Casual Friday Presents

Anxiety, Autoimmunity

And Their Nefarious Connections

A BIOGENETIX CLINICAL PRESENTATION

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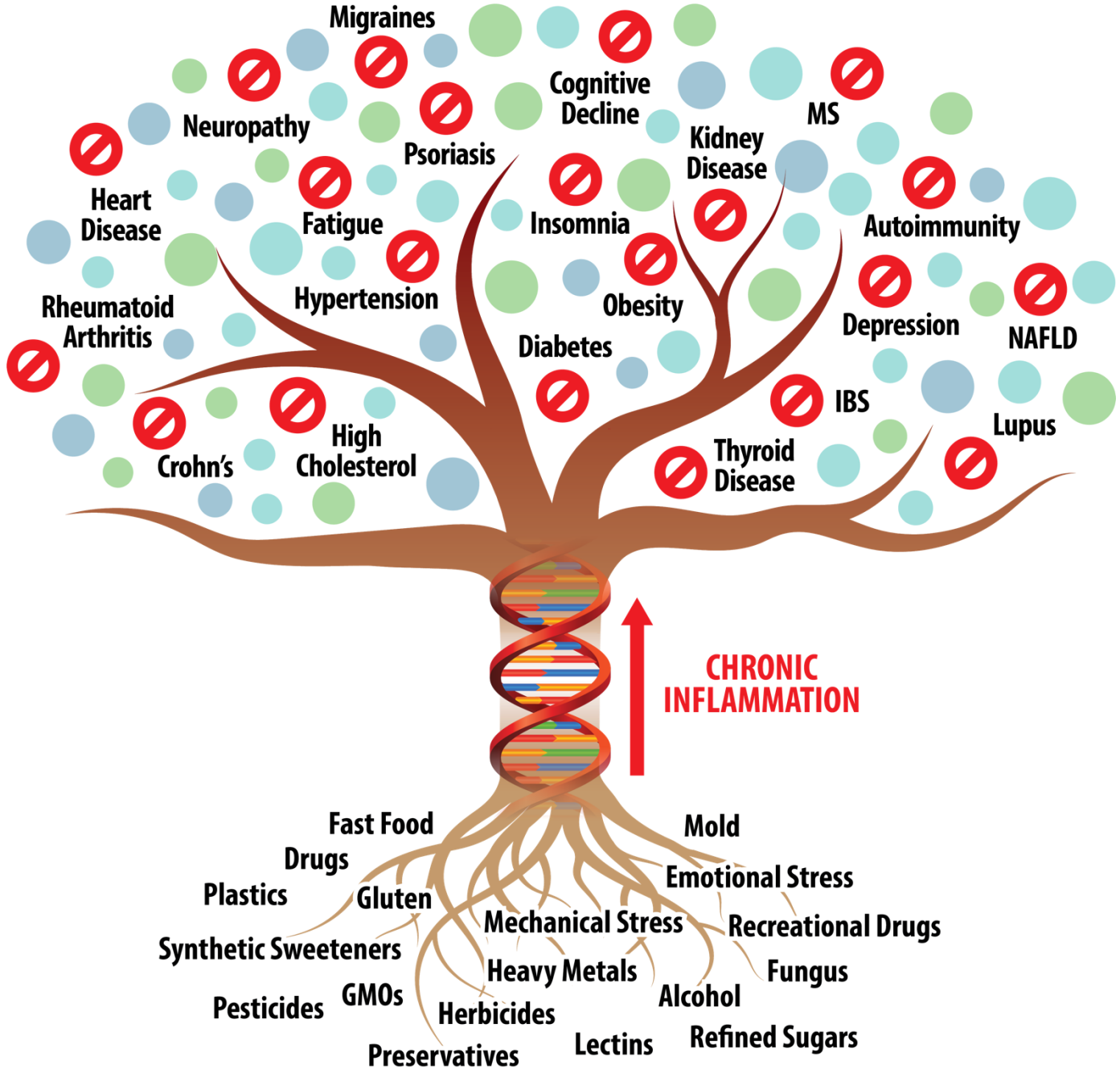
Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Autoimmunity
Rheumatoid Arthritis
Hypertension
Obesity
Depression
NAFLD
Diabetes
IBS
Lupus
Crohn's
High Cholesterol
Thyroid Disease
CHRONIC INFLAMMATION
Fast Food
Drugs
Plastics
Gluten
Mold
Emotional Stress
Mechanical Stress
Recreational Drugs
Synthetic Sweeteners
Heavy Metals
Fungus
Pesticides
GMOs
Herbicides
Alcohol
Preservatives
Lectins
Refined Sugars

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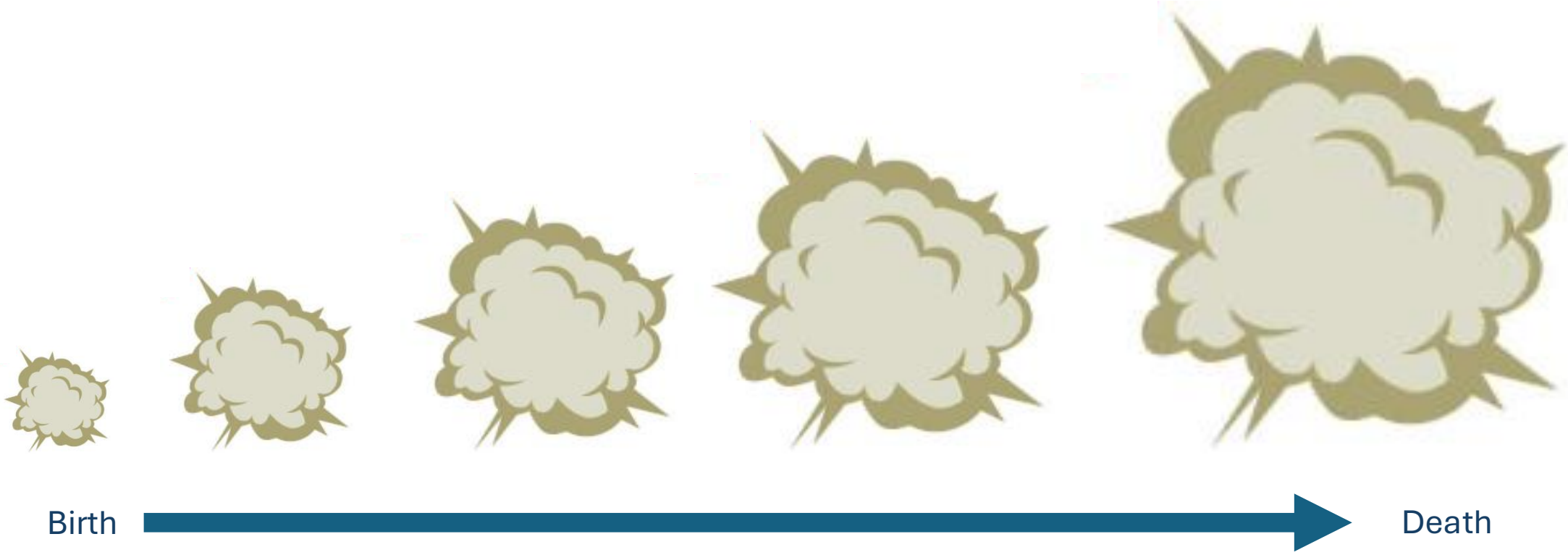
The Antigenic Cloud



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JAMA

Review

Anxiety Disorders
A Review

Kristin L. Szuhany, PhD[1]; Naomi M. Simon, MD, MSc[1]

Observations Anxiety disorders are characterized by symptoms that include worry, social and performance fears, unexpected and/or triggered panic attacks, anticipatory anxiety, and avoidance behaviors. Generalized anxiety disorder (6.2% lifetime prevalence), social anxiety disorder (13% lifetime prevalence), and panic disorder (5.2% lifetime prevalence) with or without agoraphobia are common anxiety disorders seen in primary care. Anxiety disorders are associated with physical symptoms, such as palpitations, shortness of breath, and dizziness. Brief screening measures applied in primary care, such as the Generalized Anxiety Disorder-7, can aid in diagnosis of anxiety disorders (sensitivity, 57.6% to 93.9%; specificity, 61% to 97%). Providing information about symptoms, diagnosis, and evidence-based treatments is a first step in helping patients with anxiety. First-line treatments include pharmacotherapy and psychotherapy. Selective serotonin reuptake inhibitors (SSRIs, eg, sertraline) and serotonin-norepinephrine reuptake inhibitors (SNRIs, eg, venlafaxine extended release) remain first-line pharmacotherapy for generalized anxiety disorder, social anxiety disorder, and panic disorder. Meta-analyses suggest that SSRIs and SNRIs are associated with small to medium effect sizes compared with placebo (eg, generalized anxiety disorder: standardized mean difference [SMD], −0.55 [95% CI, −0.64 to −0.46]; social anxiety disorder: SMD, −0.67 [95% CI, −0.76 to −0.58]; panic disorder: SMD, −0.30 [95% CI, −0.37 to −0.23]). Cognitive behavioral therapy is the psychotherapy with the most evidence of efficacy for anxiety disorders compared with psychological or pill placebo (eg, generalized anxiety disorder: Hedges g=1.01 [large effect size] [95% CI, 0.44 to 1.57]; social anxiety disorder: Hedges g=0.41 [small to medium effect] [95% CI, 0.25 to 0.57]; panic disorder:

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THE LANCET

SEMINAR · Volume 397, Issue 10277, P914-927, March 06, 2021

Anxiety disorders

Prof Brenda WJH Penninx, PhD [a,b] · Prof Daniel S Pine, MD [c] · Prof Emily A Holmes, PhD [d] · Prof Andreas Reif, MD [e]

Affiliations & Notes · Article Info · Linked Articles (2)

Anxiety disorders form the most common group of mental disorders and generally start before or in early adulthood. Core features include excessive fear and anxiety or avoidance of perceived threats that are persistent and impairing. Anxiety disorders involve dysfunction in brain circuits that respond to danger. Risk for anxiety disorders is influenced by genetic factors, environmental factors, and their epigenetic relations. Anxiety disorders are often comorbid with one another and with other mental disorders, especially depression, as well as with somatic disorders. Such comorbidity generally signifies more severe symptoms, greater clinical burden, and greater treatment difficulty. Reducing the large burden of disease from anxiety disorders in individuals and worldwide can be best achieved by timely, accurate disease detection and adequate treatment administration, scaling up of treatments when needed. Evidence-based psychotherapy (particularly cognitive behavioural therapy) and psychoactive medications (particularly serotonergic compounds) are both effective, facilitating patients' choices in therapeutic decisions. Although promising, no enduring preventive measures are available, and, along with frequent therapy resistance, clinical needs remain unaddressed. Ongoing research efforts tackle these problems, and future efforts should seek individualised, more effective approaches for treatment with precision medicine.

Anxiety Classifications

Clinical Anxiety Dx

- **Generalized Anxiety Disorder (GAD)**
- **Panic Disorder**
- **Social Anxiety Disorder**
- **Specific Phobia**
- **Agoraphobia**
- **Separation Anxiety Disorder**
- **Selective Mutism**
- **Substance/Medication-Induced Anxiety Disorder**
- **Anxiety Disorder Due to Another Medical Condition**

Anxiety Related Disorders

- **Obsessive-Compulsive Disorder (OCD)**
- **Post-Traumatic Stress Disorder (PTSD)**
- **Acute Stress Disorder**
- **Illness Anxiety Disorder**
- **Adjustment Disorder with Anxiety**

Symptom Oriented

- **Performance anxiety**
- **Health anxiety**
- **Relationship anxiety**
- **Existential anxiety**
- **Financial anxiety**
- **Anticipatory anxiety**
- **Situational anxiety**

Classification

- **State anxiety**
- **Trait anxiety**

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Functional Classifications

- **Cognitive anxiety** – racing thoughts, worry loops, rumination
- **Somatic anxiety** – physical symptoms (tight chest, nausea, shakiness)
- **Behavioral anxiety** – avoidance, reassurance-seeking, compulsive checking

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1. High-inflammation Anxiety Subtype (somatic)

People in this group tend to show:

- Elevated CRP
- Elevated IL-6
- Elevated TNF-α
- Sometimes altered immune cell activity
- Often HPA-axis dysregulation (cortisol rhythm abnormalities)

PMID: *31326932* (BMJ Open, DOI:10.1136/bmjopen-2018-027925)

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Clinically:

More fatigue

- More somatic symptoms (tension, pain, GI issues)
- Poor sleep
- Common comorbidities:
  - Autoimmune disease
  - Metabolic syndrome
  - Chronic infections
  - Trauma history

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Clinically:

- Inflammation can influence:
  - Serotonin metabolism
  - Glutamate signaling
  - Amygdala activity
- Some research suggests these patients respond differently to:
  - Pharmaceutical intervention
  - Anti-inflammatory strategies
  - Lifestyle interventions (sleep, exercise, diet)
- This is the subtype most relevant to autoimmune overlap.

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2. Low-inflammation (primarily neurocognitive) Anxiety Subtype

Clinically:

- Generally WNL inflammatory markers
- More centered on:
  - Cognitive threat sensitivity
  - Amygdala hyperreactivity
  - Learned fear conditioning
  - Trait neuroticism

Clinical pattern:

- Classic GAD, social anxiety, panic disorder
- Often strong family history of anxiety
- Fewer systemic physical symptoms
- These cases are less clearly linked to immune activation.

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3. Stress-sensitized / HPA-axis subtype

- This overlaps with #1, #2.

Mechanism:

- Chronic stress → cortisol dysregulation → impaired immune tolerance → increased inflammatory signaling.

Commonly discussed alongside:

- PTSD
- Early life adversity
- Autoimmune onset after prolonged stress

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4. Autoimmune-associated anxiety

A) Patients stressed about chronic disease

B) Direct immune signaling to the brain

Cytokines can:

- Cross the blood-brain barrier
- Activate microglia
- Alter neurotransmitter production

Clinically:

- Lupus
- Hashimoto’s Thyroiditis
- RA
- IBD
- MS

…all demonstrate higher anxiety prevalence.

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- Is inflammation causing anxiety?
- Is anxiety increasing inflammation?
- Are both driven by a third factor (trauma, genetics, microbiome, toxins, etc)?

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Clin Pract. 2017 Sep 15;7(4):987. doi: 10.4081/cp.2017.987

Gut microbiota's effect on mental health: The gut-brain axis

Megan Clapp [1,✉], Nadia Aurora [1], Lindsey Herrera [1], Manisha Bhatia [1], Emily Wilen [1], Sarah Wakefield [2]

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PMCID: PMC5641835 PMID: 29071061

The bidirectional communication between the central nervous system and gut microbiota, referred to as the gut-brain-axis, has been of significant interest in recent years. Increasing evidence has associated gut microbiota to both gastrointestinal and extragastrointestinal diseases. Dysbiosis and inflammation of the gut have been linked to causing several mental illnesses including anxiety and depression, which are prevalent in society today. Probiotics have the ability to restore normal microbial balance, and therefore have a potential role in the treatment and prevention of anxiety and depression. This review aims to discuss the development of the gut microbiota, the linkage of dysbiosis to anxiety and depression, and possible applications of probiotics to reduce symptoms.

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Front Immunol. 2024 May 2;15:1365871. doi: 10.3389/fimmu.2024.1365871

Dangers of the chronic stress response in the context of the microbiota-gut-immune-brain axis and mental health: a narrative review

Alison Warren [1,*], Yvonne Nyavor [2], Aaron Beguelin [3], Leigh A Frame [1]

More than 20% of American adults live with a mental disorder, many of whom are treatment resistant or continue to experience symptoms. Other approaches are needed to improve mental health care, including prevention. The role of the microbiome has emerged as a central tenet in mental and physical health and their interconnectedness (well-being). Under normal conditions, a healthy microbiome promotes homeostasis within the host by maintaining intestinal and brain barrier integrity, thereby facilitating host well-being. Owing to the multidirectional crosstalk between the microbiome and neuro-endocrine-immune systems, dysbiosis within the microbiome is a main driver of immune-mediated systemic and neural inflammation that can promote disease progression and is detrimental to well-being broadly and mental health in particular. In predisposed individuals, immune dysregulation can shift to autoimmunity, especially in the presence of physical or psychological triggers. The chronic stress response involves the immune system, which is intimately involved with the gut microbiome, particularly in the process of immune education. This interconnection forms the microbiota-gut-immune-brain axis and promotes mental health or disorders. In this brief review, we aim to highlight the relationships between stress, mental health, and the gut

Anxiety/stress can increase gut permeability

- cortisol (HPA axis)
- adrenaline/noradrenaline (sympathetic nervous system)

Impact:

- impacting protective mucus
- manipulating gut motility
- altering stomach acid / bile signaling
- altering the microbiome homeostasis

Tight Junctions get bulldozed.

Functionality imipacted.

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Volume 21, Issue 5, 31 October 2017, Pages 1160-1168

Report

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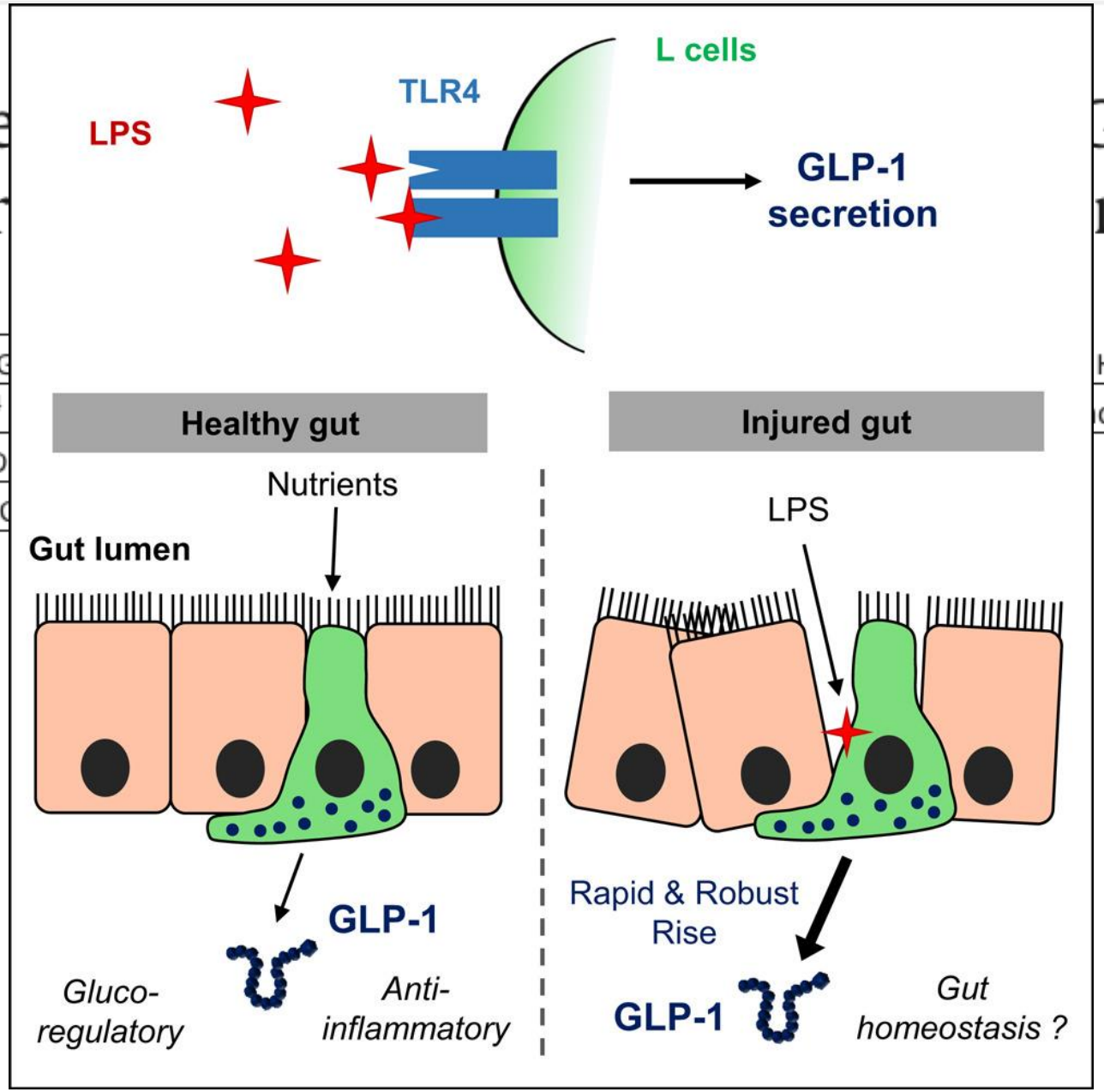
Valérie D
Jacques C



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Gut hyperpermeability → immune activation

- LPS (lipopolysaccharide) from Gram-negative bacteria
- microbial antigens
- Farming chemicals, plastics, metals
- food antigens

This triggers innate immune receptors like:

- TLR4
- immune pattern activation

Which then leads to cytokine release:

- IL-6
- TNF-α
- IL-1β

Full on systemic inflammatory issue.

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Neuropsychopharmacology. 2016 Aug 31;42(1):254–270. doi: 10.1038/npp.2016.146

Inflammation in Fear- and Anxiety-Based Disorders: PTSD, GAD, and Beyond

Vasiliki Michopoulos [1,2,*], Abigail Powers [1], Charles F Gillespie [1], Kerry J Ressler [3], Tanja Jovanovic [1]

Author information · Article notes · Copyright and License information

PMCID: PMC5143487 PMID: 27510423

conditions, types of trauma exposure, and behavioral sources of inflammation). The most parsimonious explanation of increased inflammation in PTSD, GAD, PD, and phobias is via the activation of the stress response and central and peripheral immune cells to release cytokines. Dysregulation of the stress axis in the face of increased sympathetic tone and decreased parasympathetic activity characteristic of anxiety disorders could further augment inflammation and contribute to increased symptoms by having direct effects on brain regions critical for the regulation of fear and anxiety (such as the prefrontal cortex, insula, amygdala, and hippocampus). Taken together, the available data suggest that targeting inflammation may serve as a potential therapeutic target for treating these fear- and anxiety-based

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AI Doom Cycle

Anxiety/stress

Gut permeability + microbiome disruption

Immune activation / cytokines

Brain inflammation / neurotransmitter shifts

Cycle Repeats.

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Nutrients. 2019 Oct 3;11(10):2362. doi: 10.3390/nu11102362

Effects of L-Theanine Administration on Stress-Related Symptoms and Cognitive Functions in Healthy Adults: A Randomized Controlled Trial

Shinsuke Hidese [1], Shintaro Ogawa [1], Miho Ota [1], Ikki Ishida [1], Zenta Yasukawa [2], Makoto Ozeki [2], Hiroshi Kunugi [1,*]

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PMCID: PMC6836118 PMID: 31623400

Stress-related symptom (i.e., depression, anxiety-trait, and sleep) scores decreased and cognitive function (i.e., verbal fluency and executive function) scores improved after four weeks of L-theanine administration. The reduction in sleep quality problems (disturbances in sleep latency, sleep disturbance, and use of sleep medication) was greater in the L-theanine administration compared to the placebo administration, while verbal fluency, especially letter fluency, was improved in the L-theanine administration among individuals who showed relatively low performance at pretreatment. Moreover, L-theanine administration was safe and well complied with. Therefore, L-theanine may be a suitable nutraceutical ingredient for improving mental conditions in a healthy population.

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The effects of L-theanine supplementation on the outcomes of patients with mental disorders: a systematic review

Reza Moshfeghinia [1,2,3,✉], Erfan Sanaei [4], Sara Mostafavi [1], Kasra Assadian [1], Ali Sanaei [4], Getinet Ayano [5]

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In summary, this pioneering systematic review marks the first comprehensive exploration into the effects of LT on a spectrum of mental disorders. The study's strength lies in its novelty, offering a groundbreaking examination of an under-researched area, and its broad analysis covering diverse disorders. Notably, LT supplementation demonstrated promising efficacy in reducing psychiatric symptoms, particularly in schizophrenia, anxiety disorders, and ADHD. However, the review is not without limitations. The scarcity of studies, potential publication bias, and the lack of standardized dosages underscore the need for cautious interpretation. While the findings suggest a potential role for LT in certain mental disorders, these conclusions warrant validation through further well-designed studies. Despite the current constraints, this review contributes valuable insights into the therapeutic potential of LT. Future research should focus on addressing the identified limitations, exploring individual conditions separately, standardizing dosages, and investigating the intricate mechanisms underlying LT's effects. This study serves as a crucial stepping stone, laying the groundwork for a more nuanced understanding of LT's impact on mental health and offering avenues for more targeted and effective interventions in the future.

Phys Act Nutr. 2024 Dec 31;28(4):70–74. doi: 10.20463/pan.2024.0034

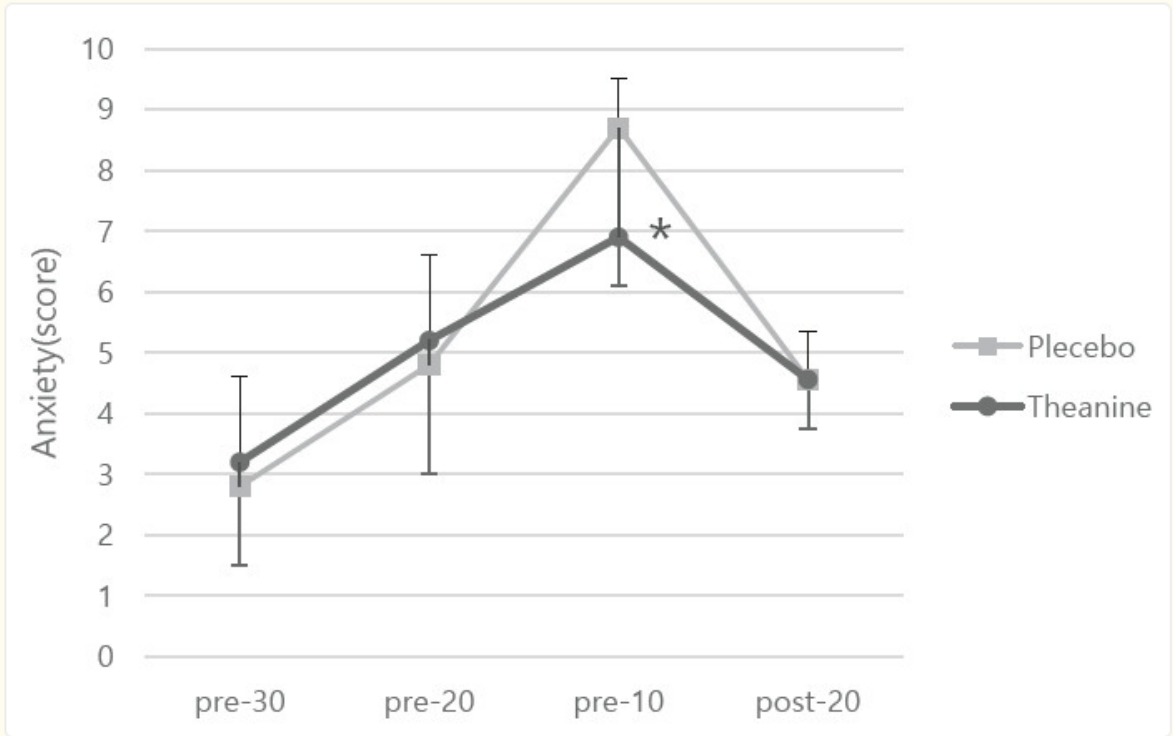
Effects of supplement L-theanine on cognitive anxiety, salivary alpha-amylase, and cortisol in archery competition

In-Soo Lim

Author in

PMCID: PM

Figure 1. Comparison of the cognitive anxiety level during pre-30, pre-3, and post-30 between Theanine and Placebo group.



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pre-30 : 30 min before competition; pre-20 : 20 min before competition; pre-10 : 10 min before competition; post-20 : 20 min after competition; *: $p<.05$.

Phys Act Nutr. 2024 Dec 31;28(4):70–74. doi: 10.20463/pan.2024.0034

Effects of supplement L-theanine on cognitive anxiety, salivary alpha-amylase, and cortisol in archery competition

In-Soo Lim

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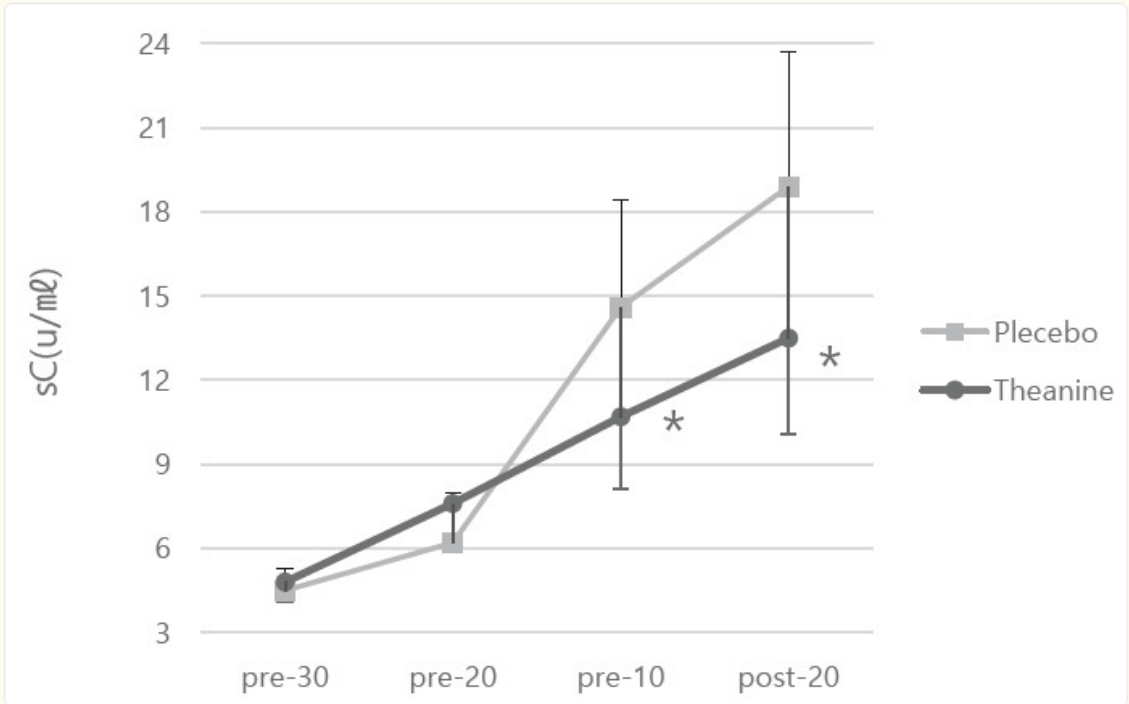
PMCID: PMC

Figure 3. Comparison of the sC level during pre-30, pre-20, pre-10 and post-30 between theanine and placebo group.



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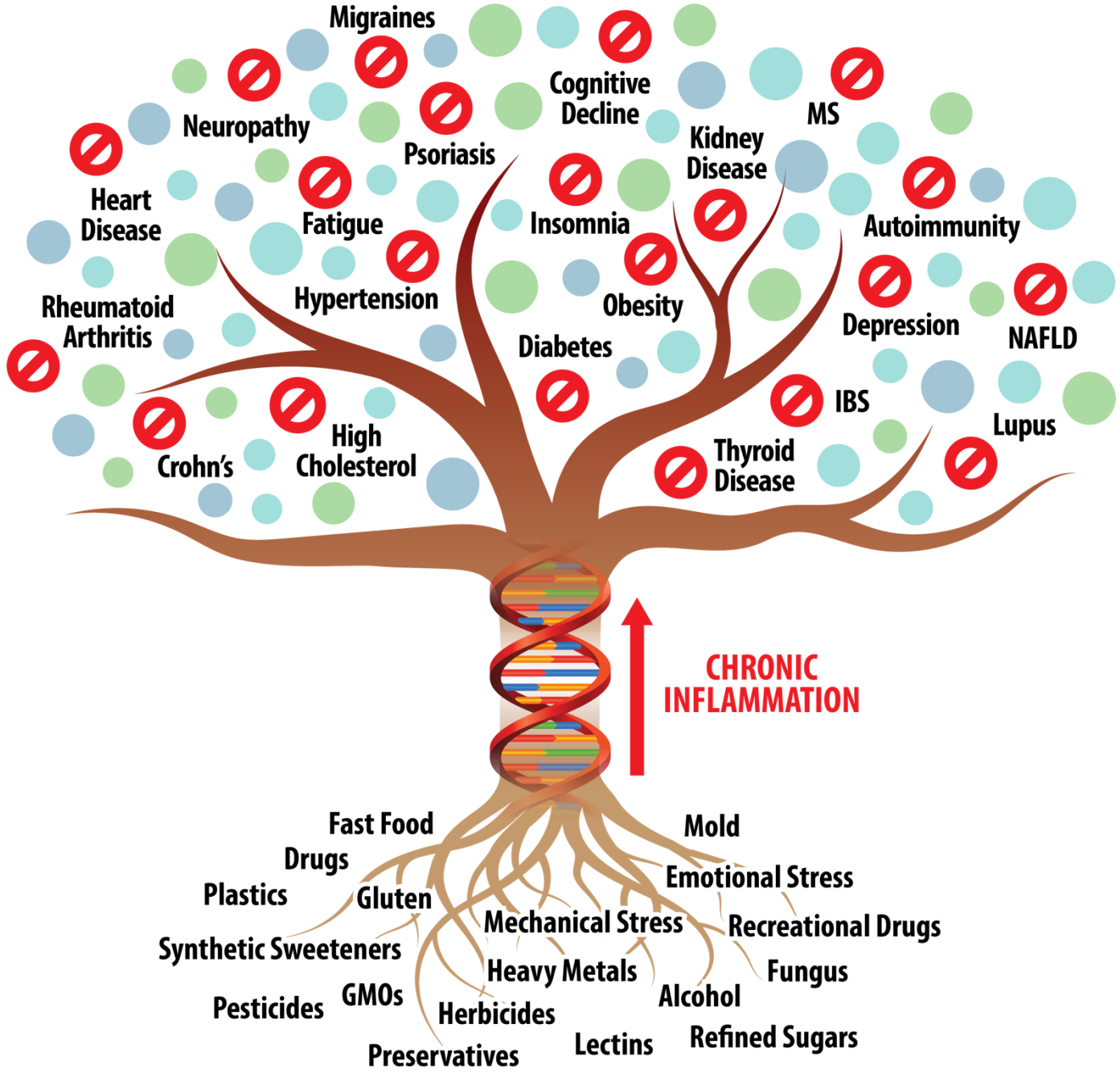
sC : salivary cortisol; pre-30 : 30 min before competition; pre-20 : 20 min before competition; pre-10 : 10 min before competition; post-20 : 20 min after competition; *: $p<.05$.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GMOs
Herbicides
Alcohol
Preservatives
Lectins
Refined Sugars

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L-Theanine

SUPPLEMENT FACTS

Serving size: 2 Capsules Servings per container: 60	Amount Per Serving	% Daily Value
L-Theanine[S1]	400 mg	**

† Daily Value not established.

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