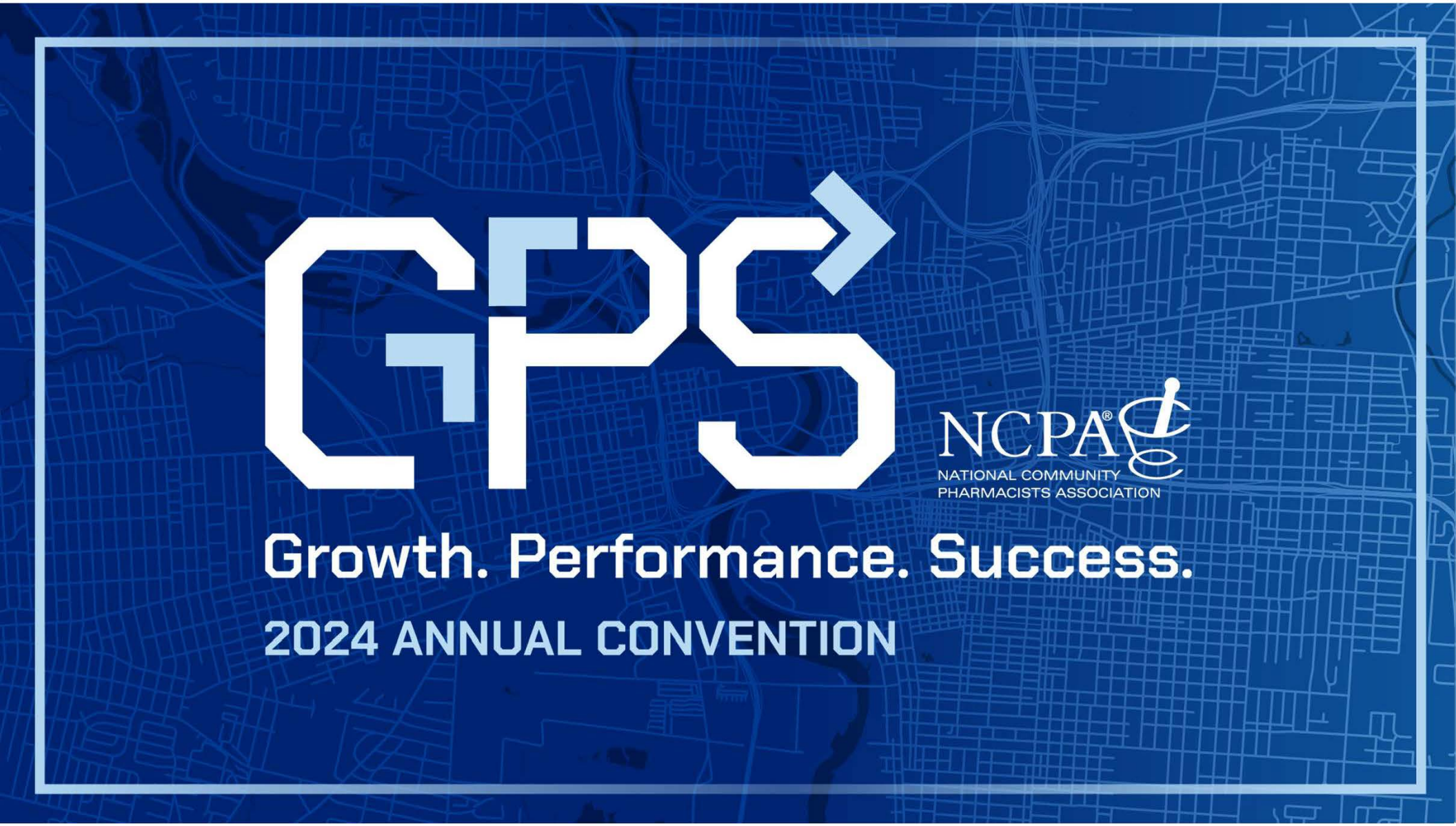
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2024 ANNUAL CONVENTION

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Beyond Serotonin: Exploring the Bidirectional Gut-Brain Connection for Managing Mental Health

NCPA 2024 Annual Convention and Expo

Columbus, Ohio

Speakers

Lara Zakaria PharmD MS CNS CDN IFMCP

Owner

Foodie Farmacist LLC

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Disclosure Statement

There are no relevant financial relationships with ACPE defined commercial interests for anyone who was in control of the content of the activity.

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Pharmacist Learning Objectives

1. Discuss the various factors that contribute to the rise of depression and anxiety.
2. Review the bidirectional gut-brain connection and its effect on the gut-brain axis.
3. Discuss personalized, evidence-based dietary and nutraceutical interventions for managing mental health.

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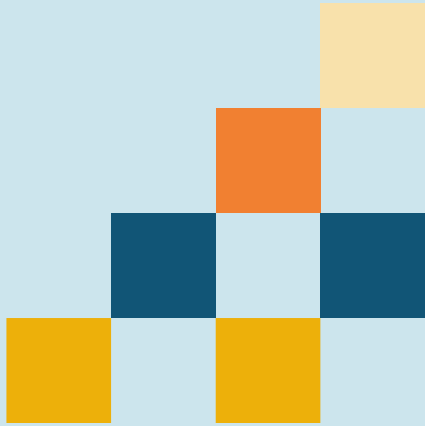
Pharmacy Technician Learning Objectives

1. Discuss the various factors that contribute to the rise of depression and anxiety.
2. Review the bidirectional gut-brain connection and its effect on the gut-brain axis.
3. Identify personalized, evidence-based dietary and nutraceutical interventions for managing mental health.



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Molecular Psychiatry www.nature.com/mp

SYSTEMATIC REVIEW OPEN

Check for updates

The serotonin theory of depression: a systematic umbrella review of the evidence

Joanna Moncrieff[1,2]✉, Ruth E. Cooper[3], Tom Stockmann[4], Simone Amendola[5], Michael P. Hengartner[6] and Mark A. Horowitz[1,2]

The serotonin hypothesis of depression is still infl
associated with lowered serotonin concentration
research. PubMed, EMBASE and PsycINFO were s
until December 2020. Systematic reviews, meta-a
serotonin and serotonin metabolite, 5-HIAA, conce
(SERT) levels measured by imaging or at post-mc
environment interactions. Studies of depression a
bipolar depression) were excluded. Two independ
using the AMSTAR-2, an adapted AMSTAR-2, or t
using a modified version of the GRADE. We did
overlapping studies. The review was registered wit
and meta-analyses, 1 collaborative meta-analysis,
synthesis, 1 genetic association study and 1 umb
quality. Two meta-analyses of overlapping studie
depression (largest $n = 1002$). One meta-analysis
and evidence that lowered serotonin concentration
overlapping studies examining the 5-HT_{1A} receptor (largest $n = 561$), and three meta-analyses of overlapping studies examining SERT binding (largest $n = 1845$) showed weak and inconsistent evidence of reduced binding in some areas, which would be consistent with increased synaptic availability of serotonin in people with depression, if this was the original, causal abnormaly. However, effects of prior antidepressant use were not reliably excluded. One meta-analysis of tryptophan depletion studies found no effect in most healthy volunteers ($n = 566$), but weak evidence of an effect in those with a family history of depression ($n = 75$). Another systematic review ($n = 342$) and a sample of ten subsequent studies ($n = 407$) found no effect in volunteers. No systematic review of tryptophan depletion studies has been performed since 2007. The two largest and highest quality studies of the SERT gene, one genetic association study ($n = 115,257$) and one collaborative meta-analysis ($n = 43,165$), revealed no evidence of an association with depression, or of an interaction between genotype, stress and depression. The main areas of serotonin research

This review suggests that the huge research effort based on the serotonin hypothesis has not produced convincing evidence of a biochemical basis to depression. This is consistent with research on many other biological markers.

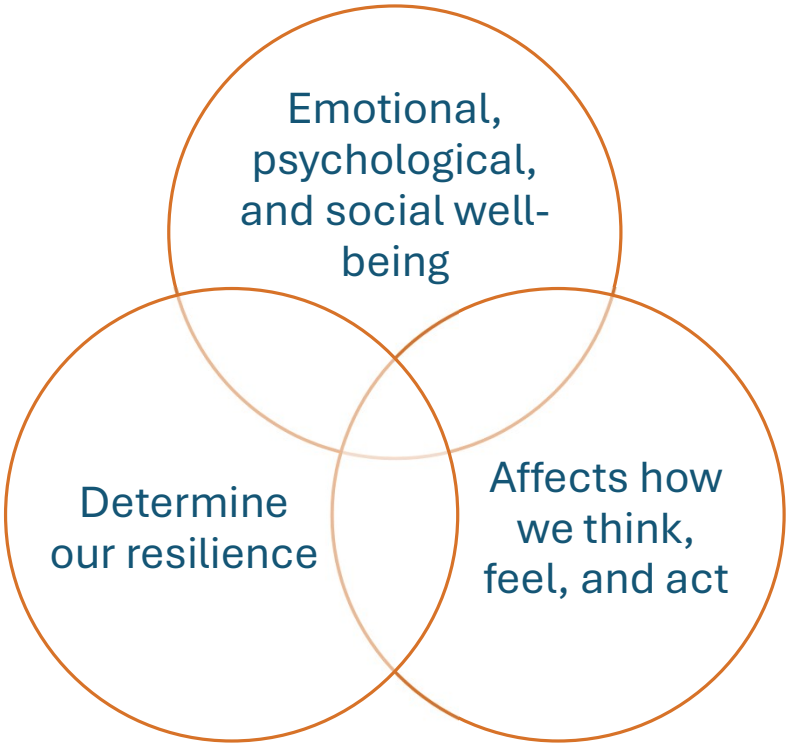
We suggest it is time to acknowledge that the serotonin theory of depression is not empirically substantiated.

Mol Psychiatry. 2022;10.1038/s41380-022-01661-0

Pharmaconutrition

Let’s make it a thing!

Mental Health includes



https://www.cdc.gov/mentalhealth/learn/index.htm

https://www.who.int/en/news-room/fact-sheets/detail/mental-health-strengthening-our-response

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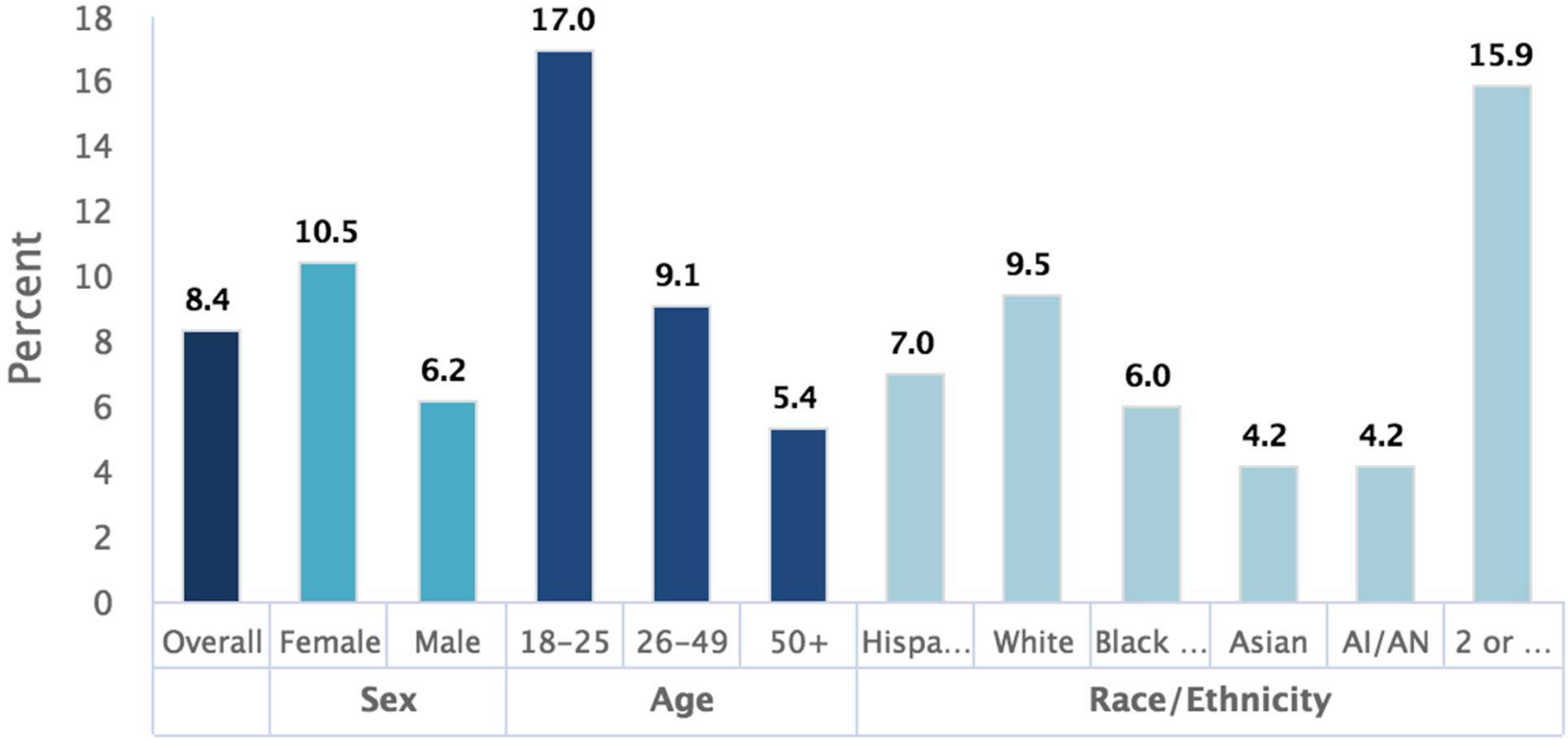
Depression & Anxiety

Incidence and pharmaceutical overview

Past Year Prevalence of Major Depressive Episode Among U.S. Adults (2020)

Data Courtesy of SAMHSA



https://www.nimh.nih.gov/health/statistics/major-depression

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Anxiety Disorders

The most common mental illness in the U.S.

Affects 40 million (18.1%) adults age 18+

Types of anxiety disorders:

- Generalized Anxiety Disorder (GAD)
- Panic disorder
- Social Anxiety Disorder
- Specific Phobias
- Obsessive-Compulsive Disorder (OCD)
- Post-traumatic Stress Disorder (PTSD)

https://adaa.org/understanding-anxiety/facts-statistics

Generalized Anxiety Disorder (GAD)

- Persistent and excessive worry about various things
- Affects 6.8 million adults
- Women twice as likely to be affected
- The disorder comes on gradually and can begin across the life cycle, though the risk is highest between childhood and middle age

https://adaa.org/understanding-anxiety/generalized-anxiety-disorder-gad

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Anxiety and Depression: Ranked top 10 causes of the global burden of disease

Anxiety disorders and depression often seen together

- Nearly ½ of those diagnosed with depression also diagnosed with an anxiety disorder

In 2019:

- 4.7% of adults aged 18+ reported regular feelings of depression
- 11.2% reported regular feelings of worry, nervousness, or anxiety

August 2020 to February 2021:

- an increase in the proportion of adults reporting **recent anxiety or depression symptoms from 36.4% to 41.5%**

https://www.psychiatrictimes.com/view/mental-health-america-crisis
Adv Nutr. 2020;11(4):890-90
https://adaa.org/understanding-anxiety/facts-statistics

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Mental Health IS Just Health

Between 2010 and 2015

- Surge in prevalence of depression, GAD, and social anxiety among adolescent/college adults
- Surge in suicide deaths
- Those living in rural areas most impacted, greater social isolation, limited access to proper mental health care

Those with severe mental disorders (including major depression):

- Have a **reduced life expectancy of up to 10–25 years**
- Higher risk of developing **obesity and metabolic syndrome**

Rates of mood and anxiety disorders have increased between 1990 and 2015

- **Despite increased treatment and medication**

J Neuro Res. 2019;97:1223–1241.
Front Psychiatry. 2018;9:513.

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Conventional Therapeutic Approaches for Management of D/A

Standard of Care: Mild-Mod Depression

Pharmacotherapy plus psychotherapy

Mild-to-moderate depression

- American Psychiatric Association (APA) and National Institute for Health and Care Excellence (NICE) both recommend psychotherapy as an initial treatment option (APA Category I)
- APA considers antidepressants an initial treatment choice (APA Category I), NICE recommends antidepressant if:
  - Unresponsive to psychosocial intervention
  - Recurrent depression,
  - Or if low-level symptoms present of ≥ 2 years
  - Additional reasons to consider antidepressants include family history, prior response to antidepressants with good efficacy and tolerability, or patient preference

DynaMed. Record No. *T116638, Major Depressive Disorder (MDD)*; [updated *2018 Nov 30]*

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Standard of Care: GAD

Psychological & Pharmaceutical Therapies

Options for psychological therapies (counseling)

- Cognitive behavioral therapy (CBT)
- Psychodynamic psychotherapy
- Mindfulness meditation
- Relaxation therapy
- Acceptance-based behavioral therapy

Medication Therapies

- First line therapy: SSRI, SNRI, and pregabalin (if not tolerant to SSRI/SNRI)
- Second-line therapy: Imipramine, bupropion, vortioxetine, Benzodiazepines, buspirone, hydroxyzine
- Other options: citalopram, divalproex, fluoxetine, mirtazapine,

DynaMed. Record No. *T114697, Generalized Anxiety Disorder*; [updated *2018 Nov 30]*

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Standard of Care: Mod-Severe Depression

Moderate-to-severe depression

- APA and NICE both recommend combination of antidepressant plus psychotherapy (APA Category I)
- APA recommends electroconvulsive therapy (ECT) for severe unresponsive major depression or urgent need for response (APA Category I)

Treatment initiation considerations

- Advise patients about potential for increased agitation, anxiety, and suicidal ideation during initial treatment stages
- Council patient to seek help promptly
- If patient responds too rapidly to initial antidepressant therapy, consider alternative diagnosis of bipolar

DynaMed. Record No. *T116638, Major Depressive Disorder (MDD)*; [updated *2018 Nov 30]*

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Standard of Care: Inadequate Response

Excluding alternative diagnoses and nonadherence

Optimize medication dose (assuming upper limit not reached, and side effect burden is tolerable)

After optimization, consider:

- Switching to another antidepressant or augmenting antidepressant with depression-focused psychotherapy
- Adding another non-MAOI antidepressant,
- Or adding another medication such as lithium, second-generation antipsychotics, or modafinil

For patients who are refractory to medications

- Electroconvulsive therapy (ECT) is most effective therapy and should be considered (APA Category I)
- Or transcranial magnetic stimulation could also be considered (APA Category II)
- **Vagus nerve stimulation** is an option for patients refractory to at least 4 adequate treatment trials, including ECT (APA Category III)

DynaMed. Record No. *T116638, Major Depressive Disorder (MDD)*; [updated *2018 Nov 30]*

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Unipolar depression in adults: Antidepressant doses*

Drug	Usual total starting dose per day (mg)¶	Usual total dose per day (mg)	Extreme daily dose range (mg)¶
Selective serotonin reuptake inhibitors			
Citalopram	20	20 to 40Δ	10 to 40Δ
Escitalopram	10	10 to 20	5 to 30
Fluoxetine	20	20 to 60	10 to 80
Fluvoxamine	50	50 to 200	25 to 300
Fluvoxamine CR	100	100 to 200	100 to 300
Paroxetine	20	20 to 40	10 to 50
Paroxetine CR	25	25 to 50	12.5 to 62.5
Sertraline	50	50 to 200	25 to 300
Serotonin-norepinephrine reuptake inhibitors			
Desvenlafaxine	25 to 50	50 to 100	50 to 400◇
Duloxetine	30 to 60	60	30 to 120§
Levomilnacipran	20	40 to 80	20 to 120
Milnacipran	12.5	100 to 200	50 to 300
Venlafaxine	37.5 to 75	75 to 375	75 to 375
Venlafaxine XR	37.5 to 75	75 to 225	75 to 375
Atypical agents			
Agomelatine§ (not available in United States)	25	25 to 50	25 to 50
Bupropion	200	300 (maximum single dose 150 mg)	100 to 450
Bupropion SR 12 hour	150	300 (maximum single dose 200 mg)	150 to 400
Bupropion XL 24 hour	150	300	150 to 450 (United States) 150 to 300 (Europe)
Bupropion hydrobromide 24 hour	174	348	174 to 522
Mirtazapine	15	15 to 45	7.5 to 60
Serotonin modulators			
Nefazodone‡	200	300 to 600	50 to 600
Trazodone	100	200 to 400	100 to 600
Vilazodone	10	40	10 to 40
Vortioxetine	10	20	5 to 20
Tricyclics and tetracyclics†			
Amitriptyline	25	150 to 300	10 to 300
Amoxapine	25	200 to 300	25 to 400
Clomipramine	25	100 to 250	25 to 300
Desipramine	25	150 to 300	25 to 300
Doxepin	25	100 to 300	10 to 300
Imipramine	25	150 to 300	10 to 300
Maprotiline	25	100 to 225	25 to 225
Nortriptyline	25	50 to 150	10 to 150
Protriptyline	10	15 to 60	5 to 60
Trimipramine	25	150 to 300	25 to 300
Monoamine oxidase inhibitors†			
Isocarboxazid	10	10 to 40	10 to 60
Phenelzine	15	15 to 90	7.5 to 90
Selegiline transdermal	6 mg/24 hour patch	6 to 12 mg/24 hour patch	6 to 12 mg/24 hour patch
Tranylcypromine	10	30 to 60	10 to 60

In: Solomon D, ed. *UpToDate*. Waltham, Mass.: UpToDate, 2022.

Initial treatment depression:

- SSRIs
- Reasonable alternatives- SNRIs, atypical antidepressants, serotonin modulators

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EBM integrative modalities

- Exercise
- Relaxation and positive activities
- Clinician-guided self-help
- “Limited data” lavender, Kava, St Johns Wort

Adjunctive therapy is critical

Pharmacotherapy and psychotherapy avert **less than half** of the disease burden

~30%–40% of those with depression do not adequately respond to pharmacological or psychological treatment

Burden of depression has not reduced – may actually be increasing - despite a substantial increase/wider availability of psychotherapies

Proc Nutr Soc. 2017;76(4):427-436
Adv Nutr. 2020;11(4):890-907

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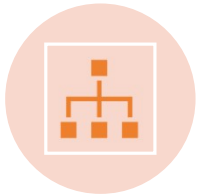
The Functional Medicine Lens



SY*STEM'S* BASED APPROACH

UPSTREAM MEDICINE

VS

"SY*MPTOM*-BASED" APPROACH

DOWNSTREAM MEDICINE

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Contributing Factors

- **Gut health and microbiome balance**
- Inflammation (and factors that contribute)
- Detoxification & environmental exposures
- Mitochondrial health
- Hormone & neurotransmitter balance
- Diet & nutritional status
- History of trauma (big T and little t)
- Connection, community and social support

Meet Claire

- 68 y/o woman
- Presenting with increased anxiety, depression, brain fog, fatigue, and disruptive GI symptoms and hives
  - Symptoms significantly impact her dietary choices and limit variety significantly
  - Reports low tolerance to stress and history significant for anxiety & depression
  - GI symptoms include belching, malodorous gas, soft/unformed stool
  - Multiple environmental sensitivities and food reactivities
  - Reports joint pain and inflammation, skin reactivity (hives), managed with diet and trigger avoidance
  - Increased risk of environmental toxin exposure due to occupation and lifestyle confirmed with laboratory analysis
- Medications
  - Occasional ibuprofen for headaches
  - Citalopram 20 mg/day (~x 6 months)

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Assessment Tools

- Health history questionnaire (HHQ)
- Medical symptom questionnaire (MSQ) + PROMISE 10
- Diet Diary (3-day written for initial)
- 24-hour recall
- Food skills and environment assessment
- Laboratory
  - Basic CBC, CMP and blood chemistries
  - Stool testing
  - Nutrition profile

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Assessment Summary

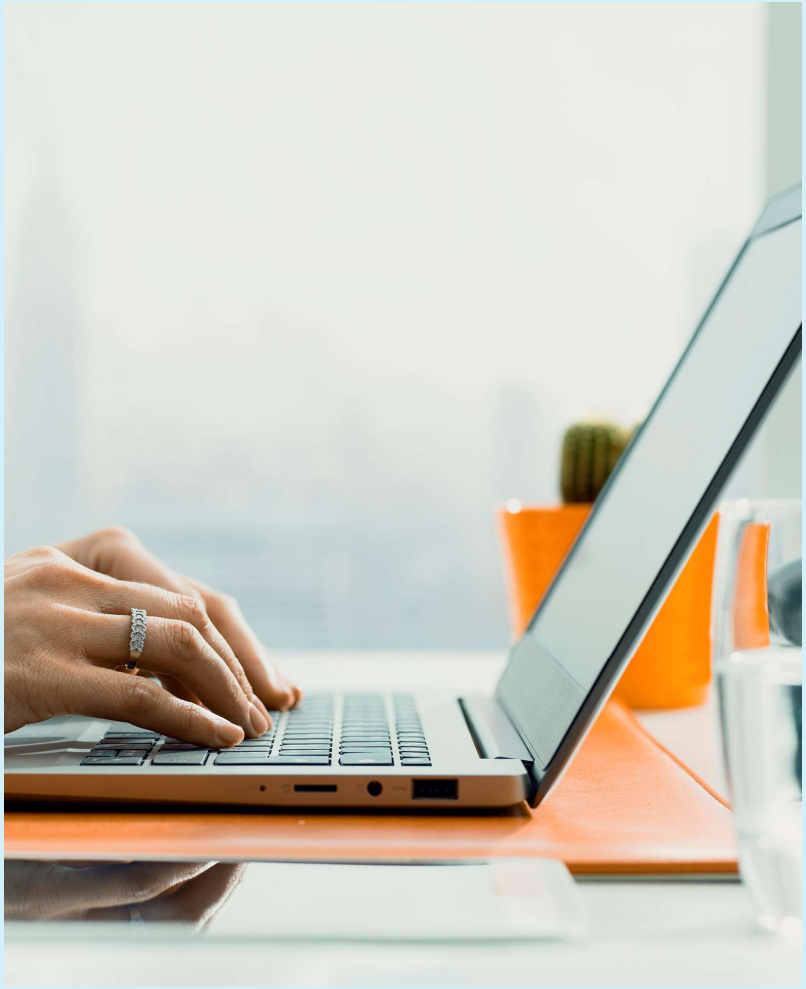
Reports low tolerance to stress and history significant for anxiety & depression

GI symptoms include belching, malodorous gas, soft/unformed stool

Multiple environmental sensitivities and food reactivities

Reports joint pain and inflammation, skin reactivity (hives), managed with diet and trigger avoidance

Increased risk of environmental toxin exposure due to occupation and lifestyle confirmed with laboratory analysis



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Proceedings of the Nutrition Society (2017), **76**, 427–436 doi:10.1017/S0029665117002026

The Joint Winter Meeting between the Nutrition Society and the Royal Society of Medicine held at The Royal Society of Medicine, London on 6–7 December 2016

Conference on 'Diet, nutrition and mental health and wellbeing'
Plenary Lecture: Mental health as an emerging public health problem

Nutritional psychiatry: the present state of the evidence

Wolfgang Marx[1], Genevieve Moseley[2], Michael Berk[2,3,4,5] and Felice Jacka[2,3,6,7]*
[1]*School of Allied Health, La Trobe University, Bundoora, Australia*
[2]*Deakin University, Food & Mood Centre, IMPACT Strategic Research Centre, School of Medicine,*
[3]*Departme*
[4]*Orygen, The N*
[5]*Florey Ins*
[6]*Centre for Adolesc*

Pharmacotherapy, such as antidepressants, and psychotherapy, such as cognitive behavioral therapy, are cornerstones of treatment; however, they avert less than half of the disease burden, suggesting that additional strategies to prevent and treat mental disorders are needed. Indeed, recent evidence suggests that despite a substantial increase in the use of psychotropics and wider availability of psychotherapies, the population burden of depression has not reduced, and may be increasing

Proc Nutr Soc. 2017;76(4):427-436.

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Treatment-resistant depression (TRD)

Precise definition of refractory or resistant depression is inconsistent in the literature

Defined as major depressive disorder (MDD) in adults who have not responded to at least two different antidepressant treatments* in the current moderate to severe depressive episode

Due to the lack of consistency in definitions of TRD, the prevalence of TRD varies widely in the literature, with **ranges of approximately 10%-45%** (US and European data)

*used for a sufficient length of time (4-8 weeks), at an adequate dose, and with adequate affirmation of treatment adherence

BMC Psychiatry. 2019;19(1):247
J Manag Care Spec Pharm. 2019;25(7):823-835

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REVIEW

The Role of the Gut Microbiota in Dietary Interventions for Depression and Anxiety

Tracey LK Bear,[1,2,3] Julie E Dalziel,[2,4] Jane Coad,[1] Nicole C Roy,[2,4,5] Christine A Butts,[3] and Pramod K Gopal[2,3]

[1] School of Food and Advanced Technology, Massey University, Palmerston North, New Zealand; [2] Riddet Institute, Massey University, Palmerston North, New Zealand; [3] The New Zealand Institute for Plant and Food Research Limited, Palmerston North, New Zealand; [4] AgResearch Ltd Grasslands Research Centre, Palmerston North, New Zealand; and [5] High-Value Nutrition National Science Challenge, Auckland, New Zealand

ABSTRACT

There is emerging evidence that an unhealthy dieta
pattern may decrease it. This nascent research sug
depression and anxiety. The relation, however, is co
choices being affected by stress and depression. Th
research evolves, all characteristics of the relation r
translated into clinical practice. A parallel and fast-g
relation, commonly termed the microbiome–gut–
function and behavior. In this review we discuss pc
of the diet–mood relation in which the gut microb
depression studies. We argue that because diet is on
nutritional intervention studies need to consider the gut microbiota as an essential piece of the puzzle. *Adv Nutr* 2020;11:890–907.

Keywords: microbiome–gut–brain axis, depression, anxiety, mood, mental health, nutritional psychiatry, microbiota, diet, nutrition

[...] *diet is a large influencer of the gut microbiota composition and function, it is likely that changes in the gut microbiota contribute to how diet (whole diet and individual components of diet) may affect depression and anxiety. Dietary patterns for positive mental health will likely support the growth of commensal microbiota, decrease the growth of pathogenic and colitis inducing bacteria, and affect gut barrier permeability and inflammation.*

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Adv Nutr. 2020;11(4):890-907.

Open access Systematic review/Meta-analyses

General Psychiatry

Effects of regulating intestinal microbiota on anxiety symptoms: A systematic review

Beibei Yang, Jinbao Wei, Peijun Ju, Jinghong Chen

To cite: Yang B, Wei J, Ju P, *et al*. Effects of regulating intestinal microbiota on anxiety symptoms: A systematic review. *General Psychiatry* 2019;**32**:e100056. doi:10.1136/gpsych-2019-100056

Received 23 January 2019
Revised 28 February 2019
Accepted 03 March 2019

ABSTRACT

Background Anxi
diseases and a va
disorders related
have indicated th
function through
intestinal microbi
is no specific evic
regulating intestir

Aims To find evi
symptoms by regu

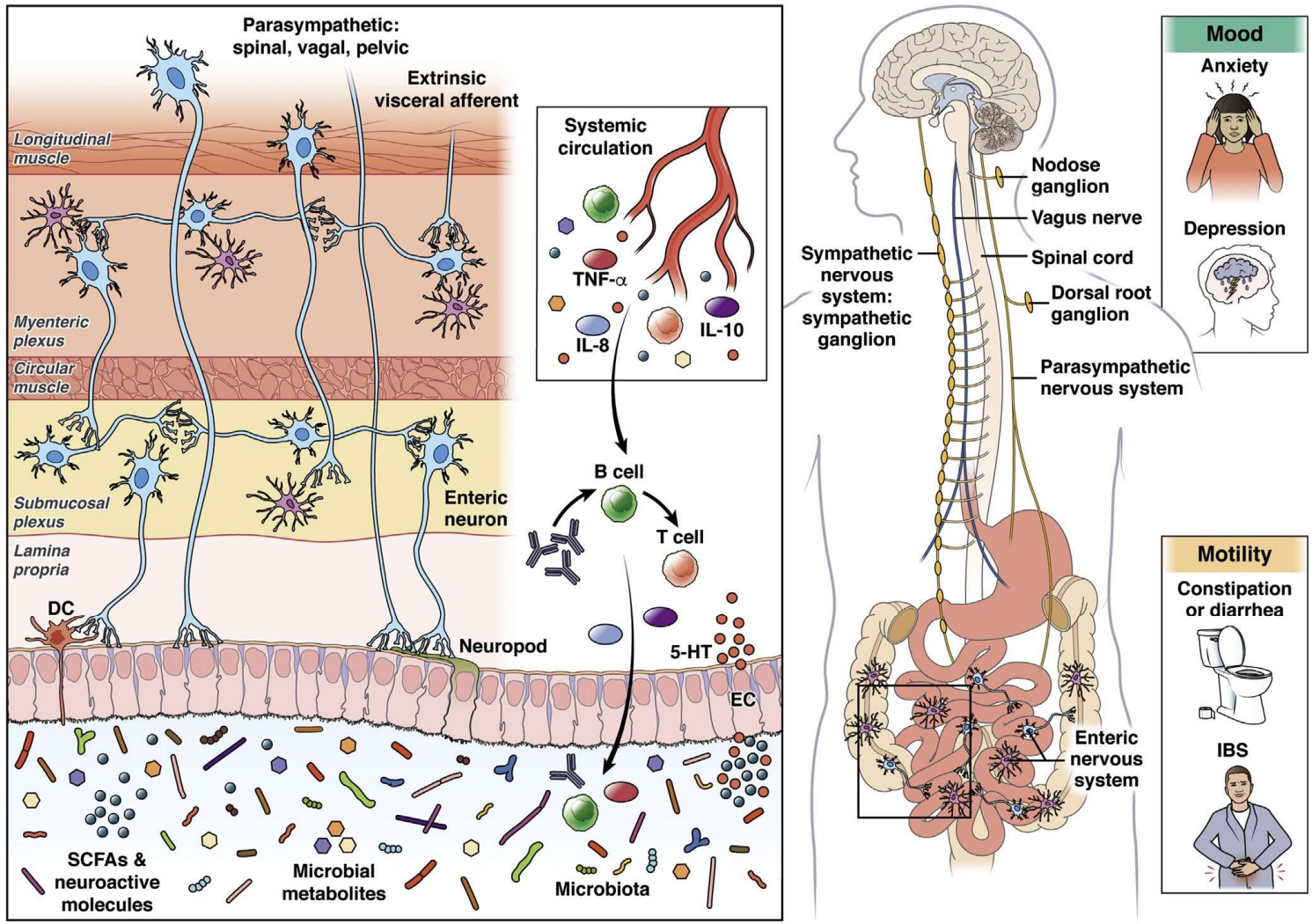
Methods This systematic review of randomised controlled trials was searched based on the following databases: PubMed, EMBASE, the Cochrane Library, OVID, Web of Knowledge, China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP databases and SinoMed. The retrieval time dated back to 25 July 2018. Then we screened research literatures based on established inclusion and exclusion criteria. Quality evaluation for each included study was done using the Cochrane risk of bias

Conclusions We find that more than half of the studies

Eleven of 21 studies showed that regulation of intestinal microbiota could improve anxiety symptoms, of which five studies conducted probiotic interventions and six studies used non-probiotic interventions like low FODMAP. That means **that 52% of studies showed a positive effect on improving anxiety symptoms by regulating intestinal microbiota**.

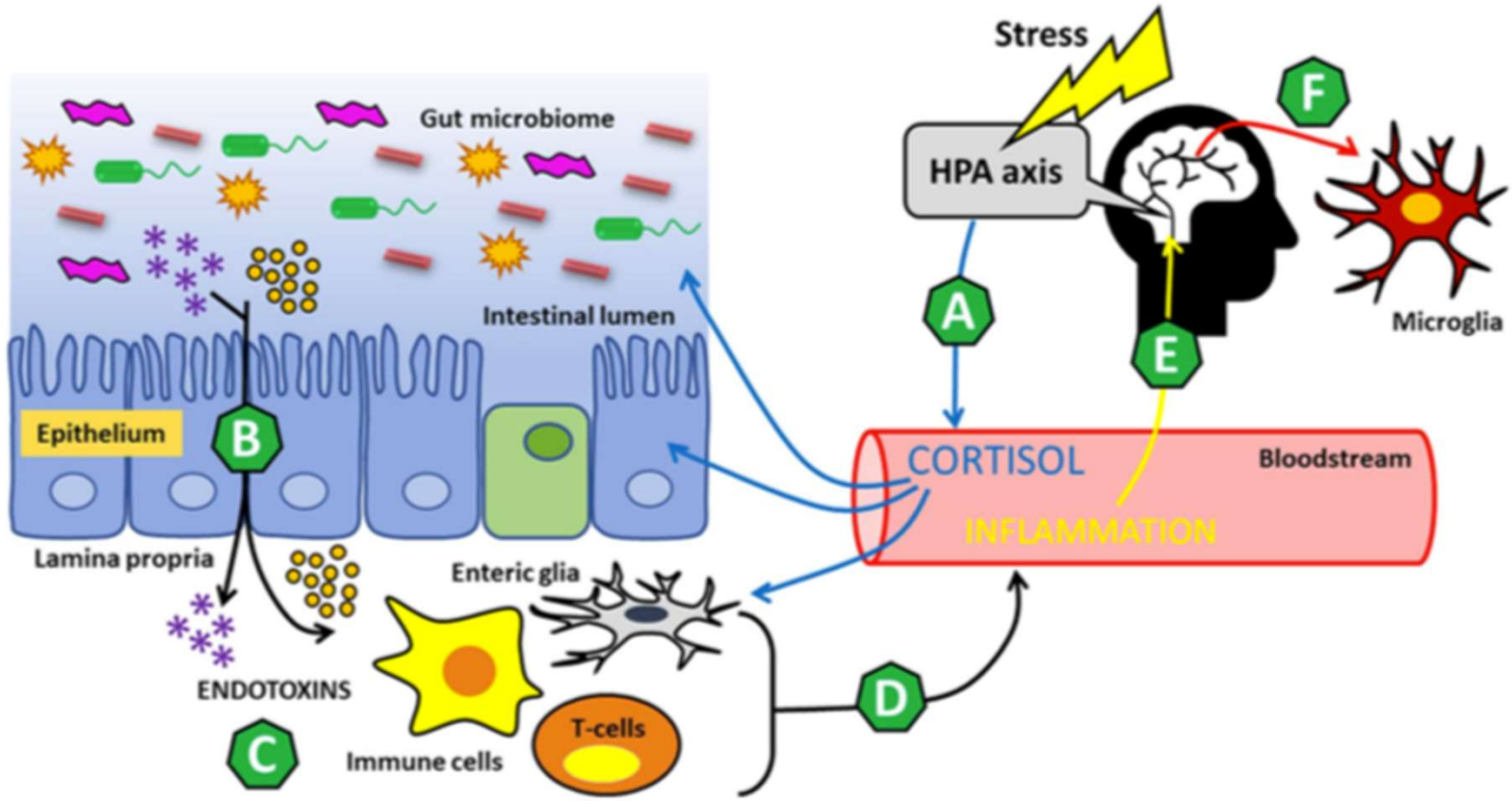
Anxiety disorder is a mental disorder with anxiety symptoms as the main clinical manifestation, with a global incidence of 3%–25%, and the incidence in chronic diseases, such as cancer, cardiocerebrovascular disease, irritable bowel syndrome (IBS), is 1.4%–70%.[1] Studies[2] have shown that up to 33.7% of people will be affected by anxiety symptoms

Gut health & Microbiome



Gastroenterology. 2021;160(5):1486-1501.

Impact of stress on bidirectional communication between the gut microbiome and the CNS



J Neuro Res. 2019;97:1223–1241.

Peirce JM, Alviña K. The role of inflammation and the gut microbiome in depression and anxiety. *J Neurosci Res.* 2019;97(10):1223-1241. doi:10.1002/jnr.24476

Stool Testing

Normal Bacterial Flora	Result		Normal
Bacteroides fragilis	4.84e8	Low	1.60e9 - 2.50e11
Bifidobacterium spp.	9.68e8		>6.70e7
Enterococcus spp.	2.53e5		1.9e5 - 2.00e8
Escherichia spp.	5.58e4	Low	3.70e6 - 3.80e9
Lactobacillus spp.	2.35e4	Low	8.6e5 - 6.20e8
Clostridia (class)	5.76e5	Low	5.00e6 - 5.00e7
Enterobacter spp.	4.45e4	Low	1.00e6 - 5.00e7
Akkermansia muciniphila	1.68e5	High	1.00e1 - 5.00e4
Faecalibacterium prausnitzii	1.78e2	Low	1.00e3 - 5.00e8
Phyla Microbiota	Result		Normal
Bacteroidetes	2.27e10	Low	8.61e11 - 3.31e12
Firmicutes	1.75e9	Low	5.70e10 - 3.04e11
Firmicutes:Bacteroidetes Ratio	0.08		<1.00

Intestinal Health			
Digestion	Result		Normal
Steatocrit	<dl		<15 %
Elastase-1	104	Low	>200 ug/g
GI Markers	Result		Normal
b-Glucuronidase	3441	High	<2486 U/mL
Occult Blood - FIT	0		<10 ug/g
Immune Response	Result		Normal
Secretory IgA	243	Low	510 - 2010 ug/g
Anti-gliadin IgA	56		0 - 157 U/L
Inflammation	Result		Normal
Calprotectin	63		<173 ug/g
Add-on Test	Result		Normal
Zonulin	199.8	High	<107 ng/g

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Stress & GI Health

Under chronic stress

- Induces inflammatory process
- GI motility issues
- Digestion compromised, nutrient absorption issues
- Changes in the microbiome balance

Front Hum Neurosci. 2017;11:316.
J Neuro Res. 2019;97:1223–1241.
Gastroenterology. 2021;160(5):1486-1501.

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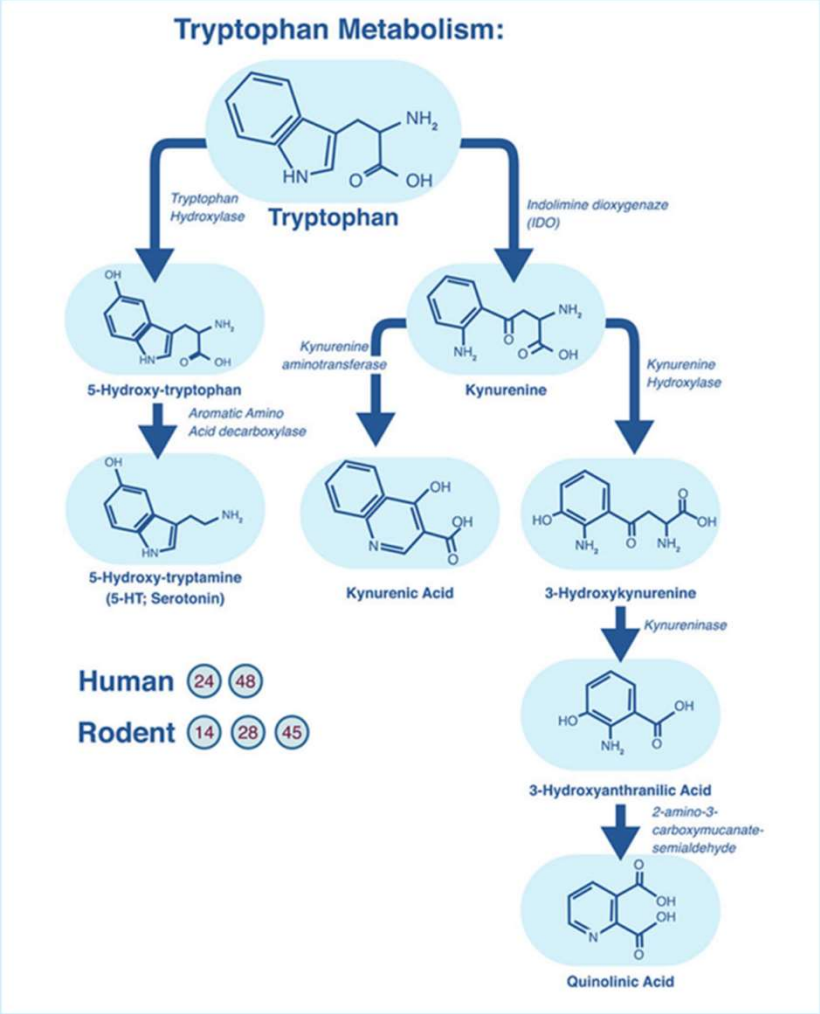
Neuroinflammation & Tryptophan Metabolism

Tryptophan is an essential amino acid precursor for Serotonin + Melatonin

Alternative pathway = Kynurenine + Quinolinic Acid (neuroinflammatory)

Commensal bacteria that metabolize tryptophan play a large role in driving the pathway



Neurobiol Dis. 2020;135:104578

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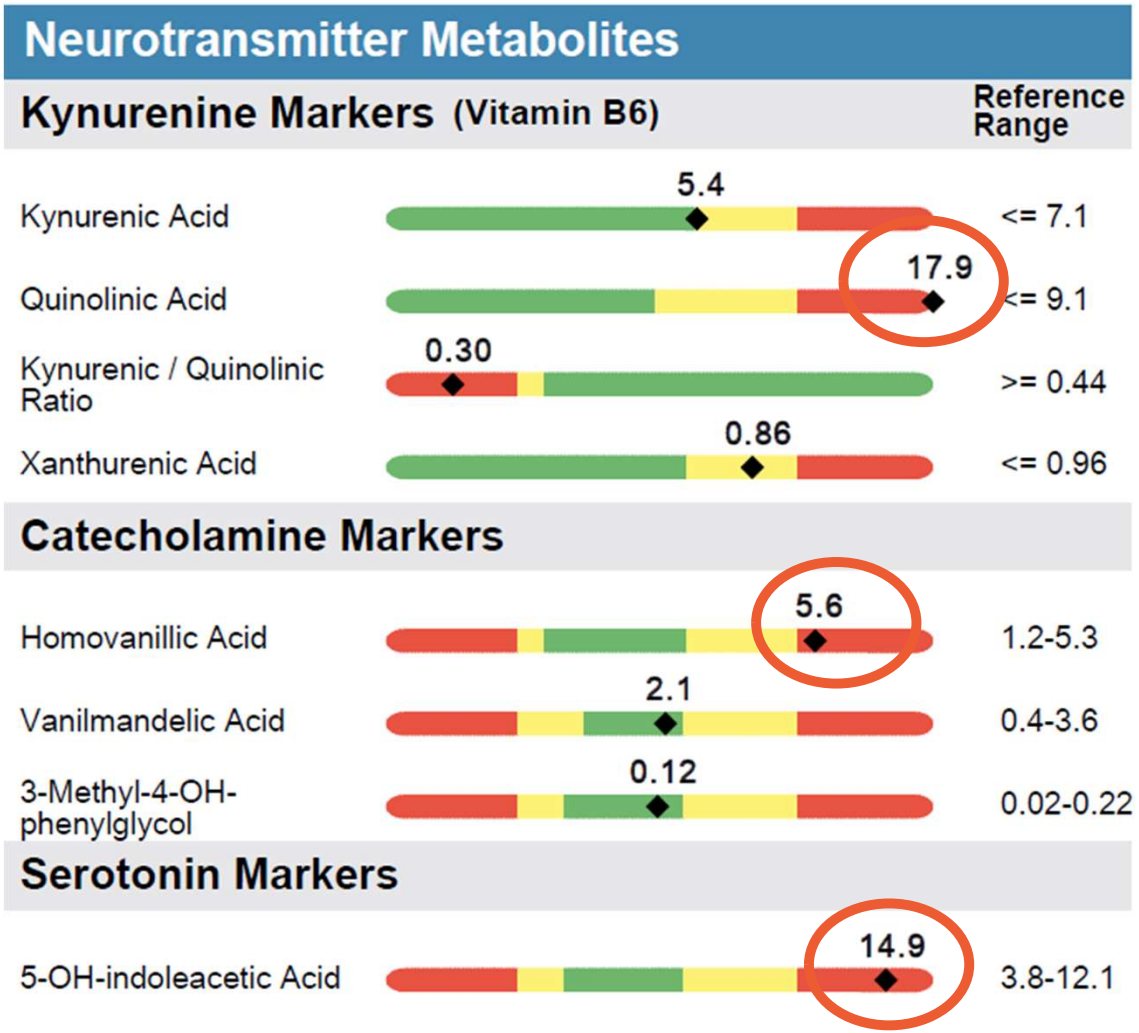
Neurotransmitter Markers



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Inflammation & Oxidative Stress

Chronic, systemic inflammation

Oxidative stress

Mitochondrial dysfunction

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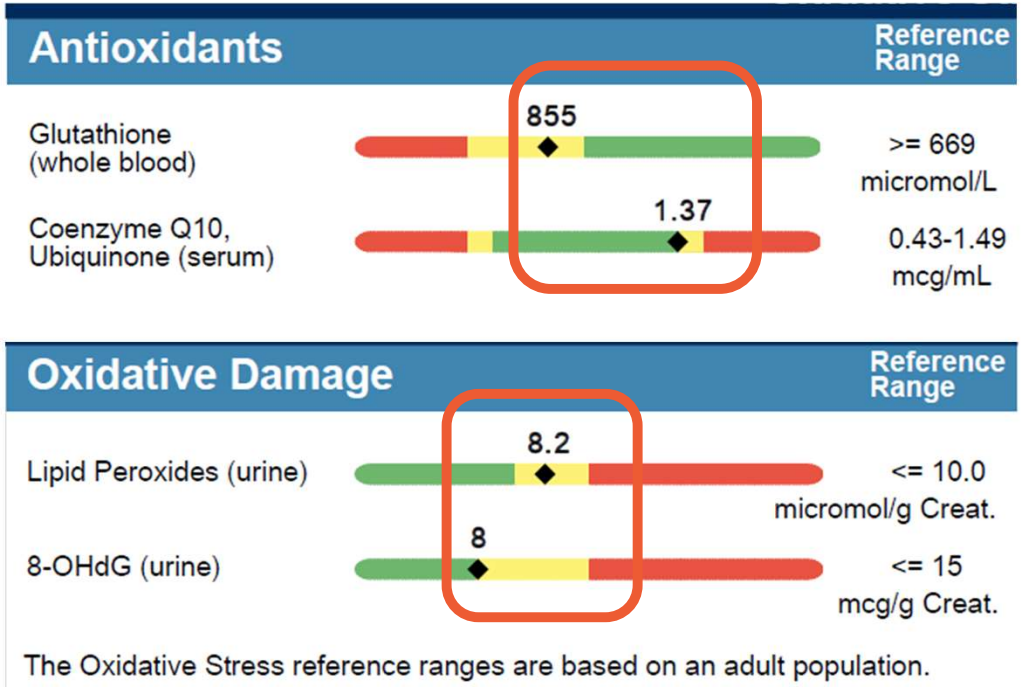
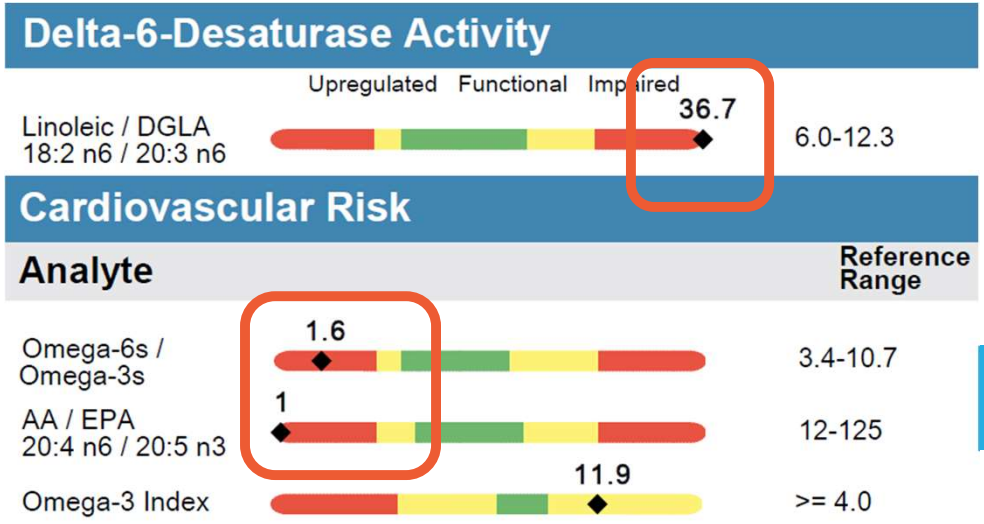
Oxidative Stress/Inflammation





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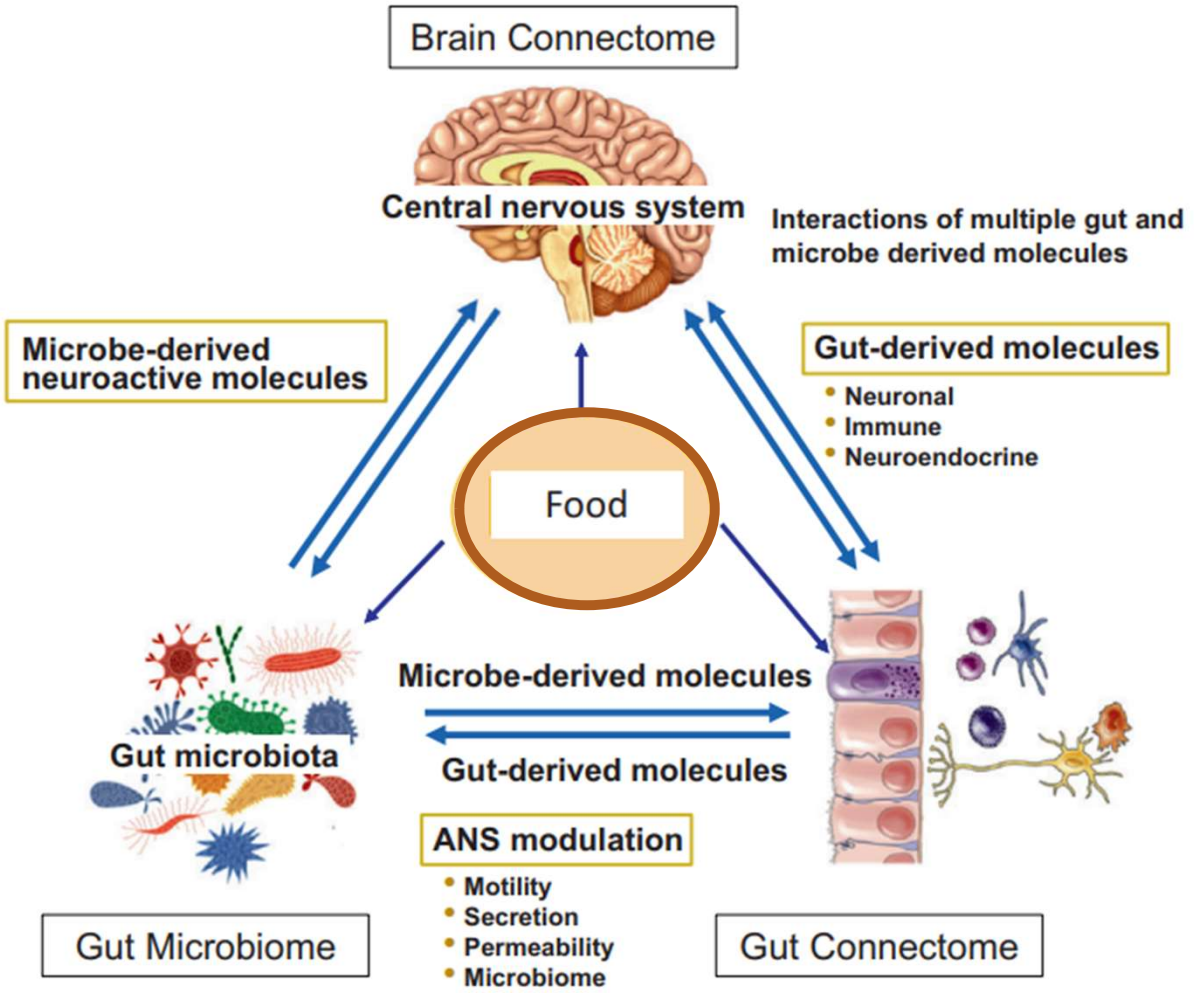
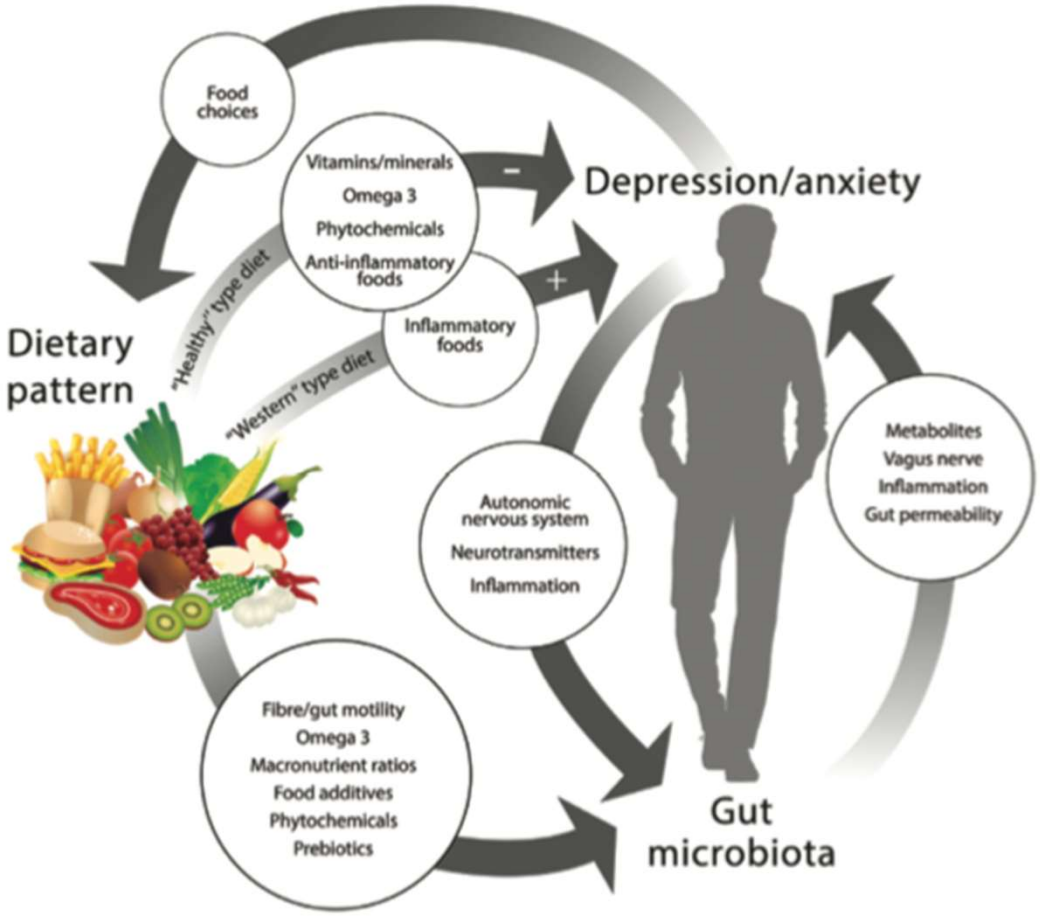


Transl Psychiatry. 2022;12(1):164

Dietary links to risk of developing depression & anxiety



Adv Nutr. 2020;11(4):890-907.

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RESEARCH ARTICLE Open Access

A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial)

Felice N. Jacka[1,4,9,10,13*], Adrienne O'Neil[1,2,13], Rachelle Opie[5,13], Catherine Itsiopoulos[5], Sue Cotton[3], Mohammedreza Mohebbi[1], David Castle[4,11], Sarah Dash[1,13], Cathrine Mihalopoulos[7], Mary Lou Chatterton[7], Laima Brazionis[5,6], Olivia M. Dean[1,4,12,13], Allison M. Hodge[8] and Michael Berk[1,3,12,13]

Abstract

Background: The possible therapeutic impact of dietary changes on existing mental illness is largely unknown. Using a randomised control
for the treatment of major

Methods: 'SMILES' was a 12
intervention in the treatme
nutritional consulting sessio
protocol to the same visit s
using the Montgomery–Åsb
remission and change of sy
repeated measures (MMRM)

Results: We assessed 166 in
n = 34). Of these, 55 were utilising some form of therapy: 21 were using psychotherapy and pharmacotherapy combined; 9 were using exclusively psychotherapy; and 25 were using only pharmacotherapy. There were 31 in

The dietary support group demonstrated significantly greater improvement between baseline and 12 weeks on the MADRS than the social support control group

These results indicate that dietary improvement may provide an efficacious and accessible treatment strategy for the management of this highly prevalent mental disorder, the benefits of which could extend to the management of common co-morbidities.

BMC Med. 2017;15(1):23.

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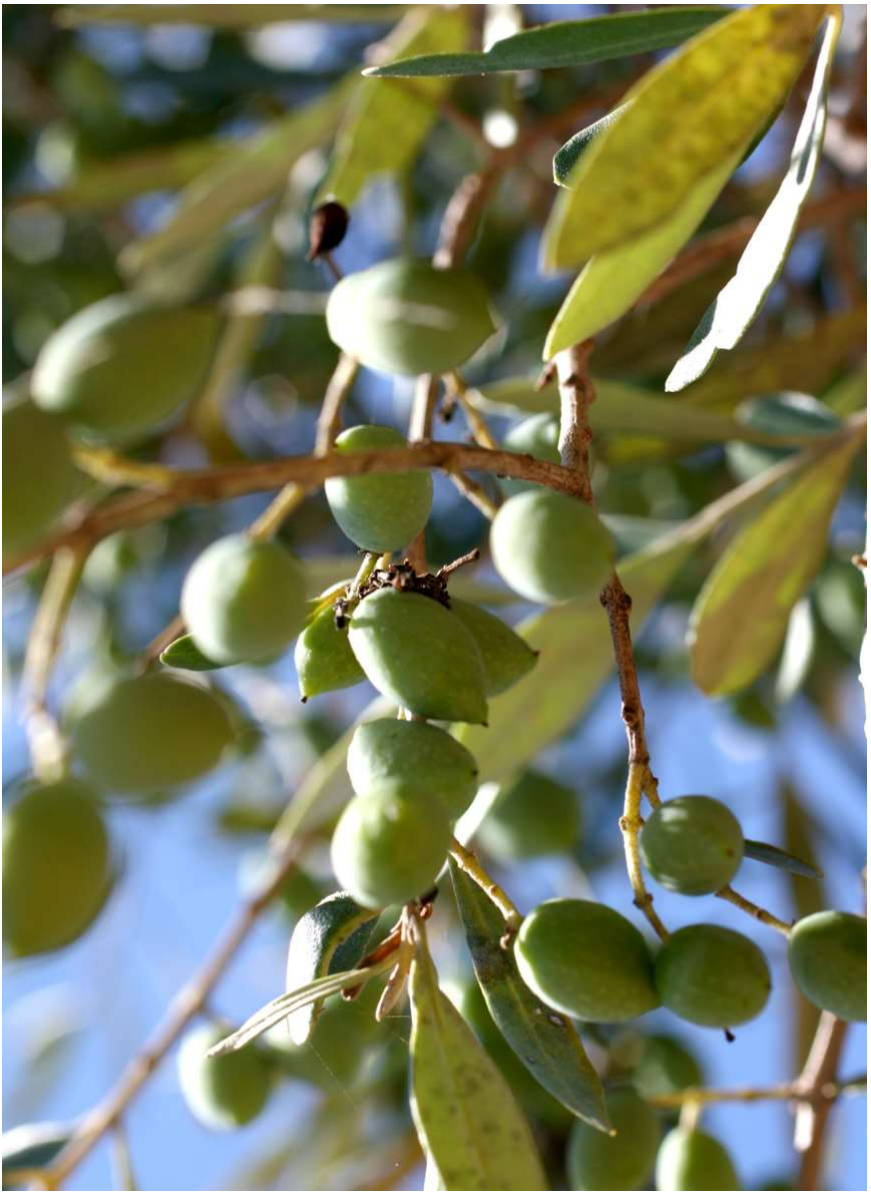

Mediterranean diet benefits

- Correlates with a reduced risk of depression (& CM comorbidities)
- Anti-inflammatory, antioxidant-rich
- Rich source polyphenols and phytonutrients
- Rich in PUFAs and MUFAs
- Positive microbiome changes

Physiol Rev. 2019;99(4):1877-2013

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Therapeutic Foods

Healthy fats

- **Extra-virgin olive oil (EVOO)**, nuts and seeds
- **Omega-3 fat sources from food** (and supplement sources 2 to 4 grams per day)
- Alpha-lipoic acid (ALA)

Micronutrients

- Zinc
- Magnesium
- Selenium
- Cit C
- Vit E
- Choline

Antioxidants

- Alliums (especially garlic) & cruciferous vegetables
- **Green tea (EGCG), resveratrol, carotenoids, quercetin**

Fiber sources

- **Non-starchy vegetables, colorful root vegetables**
- Whole Grains and legumes (limit processing)
- Traditionally fermented foods

Focus on color "eat the rainbow"

- **Phytonutrients: Organic, colorful mix of low glycemic veggies & fruit**
- **Mushrooms**
- **Herbs including turmeric, saffron, rosemary, herbal teas** (and others)

**Dietary recommendations personalized for Claire due to reactivity are in bold*

Nutraceuticals

Evidence-based nutrients & herbs to support your foundational diet

Supplement Considerations

Nutrients

- **Vitamin C**
- Essential Fatty Acids (EFA)
- Choline
- Alpha-lipoic acid (ALA)
- **Vitamin D**
- **B-Complex**
- Zinc to copper ratio
- **Magnesium**
- Selenium

Herbs & Phytonutrients

- Saffron
- St John's wort
- Curcumin
- Adaptogens
  - **Ashwagandha**
  - Holy Basil
  - Rhondiola
  - Mushrooms
- Quercetin
- Resveratrol
- Carotenoids

Nervines & GABA modulators

- GABA
- Lavender
- Kava
- **Chamomile**
- **Passionflower**
- **Valerian root**
- Hops

Targeted AA supplementation

- Tryptophan
- Tyrosine
- 5-HTP
- **L-theonine**
- Glycine

**The initial plan choices for Claire are in*

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Summary

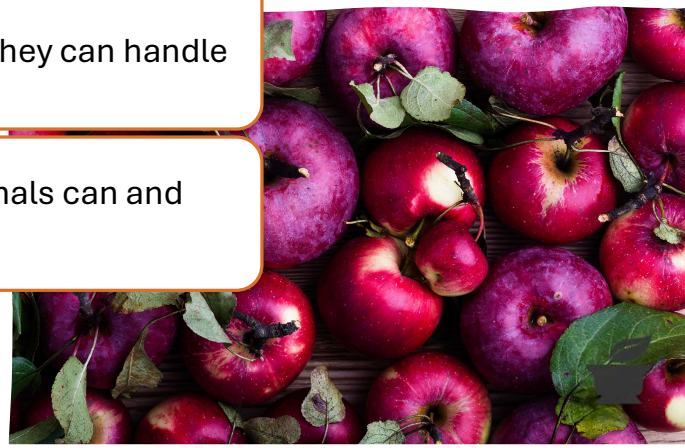
Diet, nutrition, and herbs can be a powerful strategy to help patients improve their mental health

There are multiple mechanisms beyond SSRIs and the serotonin pathway that impact depression & anxiety, including inflammation, microbiome balance, gut barrier integrity, neurotransmitter and hormone, and HPA-axis balance

Interventions including diet, targeted nutrients, herbs, and lifestyle modification (sleep, meditation, limbic retraining, and movement)

Interventions should always be tailored to the individual, integrated slowly at a rate they can handle

Physicians, nutritionists, pharmacists, and other allied and mental health professionals can and should work collaboratively to reduce the burden of mental health



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Questions?

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