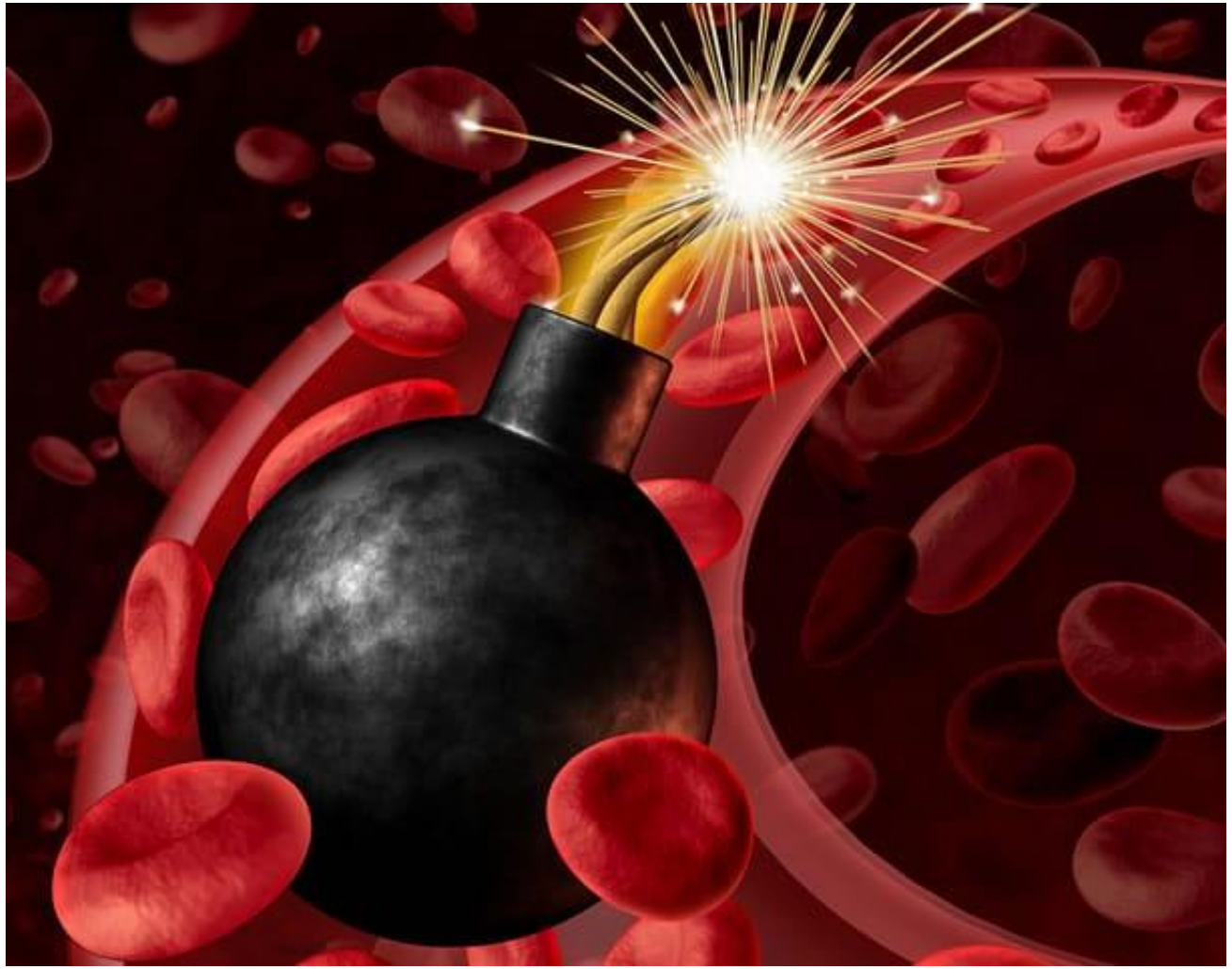
- Inflammation is a natural characteristic of a healthy immune response. Something is threatening the body and must be destroyed.
- Problems arise when the response turns into a Mr. Hyde.
- The response can be disproportionate.
- The response can attack healthy and necessary parts of the body.
- The response can become chronic.
- Chronic inflammation has been strongly correlated with cardiac disease, Type 2 diabetes, cancer, obesity, Alzheimer's, asthma, inflammatory bowel disease, and auto immune conditions.

Inflammaging

Inflammaging is a term used to describe chronic inflammation in older people.

As we age, inflammation is more likely to increase or become chronic.

Chronic inflammation also causes us to age more quickly.



Can Our Microbiome Come to the Rescue

- Research looks for correlations and large subject sets to increase confidence levels and establish significance.
- A significant difference may or may not mean much.
- The same food could help some, hurt others, and have no effect on the rest. Or it could be helpful or harmful in ways that are not considered by the research protocol.
- The concern applies to drugs as well as foods.
- The same drug may save some, harm others, and have limited or unmeasured effect on others.
- What makes the difference and how do we know?
- Increasingly, it looks like our individual microbiomes could be the key.

Choline (To Eat or Not To Eat) That Is the Question

- Eggs are rich in choline.
- Essential nutrient required to maintain cell structural integrity and produce critical neurotransmitter acetylcholine.
- High levels correlate with healthy hears and minds.
- Gut bacteria break down choline into trimethylamine (TMA). The liver converts TMA into trimethylene N-oxide (TMAO).
- Increased TMAO levels are linked to cardiovascular disease and strokes. Study So do you add or avoid choline?
- Healthy microbiomes do not convert choline into TMAO.
- Answer is to improve microbiome and avoid choline until you do.

Dysbiosis

- When the ecology is seriously imbalanced, the condition is referred to as dysbiosis, itself not subject to exact definition.
- It is characterized by a lack of diversity, loss of beneficial bacteria, and a rise in pathogenic bacteria.
- Associated with pathogenesis of both intestinal and extra-intestinal disorders.
- Intestinal disorders include inflammatory bowel disease, irritable bowel syndrome (IBS), and celiac disease.
- Extra-intestinal disorders include allergy, asthma, metabolic syndrome, cardiovascular disease, and obesity. Article

Factors in Development and Alteration

Birthing	Infant feeding method	Diet
Probiotics and Prebiotics	Environment	Stress
Lifecycle	Diseases	Toxins

Applying Microbiome Knowledge

- Look for correlations between illnesses and conditions and the presence or absence of specific bacteria.
- Use animal subjects to create and ameliorate conditions by manipulating bacteria.
- If amelioration is successful, test application in humans.
- Inevitably find too few bacteria that control inflammation and too many the increase it.

Correlation with Diseases

Researchers have found strong correlations between microbiome bacteria differences and numerous diseases and conditions. Those correlations are no longer in doubt.

But correlation does not imply causation. Do the microbiome differences cause the problem? Does the problem lead to microbiome changes? Or does something else cause both?

Recent research appears to support the theory that the changes to the microbiome are in fact causative in many cases.

Increasingly, both animal and human studies are finding that improving the microbiome can help cure or treat the condition.

COVID-19 and the Microbiome

- Similar to other diseases, COVID-19 patients show high density of pathogens and low diversity in the lungs, particularly marked decreases of beneficial bacteria.
- The same changes occur in the gut microbiome.
- Still to be determined is the extent to which the changes reflect the disease or contribute to it
- Also to be determined is whether there are interventions that alter the microbiome in a positive way and if so, whether they alter the course of the disease.

High Risk COVID-19

- It is known that COVID-19 ranges from asymptomatic to mild to severe.
- Certain conditions, such as old age, diabetes, and obesity correlate with both higher risk of severe COVID-19 and specific microbiome compositions that increase inflammation.
- Recent studies, show that the correlation between those microbiome markers and severe COVID is even higher than the correlation with the known risk factors. Article
- If further studies show the same results, it could create a pathway to preventing or treating severe COVID through the microbiome.

Examples of Physical Conditions Correlate with Bacteria Composition

- Irritable bowel syndrome (Y)
- C. Difficile
- Type 2 diabetes
- Cardiovascular disease
- Obesity
- Cancer
- Metabolic syndrome
- Autoimmune diseases
- Crohn's Disease
- Melanoma Immune Booster

Examples of Mental Conditions that Correlate with Bacteria Content

- Major depressive disorders (Y)
- Anxiety (Y)
- Parkinson's Disease (PD) (Y)
- Social deficits (Y)
- Amyotrophic lateral sclerosis (ALS), Lou Gehrig's disease (Y)
- Autism (Y)
- Multiple Sclerosis (MS) (Y)
- Alzheimer's Disease (AD) (Y)
- Senescence (Y)
- Personality (Y)

Improving Microbiome

- Mediterranean, DASH, and MIND Diets
- Probiotics
- Prebiotics
- Exercise
- Plant Based Diet
- High Fiber Diet
- Exercise
- Polyphenols
- Sleep

Harming Microbiome

- Artificial Sweeteners
- Glyphosate
- Fried Foods
- Processed Foods
- Multiple Food Additives
- Low Fiber Diets
- Refined Sugar
- Emulsifiers
- Antibiotics
- Toxins in Foods, Cleaning Products, Personal Care Products, Environment

Short-Chain Fatty Acids (SCFA's)

- Most common ones are acetate, propionate, and butyrate.
- Primary source of energy for endothelial cells, lining of the intestine that form a critical barrier to keep out pathogens.
- Play a major role in balancing inflammation and immunity responses.
- Produced from fermentation of plant-based fibers that survive digestion.
- Western diet has created continual reductions in SCFA's.
- Normally, maintaining high levels of SCFA's would be desirable.

Theory and Limitations

- Healthy microbiome is populated by diverse and beneficial bacteria with relatively few pathogenic varieties.
- Beneficial bacteria not only serve healthy functions but also crowd out pathogenic ones.
- The purpose of probiotics and prebiotics is to provide more beneficial bacteria directly or through foods that stimulate the bodies own production.
- It is not totally clear how well they work, whether they make it to the intestines, or whether they stay in the body but there is strong evidence to support their effectiveness.

Probiotics and Prebiotics

- Probiotics - live microbial food supplements that beneficially affect the host animal by improving its intestinal microbial balance. Basically, food products that contain live beneficial bacteria that survive into the intestines and improve the concentration and balance.
- Some research indicates that dead probiotics may work. Abstract
- Prebiotics - nondigestible food ingredients that beneficially affect the host animal by selectively stimulating the growth, activity, or both of one or a limited number of bacterial species already resident in the colon. Basically, foods that survive to be fermented in the colon.

Probiotic Foods

Includes many fermented foods but not all fermentation is probiotic. Not proven but may require live bacteria.

Examples include:

Sauerkraut	Kimchi	Yogurt
Kombucha	Kefir	Miso
Tempeh	Fermented Pickles	Green Olives
Cheddar Cheese	Cottage Cheese	Natto
Gouda Cheese	Apple Cider Vinegar	Balsamic Vinegar

How to Add Prebiotics

Certain foods survive digestion and are fermented in the intestine. There is a huge list of possible foods. Raw foods are usually more effective than cooked.

Examples include:

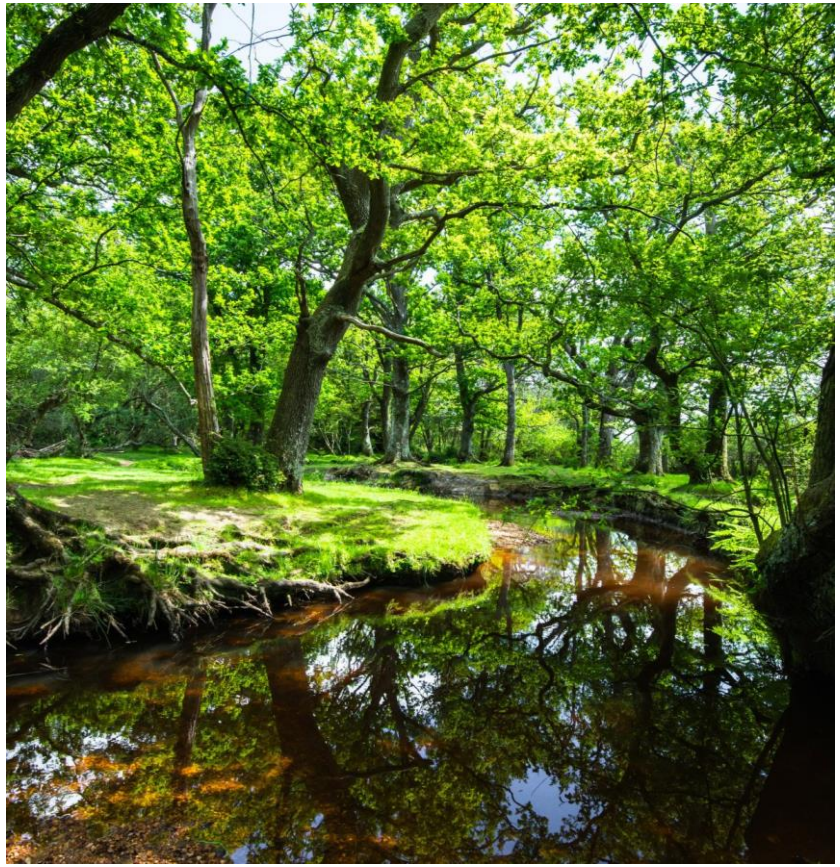
Garlic	Leeks	Onions
Blueberries	Bananas	Asparagus
Whole Oats	Apples	Spinach
Beans	Cocoa	Walnuts
Barley	Flaxseeds	Sweet Potatoes

Dietary Changes vs. Probiotics for Anxiety

- Meta-study of review of 21 studies compared outcome including probiotic supplements, probiotics, and dietary changes.
- All showed improvement but dietary changes had the greatest, followed by probiotics, and then supplements.
- Not all studies distinguished between probiotic foods and probiotic supplements. Study

Exposing Children to Nature Improves the Microbiome

- Study in Finland compared changes in microbiome in children 3-5 by allowing them to play in a mini-forest they created.
- Similar results to children who took daily trips to the forest.
- Intervention was only 28 days.
- Marked increase in diversity as well as increases in bacteria known to support healthy immune systems. Article Study
- May help to explain reduced levels of asthma and allergies in rural children.



[Video]

FMT

About 50% of Fecal Matter Is Bacteria

Fecal Microbiota Transplants (FMT)

- As disgusting at is sounds, literally implanting healthy feces into the guts of those with unhealthy microbiomes
- Extensive success with mice but also used with humans
- Yellow Soup - Practice reported as far back as the 4th century. Chinese doctor Ge Hong documented feeding dried or fermented stool from healthy people to cure diarrhea.
- Over time, scientists are experimenting with implantation of specific bacteria.

Video

Cause and Treatment

- Not surprisingly, the culprits seem to be too few that are anti-inflammatory and too many that increase inflammation.
- Modern research is looking at whether dietary interventions or fecal transplants can help address mental health conditions. Does not necessary indicate the relationship is causal.
- Fecal transplants from anxious or depressed mice and humans into healthy mice led to symptoms of anxiety and depression.
- Similarly, transplants from health donors improved symptoms in mice.

What Makes FMT Work?

- Assumed that it was the implantation of living healthy bacteria that effectively combated C. difficile.
- Small sample experiment (5 patients) used sterilized fecal matter, or fecal filtrate transfer (FFT), which would have eliminated bacteria.
- All 5 were free of diarrhea or other C. difficile symptoms when tested six months later.
- “This finding indicates that bacterial components, metabolites, or bacteriophages mediate many of the effects of FMT, and that FFT might be an alternative approach, particularly for immunocompromised patients.” study

Microbiome and Sleep

- Two groups of mice, one allowed to breath normally and the other intermittently deprived of air during sleep.
- Fecal transplant from each group to other mice.
- Those receiving the transplant from the well rested mice showed normal daytime patterns.
- Those receiving the transplant from the sleep deprived mice slept longer and more often during normal waking times.
    - Article Abstract

FMT Improve Symptoms in Children with Autism

- Those suffering from autism frequently suffer gastrointestinal complications.
- Antibiotics often have positive impact on GI issues and concomitantly marginally improve autism characteristics.
- Antibiotics also have serious side effects and the benefits disappear when the treatment is stopped.
- FMT found to have greater impact on GI issues but still a significant reduction in autism characteristics.
- Surprisingly, the conditions continued to improve after treatment and maintained as of a two-year follow-up. Article

Can We Reverse Aging?

- We know that the microbiome deteriorates with age with resulting weakened immune systems and increased inflammation.
- Many studies have been done with animals, primarily mice and fish, that show that fecal transplants between young and old tend to restore the aging microbiome.
- We also know that the microbiome tends to equalize among those sharing a household.
- In this study, looking at the immune system of mice, they found that both fecal transplants and cohousing had exactly that effect. Study
- In a different study, older kingfish received fecal transplants from young kingfish resulting in a 37% life extension, reduced age-related behavioral decline, and youthful level of gut diversity. Abstract

Psychedelics

- Let’s take a look at so-called psychedelics.
- There are many uses for psychedelics but our primary focus will be on how they are used therapeutically.

Common Names – Common Definitions

- Hallucinogens – causing hallucinations
- Psychedelics
  - Cambridge Dictionary - causing unusually strong experiences of color, sound, smell, taste, and touch, and other mental effects such as feelings of deep understanding or hallucination (= imagining things that do not exist)
  - Miriam-Webster - of, relating to, or being drugs (such as LSD) capable of producing abnormal psychic effects (such as hallucinations) and sometimes psychotic states
- Entheogens
  - Medical Dictionary - A psychoactive substance, usually one derived from plants or fungi or from the secretions of animals such as toads, ingested by a shaman or another participant in a ritual in order to produce visions or gain mystical insight.

Take Home Message

Psychedelics are safe and effective ways to treat mental health conditions, such as depression, anxiety, addiction, and PTSD.

They are far more effective and safe than available therapy or pharmaceutical options.

They are far safer than available pharmaceutical options.

There is no longer any debate about those conclusions, just an onerous and lengthy process necessitated by criminalization.

But appreciate they are powerful and should be treated with respect.

Uses

- Common to bifurcate between medical and recreational use, something we will avoid since it is both too limited and inaccurate.
- Medical is a legitimate category but must be differentiated from health, a broader and more accurate concept.
- Medical is generally related to treatment of a disease, condition, or illness.
- Health includes health promotion and need not relate to a problem. For instance exercise promotes health but need not be treatment for an illness.
- There are many uses that enhance the individual but in ways unrelated to health.
- There also are truly recreational uses. Of course recreational comes from re-create.

Spiritual vs. Medical

- Psychedelic substances have been used in multiple cultures over thousands of years.
- Different cultures use different words and different professionals to address health and spirituality, sometimes overlapping.
- For health and spirituality practices, some cultures use intermediaries and others use direct relationships, or some combination of both.

Nothing New Under the Sun

- 60 years ago we knew what psychedelics do, how they can be used therapeutically, and that they were safe if treated with respect.
- The FDA process is not required for knowledge or data but rather to address DEA scheduling.
- The only remaining questions are how new regulations will be drafted and how they will be designed to monetize substances that either grow naturally or can be produced for pennies.

FDA Breakthrough Designation

- Breakthrough designation, introduced in 2012, rarely used and reserved for treatments for serious and life-threatening conditions that may be better than existing ones.
- 2017 - FDA Designates MDMA As 'Breakthrough Therapy' For Post-Traumatic Stress Disorder (PTSD)
- 2018 – Designated Compass Pathways – psilocybin, limited to severe, treatment resistant depression
- 2019 - Designated Ursona Institute's phase 2 clinical trials using psilocybin to treat depression, not limited to treatment resistant patients

Examples of Psychedelics

- There are many compounds that have psychoactive effect.
- Some grow naturally, others are compounded based on naturally occurring compounds, and other are purely chemical.
- No agreement on what is or is not a psychedelic.
- MDMA and Ketamine are examples of ones that may or may not be called psychedelics.
- The following slides are examples.

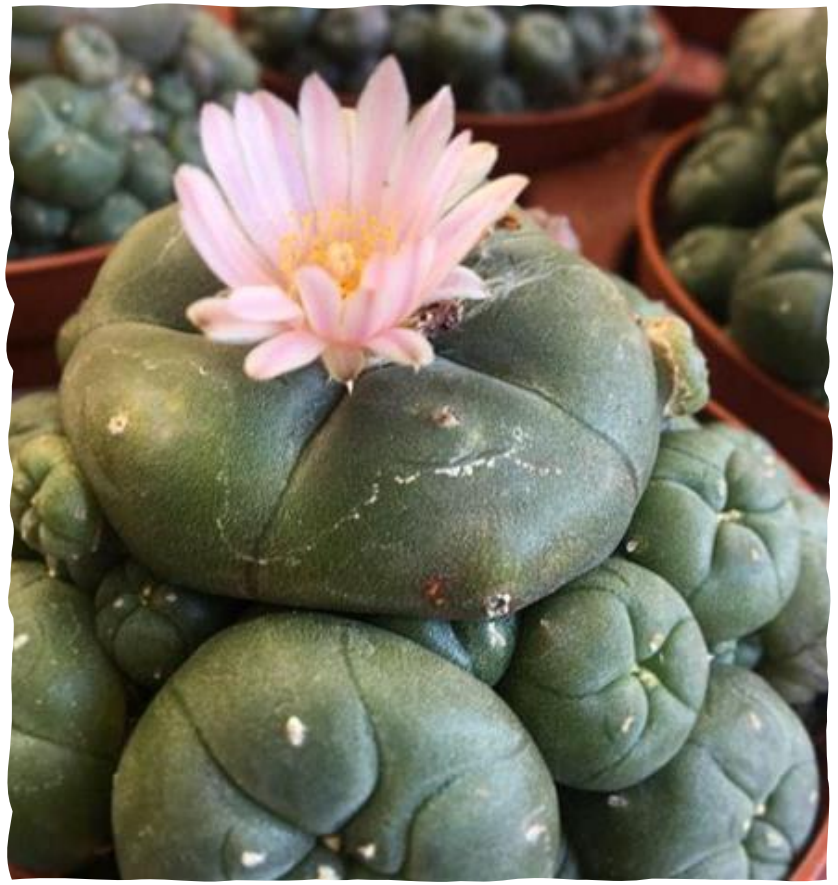
LSD

- Lysergic Acid Diethylamide
- Commonly referred to as ‘acid’
- First synthesized in 1938 by Albert Hoffman
- Made from lysergic acid, which is found in ergot, a fungus that grows on rye and other grains
- 2016 lifetime prevalence 1.2% ages 12-17, 8.3% ages 18-25, and 10.8% ages 26 and older

Psilocybin

- Magic Mushrooms or Shrooms
- 4-phosphoryloxy-N,N-dimethyltryptamine
- Active ingredients are psilocybin and psilocin. Psilocybin molecules too large to reach brain. Broken down to psilocin by liver.
- Naturally occurring in over 180 species of mushrooms found in numerous locations
- Climate change increasing natural growth areas

Mescaline



- Commonly called peyote or buttons
- Found naturally in various cacti, including the Peyote cactus, and some species of beans
- Used for centuries in religious rituals by native peoples
- Schedule 1 drug but legal in certain religious ceremonies registered by the Native American Church

MDMA

- Commonly known as Ecstasy or Molly
- Synthetic first synthesized in Germany in 1912, possibly as an appetite suppressant
- 3,4 methylenedioxymethamphetamine
- Acts as both stimulant and psychedelic
- No commercial use developed and patent ran out

Ayahuasca

- Herbal drink made from plants growing in the Amazon jungle
- Combination of two or more plants
- flowering vine (*Banisteriopsis caapi*), often referred to as B. Caapi
- And shrub chacruna (*Psychotria viridis* or *Diplopterys cabrerana*)
- Chacruna contains Dimethyltryptamine (DMT or N,N-DMT) but the body cannot synthesize it
- B. Caapi allows the body to synthesize DMT
- DMT occurs naturally in the human body and brain

Salvia Divinorum

- Powerful, short acting psychedelic drug native to Mexico and used in religious rites.
- Psychedelics, such as psilocybin and LSD, work through serotonin receptors.
- Salvia works on the kappa opiate receptors (different than mu opiate receptors related to pain and affected by opium and heroin).
- Salvia led to different experience than psilocybin and LSD but with some similarities.

Ketamine

- Also known as K or Special K
- Synthetic developed as an anesthetic or to relieve pain and discomfort during medical tests and procedures
- Even though not approved for depression, off label use is legal with a prescription

Other Natural Psychedelics

- San Pedro – cactus of the Trichocereus genus containing mescaline similar to peyote
- Iboga – Tabernanthe Iboga – Black Bugbane – Sacred Wood
  - Shrub found in African Rain Forests
  - Contain the psychedelic Ibogaine (12-methoxyibogamine)
  - Similar to LSD in effect but lasts for up to 20 hours
  - Iboga extracts used to treat opioid addictions
- 5-MED - 5-MeO-DMT - 5-methoxy-N,N-dimethyltryptamine
  - Related to but not DMT found in ayahuasca
  - Found in numerous plants and venom of *Bufo alvarius* toad
  - Extremely potent and more intense than other psychedelics
  - Short acting so fits Western medical model

Traditional Uses

- Psilocybin traditionally used in Mexico
- Ayahuasca traditionally used in South America
- Ibogaine traditionally used in Africa
- LSD, a more recent discovery and a synthetic, was mostly used North America and Europe

Medical Model

- Recent research has focused on diagnosed mental health issues and has adhered to strict medical models.
- Partially that is justified because of the prevalence of often debilitating depression, anxiety, addictions, and PTSD and the lack of effective alternative treatments.
- But in reality, the primary reasons are selling it to the public, raising capital, and most importantly, avoiding FDA and DEA prohibitions.

Conditions with Clinical Evidence of Improvement with Psilocybin

- Long term clinical depression
- Long term clinical anxiety
- Alcohol addiction
- Smoking addiction
- Cancer or terminal illness induced depression of anxiety.
- Obsessive-Compulsive disorders
- PTSD
- Criminal behavior

Cancer or Terminal Condition Depression

- Original LSD studies in the 50's and 60's were on terminally ill cancer patients for the purpose of pain relief.
- While it achieved its purpose, it also relieved the depression in almost all and allowed them to come to terms with their illnesses and enjoy their remaining time.
- Johns Hopkins has recently taken the lead among medical centers in psilocybin research, including with the terminally ill.

Bill Wilson – Founder of AA

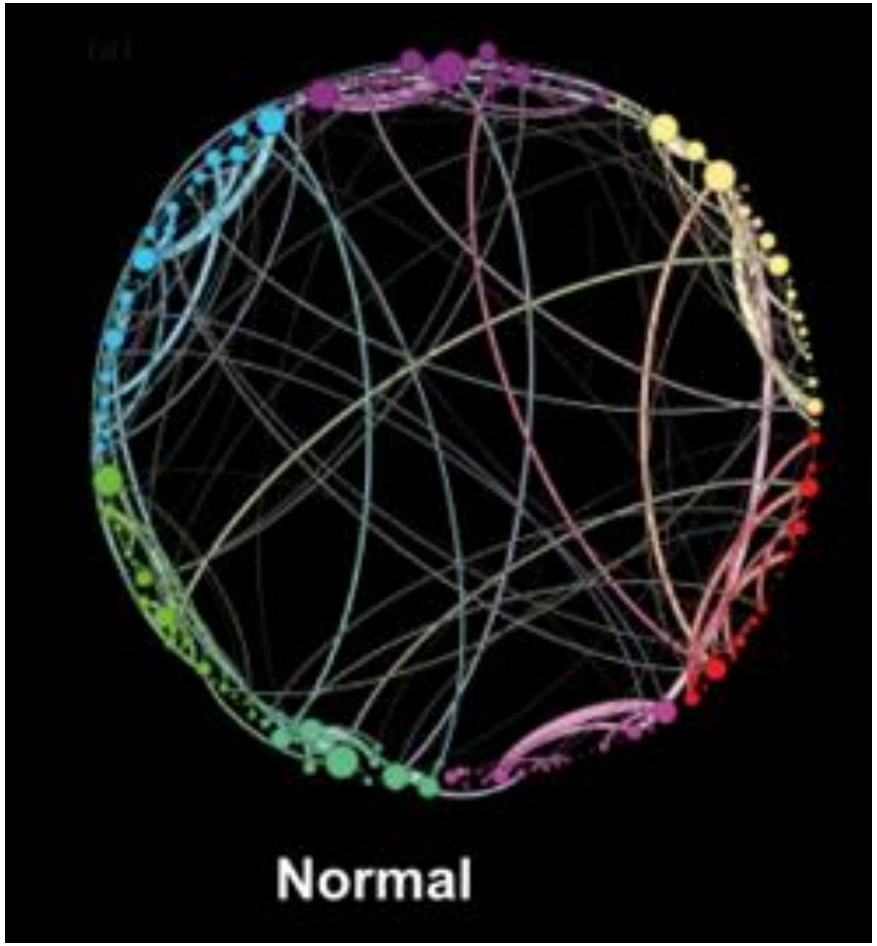
- Wilson a regular user of LSD. This all occurred when LSD was legal.
- He believed it had great potential to help alcoholics overcome their addictions but was careful to say little publicly.
- Most of what he believed was found in personal letters of his.
- One quote - "The vision and insights given by LSD could create a large incentive – at least in a considerable number of people.“
- AA considered including LSD but rejected it as too controversial.
- Wilson defended his use of LSD but dropped off the AA governing board in 1958 to be free to continue his “experiments”.

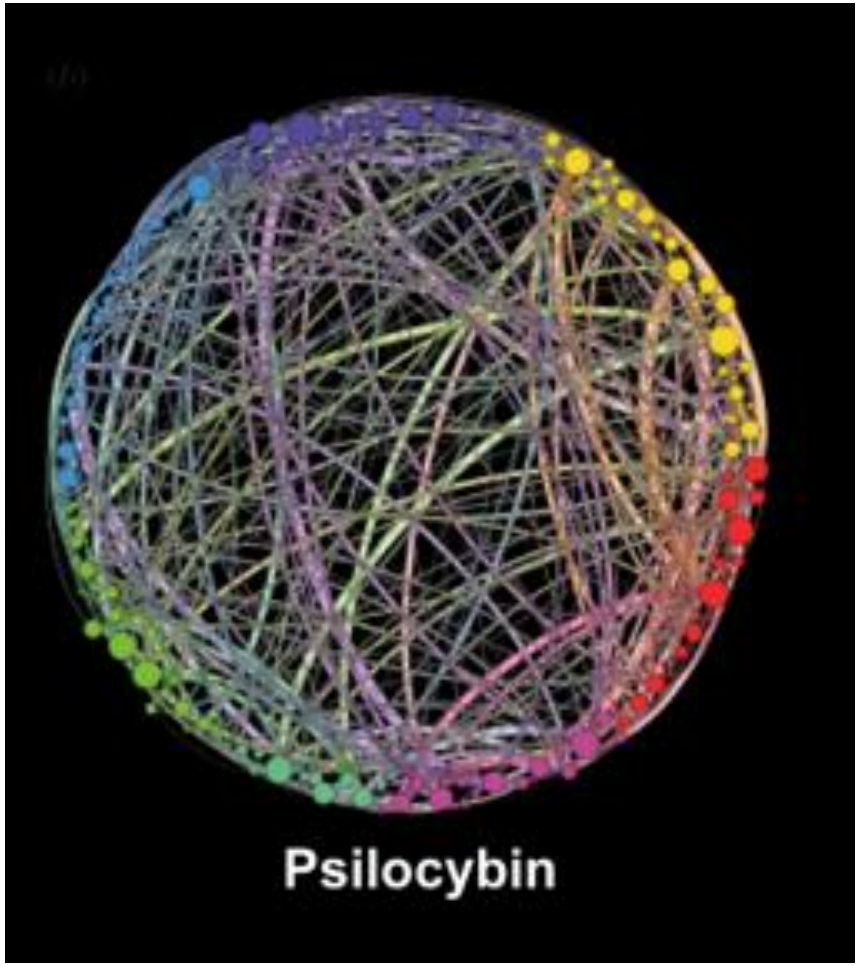
How it works

- Research has been so limited that we have much more to learn about how psychedelics work.
- The primary model is based on relearning, creating new pathways based on current inputs to replace some that have developed historically but are neither adaptive or healthy.
- Think of ski trails or forest paths.
- We know there is greatly enhanced brain activity and new connections developed but we do not know the extent it is based on excitatory factors vs. inhibitory factors or a combination of both.

How Does it Work in the Brain?

- Decreases localized in important hub structures in the brain, such as the thalamus, posterior cingulate cortex and medial prefrontal cortex - structures important for information integration and routing
- Highly significant correlation between the magnitude of decreases in oscillatory activity in the PCC and reports of ego-disintegration
- Stimulation of serotonin 2A receptor disrupts coupling between the firing of certain cells types and the rhythmic oscillations of larger populations of neurons in the cortex.
- Psychedelics have a disorganizing influence on cortical activity which permits the brain to operate in a freer, less constrained manner than usual.





Active Links

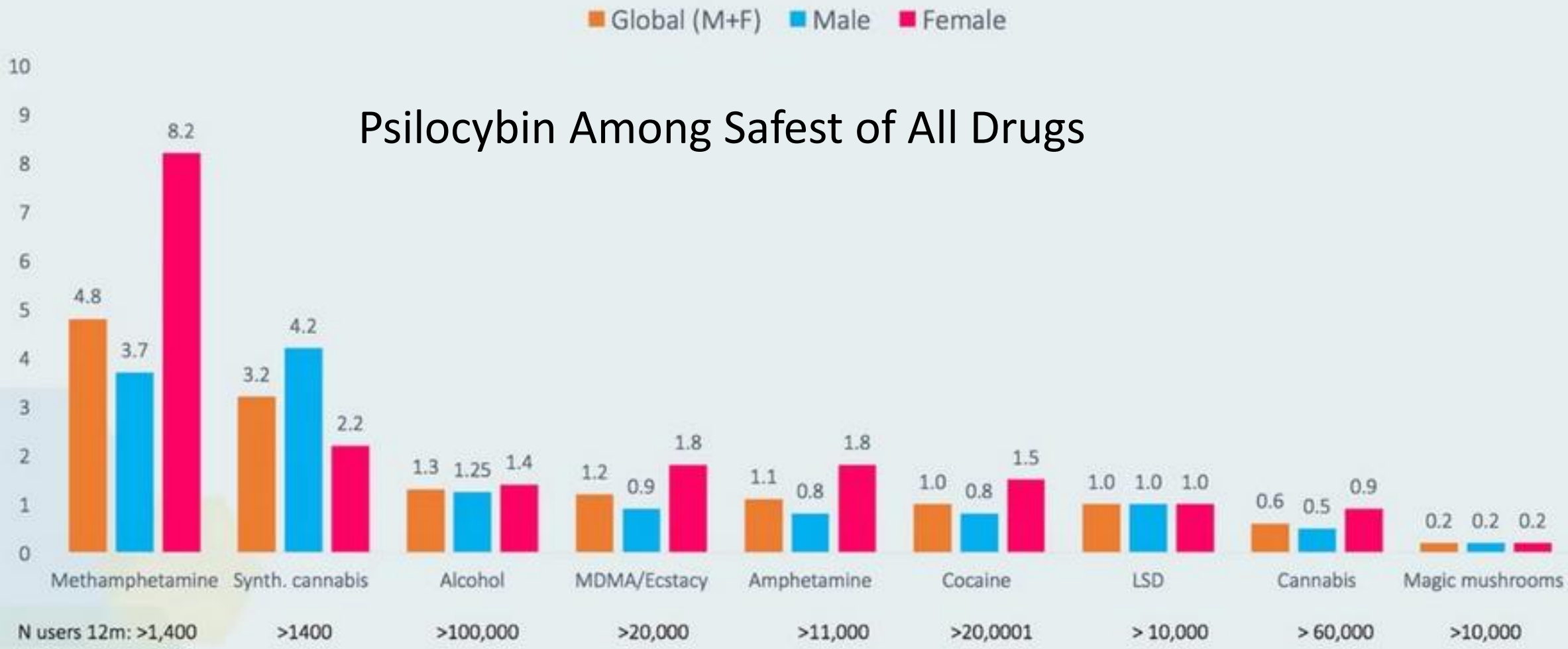
[Study]

Effects of psilocybin on hippocampal neurogenesis and extinction of trace fear conditioning

- Mice taught to associate auditory signal with electric shock.
- Study measured rate of unlearning when shock no longer used.
- Three groups – saline (control), low dose psilocybin, high dose
- Low dose resulted in much greater rate of unlearning than high dose or control but high dose marginally faster than control.
- Both high and low dose resulted in neurogenesis in the hippocampus but low dose had larger effect. Study
- Appears that different dosing levels may be appropriate for different purposes e.g. PTSD vs. Depression or Addiction

- There have been anecdotal accounts of people having psychotic breakdowns using psychedelics.
- No solid research or clinical analysis
- One common theory is that psychedelics could trigger a psychotic episode in someone who was pre-psychotic.
- Researchers generally screen out those who appear to be unstable.
- While there have been no known episodes in any of the trials, no way to know if it is because or the screening, the protocols, the support, or because it is not a legitimate concern.

GDS2017 Global comparison of emergency medical treatment seeking – GDS2017 all substances



Psilocybin Among Safest of All Drugs

GLOBAL DRUG SURVEY

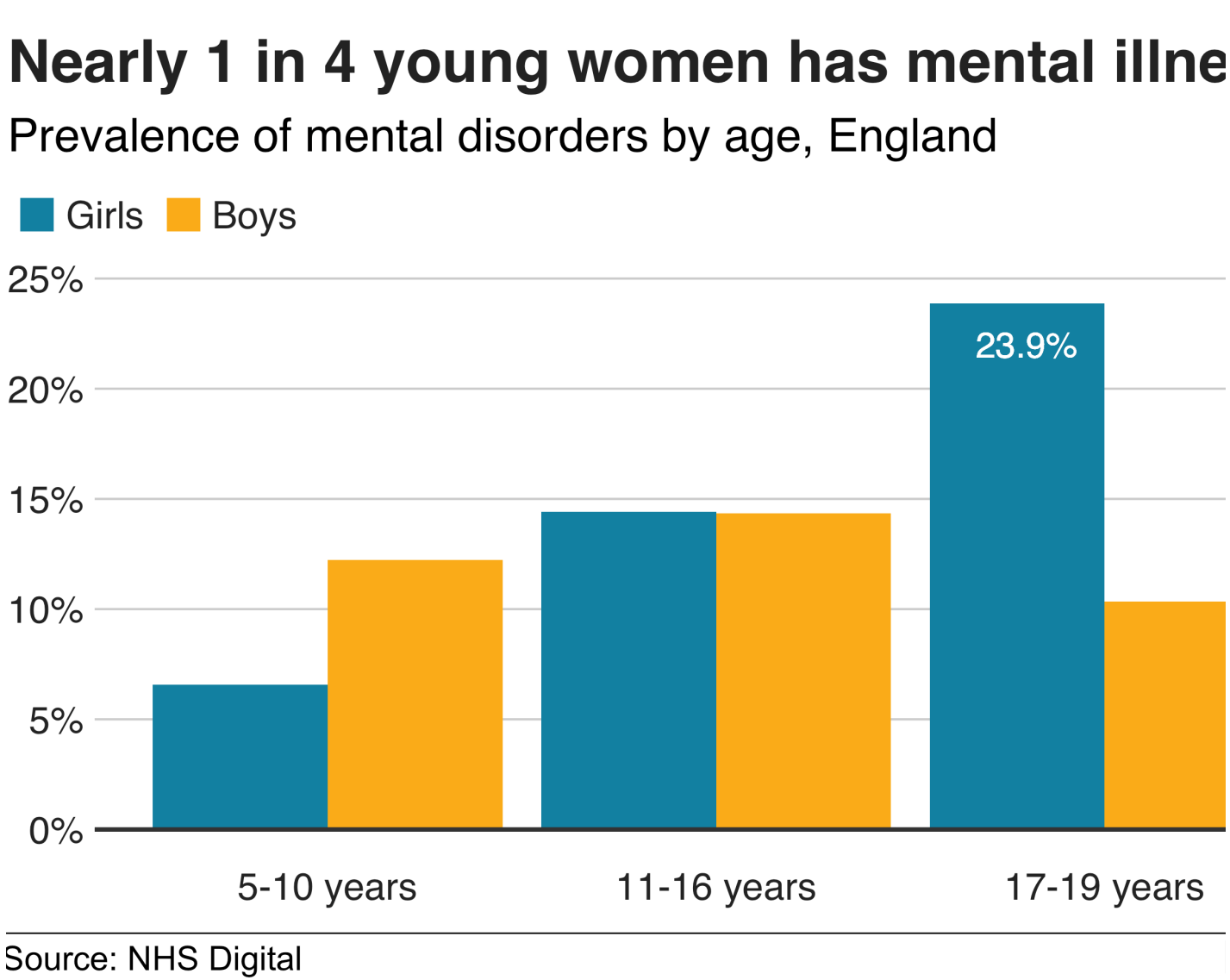
2017

Lasting Changes with Psilocybin

- Johns Hopkins 2011 study looked at lasting changes among those who had participated in various studies receiving 2-5 doses.
- Measured 14 months after last dose and found in 60% of subjects.
- Changes were in openness, including imagination, aesthetics, feelings, abstract ideas, and broad-mindedness. Openness is a well researched primary personality trait measured with well validated inventories.
- Changes were greater than measured over decades of life experiences and unheard of in adults after the age of 30. Study

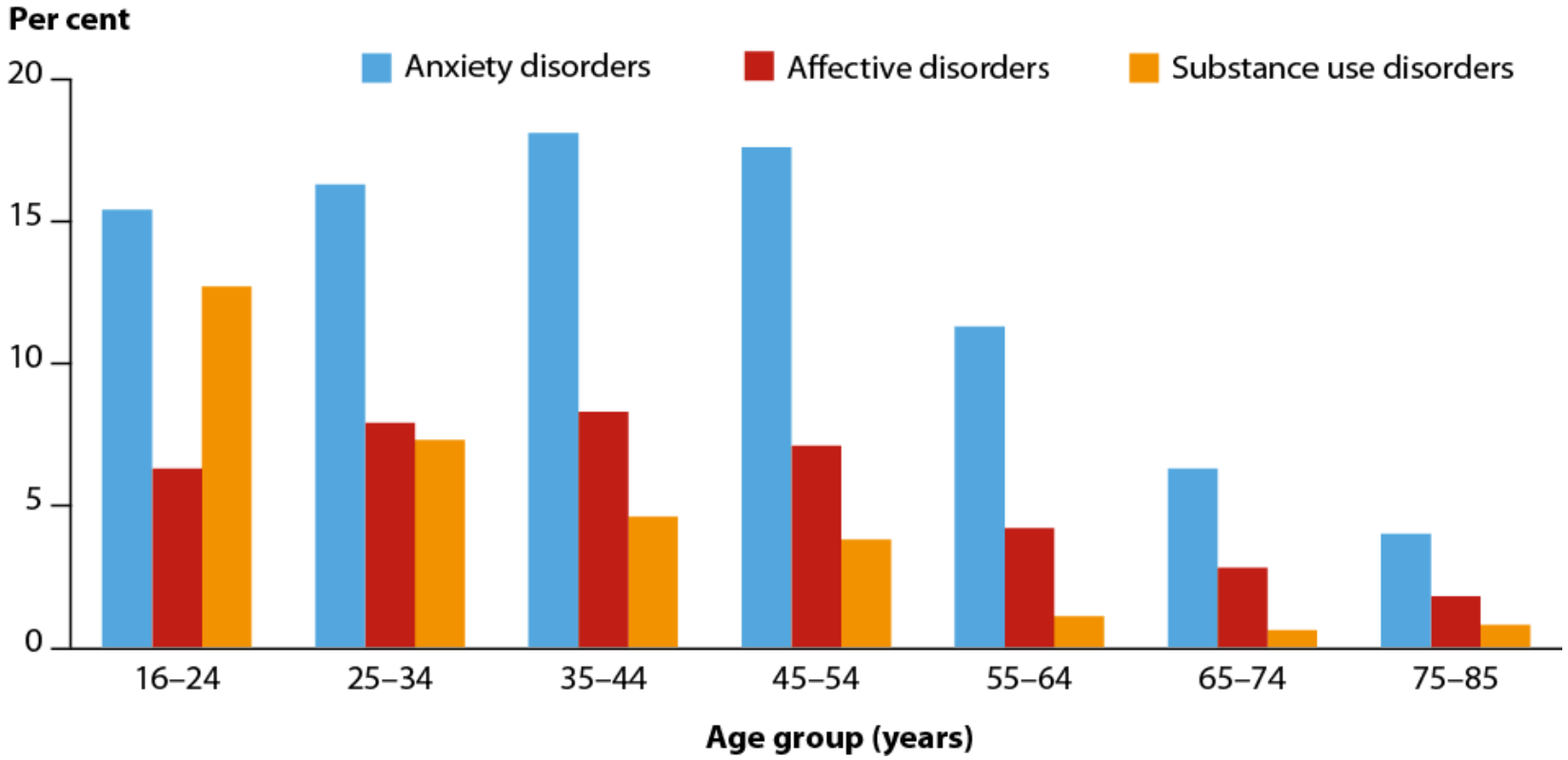
Johns Hopkins Statistics

- An estimated 26% of Americans ages 18 and older -- about 1 in 4 adults -- suffers from a diagnosable mental disorder in a given year.
- Approximately 9.5% of American adults ages 18 and over, will suffer from a depressive illness each year.
- Approximately 18% of people ages 18- 54 have an anxiety disorder in a given year.



Mental Illness Among Young People in England

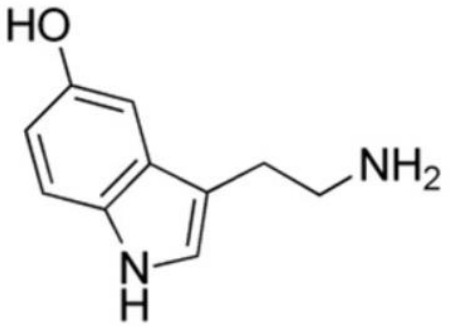
Australia Prevalence of Disorders



Symptoms vs. Causes

- Low levels of serotonin correlate with depression (but really quite more complicated).
- Assumption was increasing serotonin by reducing reuptake or inhibiting Monoamine Oxidase (MAO) which annihilate serotonin would treat depression.
- Limited impact may be based treating symptom rather than cause.
- Ear lobe crease
- Beta amyloid plaques and tau tangles

Serotonin



- One of many neurotransmitters also a hormone. Acts as neurotransmitter in brain but as hormone in digestive system.
- 5-hydroxytryptamine, or 5-HT
- Over 90% produced in the digestive system.
- Made from the essential amino acid tryptophan
- Tryptophan enters the body through diet
- Complex effects not fully understood but important in digestion and sleeping as well as regulating mood

Pharmaceutical Treatment of Depression

- Most common treatments for depression are Monoamine oxidase inhibitors (MAOI's) and Selective Serotonin Reuptake Inhibitors (SSRI's).
- Both increase the amount of serotonin, SSRI's by preventing reuptake and MAOI's by inhibiting MAO from breaking it down.
- MAOI's also prevent breakdown of norepinephrine and dopamine.
- Neither corrects and conditions.
- Both work for most people in the short term but with multiple, and often dangerous, side effects.

Psilocybin and Serotonin Receptors

- Psilocybin (chemically known as 4-phosphorryloxy-N, N-dimethyltryptamine
- Serotonin 2A receptor (5-HT2AR) agonist
  - 5-HT is serotonin
  - 2A is the receptor
  - Agonist excites, antagonist inhibits
- Attaches to 2A and no psychedelic effect if 2A blocked
- Also binds to many other 5-HT receptors but scientists are not sure of how they interact.
- Similar psychedelics, like LSD, bind to same receptors.

Correcting Serotonin Systems

- Serotonin, 5-hydroxytryptamine (5-HT), is a neurotransmitter
- Modulating cognition, reward, learning, memory, and numerous others
- 90% or more of serotonin is manufactured in the gut.
- More and more studies on depression are focusing on the health of the human microbiome and diet and exercise.
- Studies of psychedelics are focusing on how they reorder the way the body creates and uses serotonin rather than adding more or preventing reductions.
- Serotonin does many positive things but also not so positive. Systems working as designed more critical adding or subtracting neurotransmitters.

Serotonin Reordering

- Studies of psychedelics are focusing on why and how they appear to reorder the way the body creates and uses serotonin rather than simply trying to add more or prevent reductions.
- Serotonin does many positive things but also things that are not so positive. Having systems work as they are designed is more critical than simply adding or subtracting a single neurotransmitter.
- Improves connection quality between neurons
- Inhibitory action – prevents over-excitement of neurons and so fosters relaxation, calmness, happiness, and focus

Increased amygdala responses to emotional faces after psilocybin for treatment-resistant depression

- Psilocybin with psychological support was used successfully to treat depression.
- Amygdala responses to fearful faces were increased one day after psilocybin session.
- Increased amygdala responses predicted positive clinical outcomes.
- Psilocybin assisted therapy treats depression by reviving emotional responsiveness. Study

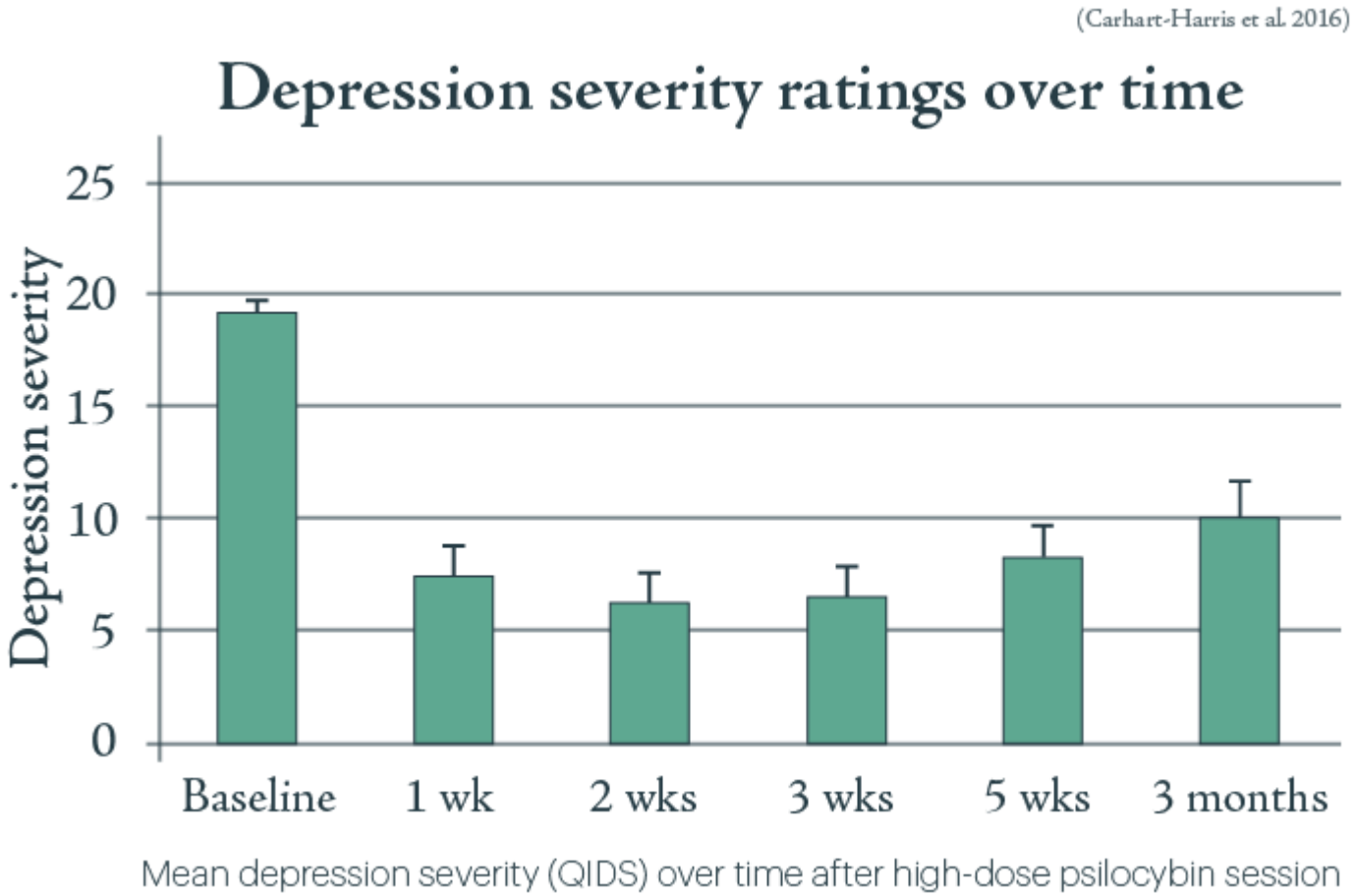
Compare to SSRI's

- SSRI's result in decreased amygdala responsiveness, blunting feelings.
- Explains why SSRI's similarly blunt positive feelings since there is no scientific explanation of how suppressing negative, but not positive amygdala reactions could occur.
- It appears psilocybin works to confront and integrate negative emotions rather than avoidance and disconnection
- Julie Holland is a psychiatrist who is currently serving as the medical monitor for a study of MDMA and psychotherapy in veterans with PTSD.
- Those medications (SSRI's), Holland said, "are sort of sweeping symptoms under the rug. Psychedelic psychotherapy takes the rug out back and beats the hell out of it and vacuums the floor and puts the rug back down."

Which Would You Choose Treat Depression?

	Prosac (SSRI)	Psilocybin
Effectiveness	1-3% more effective than placebo	Over 80% effective
Usage	Possibly Lifetime	Often single dose
Erosion	Loses effectiveness after 6 months	Limited or no erosion
Side Effects	Serious and Numerous	Minimal
Ability to Feel	Depressed	Enhanced
Interpersonal	Seriously interferes	Enhanced

The Beckley/Imperial Psychedelic Research Programme - study

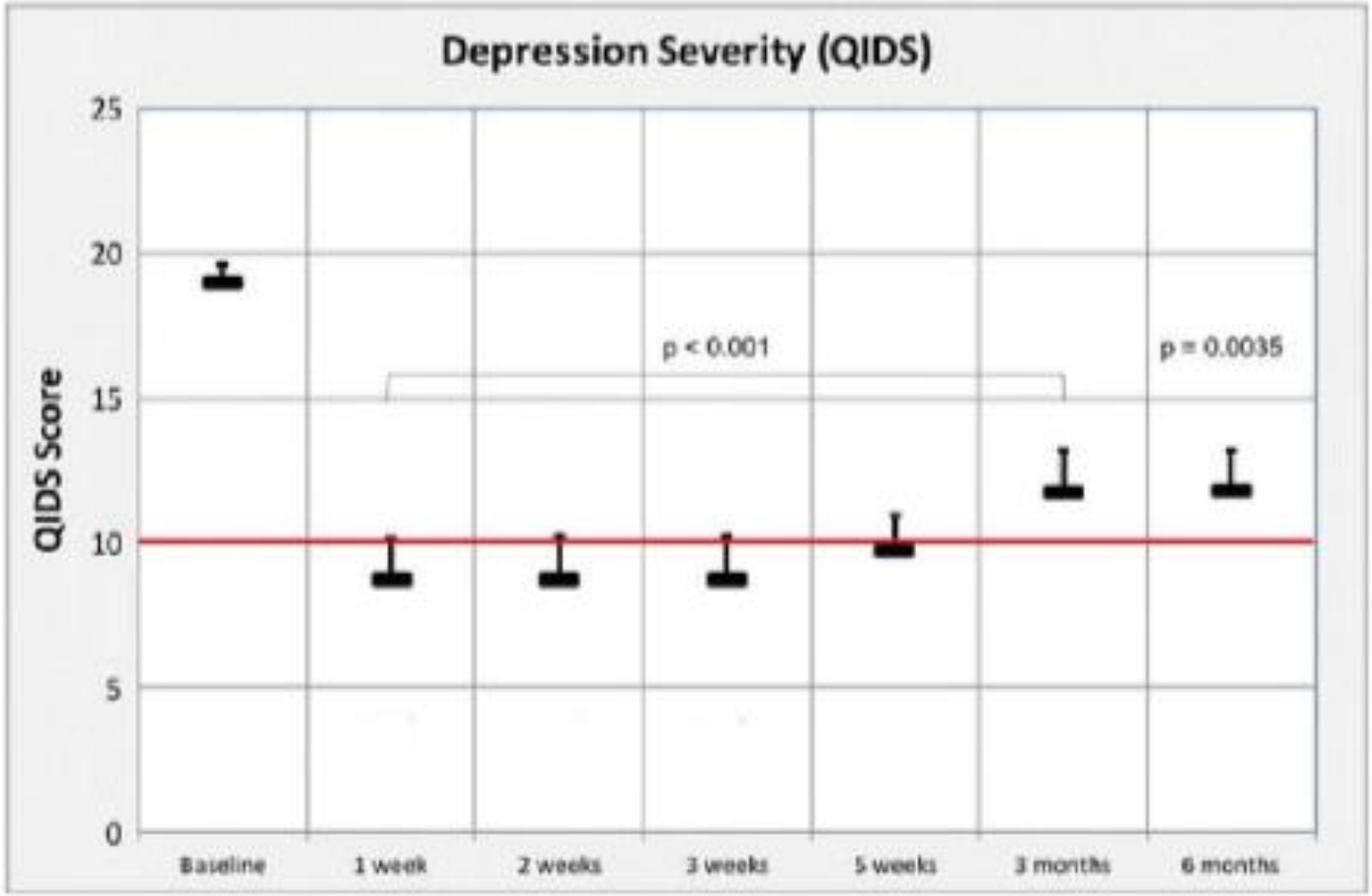


Depression severity determined by self-rated 16-item QIDS. QIDS scores of 16–20 are considered to reflect severe depression, scores of 11–15 are considered moderate depression, scores of 6–10 are considered mild depression, and scores of 5 and less are considered absent depression.

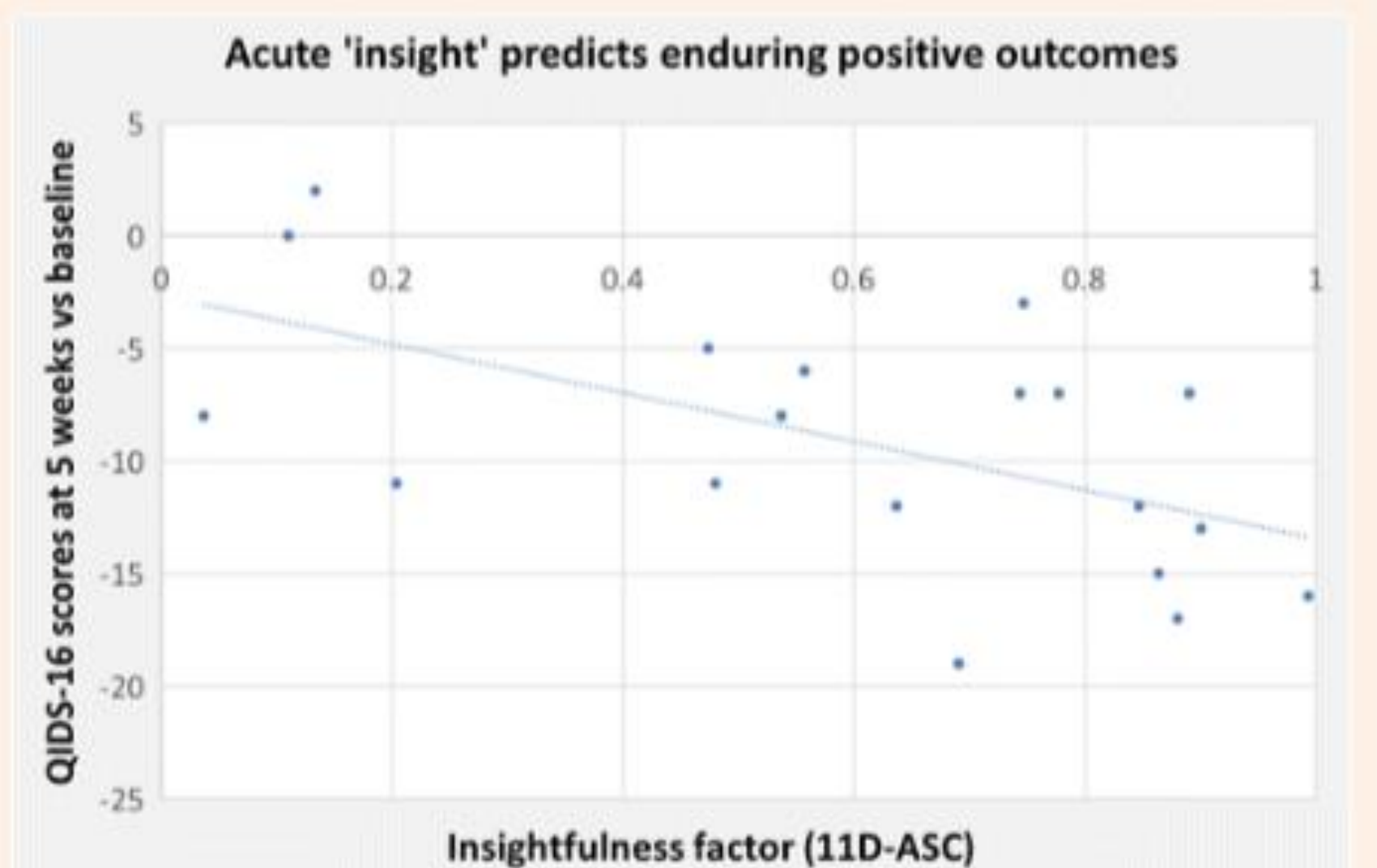
Overview of Results

- All 12 participants improved after psilocybin
- 67% were in remission (depression-free) at 1 week post-treatment
- 42% were still in remission after 3 months

Follow up Study



Self Reported Insightfulness Correlated with Positive Outcomes



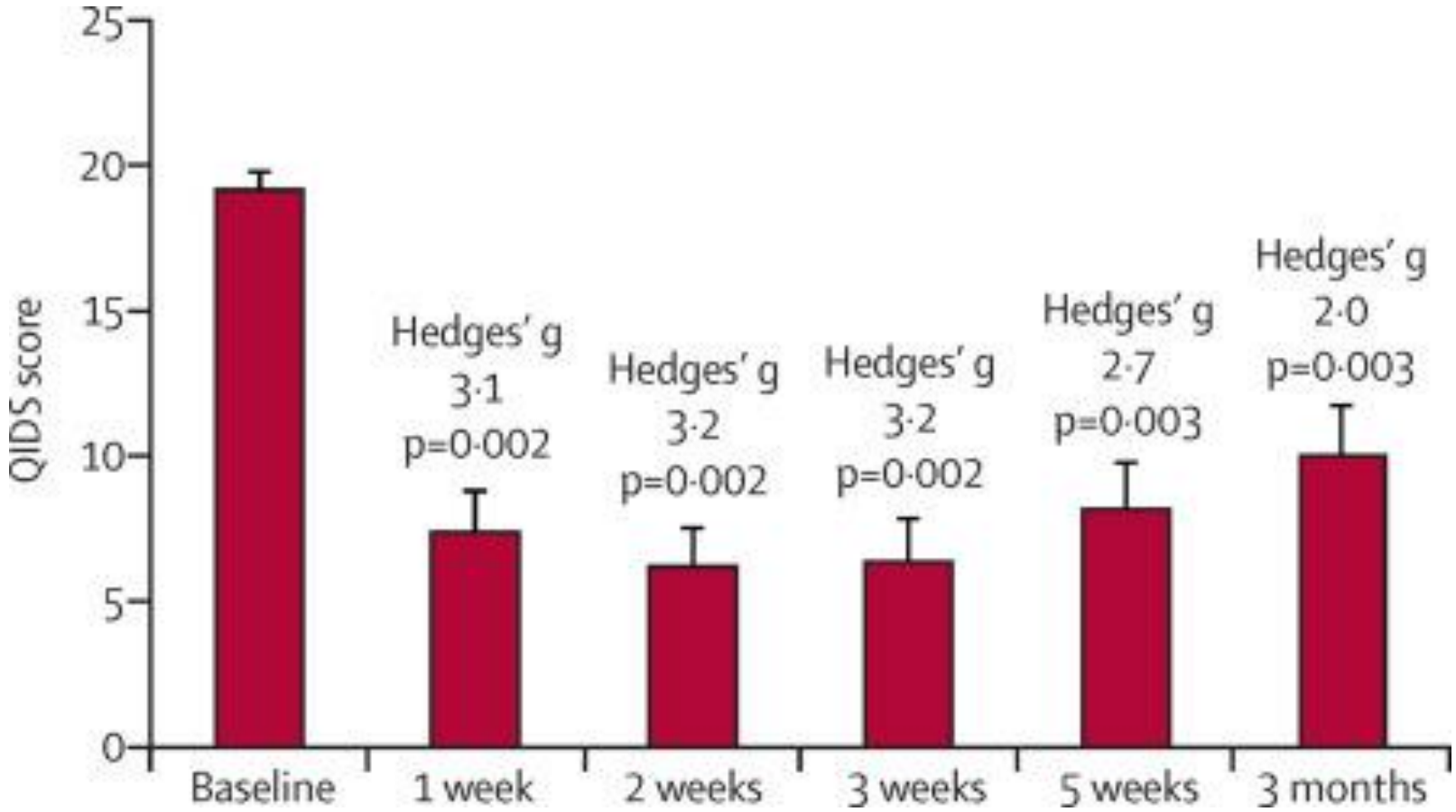
Psilocybin for Depression and Anxiety Related to Life-Threatening Cancer

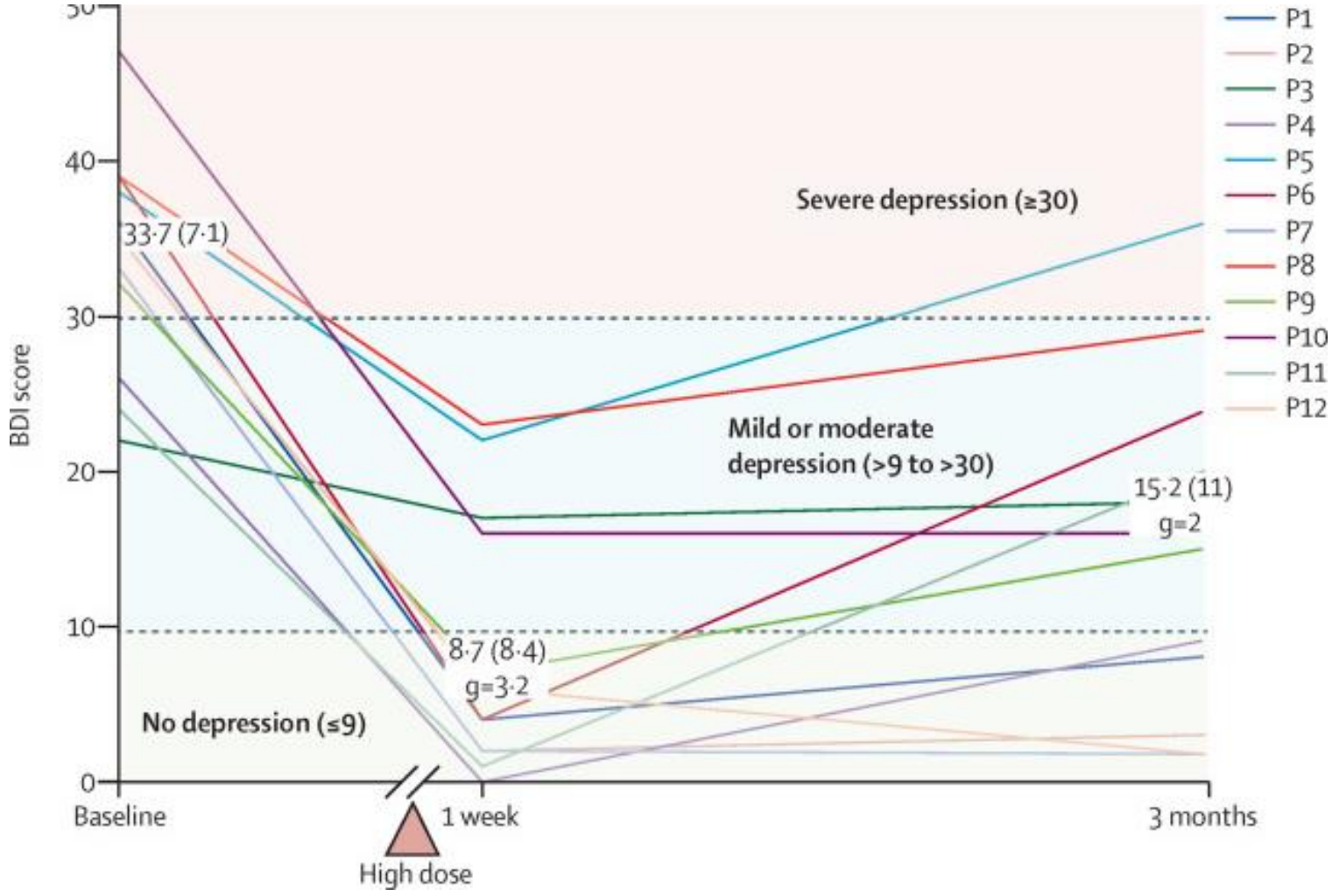
- Johns Hopkins study immediate and long term impact.
- At 6-month follow-up, these changes were sustained, with about 80% of participants continuing to show clinically significant decreases in depressed mood and anxiety. Study
- Similar results NYU study – 60-80% at 6 month followup Study
- Research reports have to report Adverse Events (AE), both medical and psychiatric – Psylocybin studies, including these, inevitably include “No AE’s”.

Robin Carhart-Harris Study

- Treatment of unipolar treatment-resistant depression with psilocybin
- Treatment-resistant means pharmaceuticals did not work.
- Two doses each, small dose to assess tolerance and then stronger ‘therapeutic’ dose
- Small sample size but extraordinary results, particularly since subjects were the most difficult to treat with no reasonable alternative.
- Results were primarily responsible for Breakthrough status granted by FDA to immediately move to the next phase of testing.
- Results published in Lancet, probably most prestigious medical journal in the United Kingdom Study

Overall Depression Inventory Results





Individual Results

2020 Johns Hopkins Study

- Psilocybin four times more effective than anti-depressants.
- (Short-term evaluation - Anti-depressants, even when effective, tend to stop working after 6 months.)
- Extent of mystical experience correlated with extent of reduced depression.
- No adverse effects.
- More effective and longer lasting than ketamine. Study

Chronic Traumatic Encephalopathy(CTE)

- Brain degeneration caused by repeated head trauma.
- Can only be diagnosed by autopsy.
- Debilitating condition that causes cognitive impairment, impulsive behavior, depression, apathy, short-term memory loss, difficulty planning and carrying out tasks, emotional instability, substance abuse, and suicidal thoughts or behavior.
- Often results in unprovoked and uncharacteristic violence and homicides.
- Prevalent in athletes in sports such as football, soccer, and hockey.
- No known treatment or even palliative care.

Video

MDMA, Molly, or Ecstasy

- MDMA has been granted breakthrough status by the FDA as a treatment for PTSD.
- It is also being used to improve relationships, often as part of marriage counseling.

MDMA Reopens Critical Learning Period

- “A critical period is a developmental epoch during which the nervous system is expressly sensitive to specific environmental stimuli that are required for proper circuit organization and learning.”
- This critical period closes by the time we reach adulthood.
- “Closure of critical periods limits the ability of the brain to adapt even when optimal conditions are restored.”
- “single dose of . . .(MDMA) reopens the critical period for social reward learning “
- Excerpts taken from Abstract

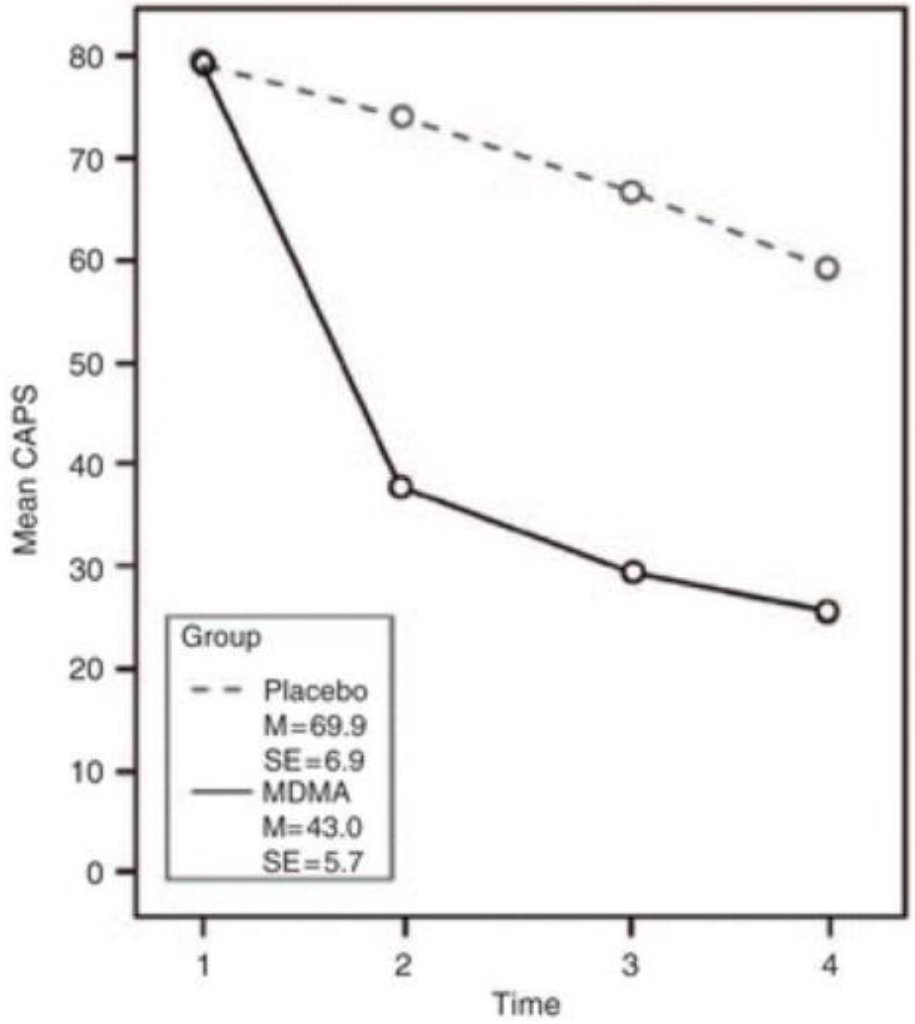
MDMA and Couples Therapy

- In the late 1970's and early 1980's, MDMA showed tremendous effectiveness in couples therapy.
- So of course the DEA, in 1985, decided to list it as Schedule 1 and stop all further research.
- That research has started again and showing the same results we knew about 40 years ago.

MAPS Funded MDMA PTSD Results

- Multidisciplinary Association for Psychedelic Studies (MAPS) has funded multiple small studies to establish the efficacy of MDMA (Ecstasy, Molly) on PTSD
- As in other psychedelic research studies, subjects were those with treatment resistant conditions that had failed to respond to all known psychotherapeutic and pharmacological interventions.
- Results led to FDA granting Breakthrough status for MAPS to proceed to phase 3 testing.

Results in One Proof Principle Study



Time 1: Baseline < 4 weeks before first experimental session and after discotinuing any psychotropic medications
Placebo=79.6 (8.1), MDMA=79.2 (6.6)

Time 2: 3-5 days after first experimental session
Placebo=74.1 (10.3), MDMA=37.8 (8.4)

Time 3: 3-5 days after second experimental session
Placebo=66.8 (8.0), MDMA=29.3 (6.5)

Time 4: 2 months after second experimental session
Placebo=59.1 (9.4), MDMA=25.5 (7.7)

Second MAPS Phase 2 Study

- 28 people suffering from PTSD, mean period of duration of over 29 years
- All prior pharmaceutical and therapeutic intervention without success.
- Study combined MDMA with Cognitive Behavioral Therapy (CBT).
- Half diagnosed with major depression, another quarter with depression.
- All but one had suicidal ideations with many having attempted suicide.
- All showed improvement with 76% no longer meeting diagnostic criteria for PTSD 12 months after completing treatment.
- There were no adverse events. Study

Why It Works

- No one knows for sure but there are logical reasons why it works so well.
- Trauma theorists believe emotional engagement is necessary for processing traumatic experiences.
- Under the influence of MDMA, people are able to remain emotionally connected while working with difficult traumatic material.

Smoking Cessation

- While many have effectively quit smoking, it is often after many tries and hardcore smokers have particular difficulty quitting.
- Reduction in smoking has been accomplished primarily through price increases (high taxes) and inconvenience (no smoking in workplaces, restaurants, etc.)
- Smoking cessation through non-pharmaceutical methods such as hypnosis and therapy have extremely low success rates.
- The ‘Patch’ is effective at the 6^{th} month mark in 20% of cases.
- Varenicline (Chantix) is effective after 6 months in 30% of cases.

Which Would You Choose to Quit Smoking?

Effectiveness	**30%**	**80%**
Cost	$405 - $515	$30 - $50
Side Effects	Seizures, New or worse heart or blood vessel (cardiovascular) problems, Sleepwalking, Allergic (can be life-threatening), Serious skin reactions (some of these skin reactions can become life-threatening), Nausea, Sleep problems, Constipation, Gas, and Vomiting	Nausea, Temporary Panic Attack
Risks	New or worse mental health problems, such as changes in behavior or thinking, aggression, hostility, agitation, depressed mood, or suicidal thoughts or actions	May trigger breakdown for those in pre-psychotic state
Other Side Effects	These are not all the side effects of CHANTIX. Ask your healthcare provider or pharmacist for more information.	

Guess Which?

- Chantix vs. Psilocybin
- Federal Regulators Approved
- Alternatives such as nicotine patch and hypnosis less than 20% effective

Dr. Roland R. Griffiths, Ph.D. - TedMed Talk

- Professor in the Departments of Psychiatry and Neurosciences at the Johns Hopkins University School of Medicine.
- Using unusually rigorous scientific conditions and measures, Johns Hopkins researchers have shown active agent in “sacred mushrooms” can induce mystical/spiritual experiences descriptively identical to spontaneous ones people reported for centuries.
- Griffiths said, “I had a healthy skepticism going into this”.
- More than 60% met criteria for a “full mystical experience” by psychological scales.
- One third said it was the spiritually most significant experience of their lives and more than two thirds rated among the five most significant.
- In 2 month follow-up, 79% reported moderately or greatly increased well-being or life satisfaction compared to placebo. Confirmed by friends, family members, and co-workers.
- Psychological tests and subjects’ own reports showed no harm to study participants, Link

Dr. Roland Griffith

- TedMed Talk