

Psychiatry Redefined

The Evolution of Psychiatry: From the Measureless Medicine to Precision Healing

by James Greenblatt, MD

Measuring the Mind

Measurement is the basis of all scientific medicine. Clinical diagnoses, treatments, and success rates all rely on definitive, quantifiable data that can be accurately assessed, evaluated, and monitored. Numbers allow physicians to create comparable references and scales that identify and characterize a condition and its severity. Discrete data are vital for effective medical care in every category of health and allows researchers and clinicians to communicate with each other, to patients, and to the public. Technology has generated an era of precision medicine with tremendous potential for early detection and targeted treatment strategies. There currently appears to be no end in sight for advanced technology and the development of tests, devices, and, yes, even medications that improve healthcare practices for the growing and aging global population.

While modern information and innovation has driven the progress of diagnostic and treatment methods for physical health, the same cannot be stated for mental health practice. Traditional psychiatry has taken the role of the “measureless medicine” due to a lack of consistent, objective markers utilized. It is difficult to measure and quantify thoughts, feelings, and moods because each patient’s perspective and experience is unique. Clinical diagnosis of a specific mental health condition relies on subjective symptom scales

that attempt to categorize by the most commonly reported symptoms. The continually poor outcomes demonstrate that efforts to improve psychiatric treatment have been slow and resulting in more prescription medications but not always improvement in clinical outcomes, rates of recovery and, most important, remission of symptoms. Attempts to refine mental health diagnoses have only led to a thicker, heavier DSM volume and more turns of the revolving door representing failed prescriptions.

A set of objective markers for mental health is elusive because mental illness is not one disease. Even within conditions such as depression or schizophrenia, symptoms and severity often vary significantly in nature and degree. Consequently, there is not one test that can diagnose every case, nor is there one treatment protocol that applies to every patient under a diagnostic label. Furthermore, the typical approach to psychiatric treatment fails because traditional methods ignore the clear connection between the body and the brain. Indeed, many mental health sufferers first mention their symptoms to their primary care physician because of physical complaints that accompany their psychological struggles. Standard psychiatric evaluations neglect to assess or consider physical symptoms, diet, or other lifestyle behaviors that are linked to brain function. Mental illness is complex and multi-factorial,

requiring a comprehensive analysis of the biochemical, physical, genetic, social, and environmental influences that induce and differentiate each patient’s condition. This perspective describes the framework of integrative psychiatry, which takes into account the whole person as a function of a unique biochemical makeup and nutritional needs that must be balanced to restore and maintain physical and mental wellness.¹

A Unique Set of Stripes

Biochemical individuality is a core concept of integrative and orthomolecular psychiatry. A comprehensive evaluation of the physical, genetic, biochemical, psychological, and environmental variables unique to each patient highlight specific imbalances throughout the brain and body that can be targeted with nutrition and dietary supplements in virtually all psychiatric conditions. Plenty of evidence supports the conclusion that psychiatric illness involves structural, biochemical, and metabolic abnormalities that influence mood and behavior. New imaging technology confirms that the anatomy of the brain and the integrity and connectivity of neurons is different in individuals with all types of mental illnesses, suggesting that specific and measurable biomarkers exist. Single or combinations of nutrient deficiencies manifest in varying forms and degrees of brain dysfunction based on their direct

and indirect effects on neurotransmitter concentrations and ratios.¹

The zebra is a beautiful and highly recognizable creature with its distinctive and striking alternation of white and black stripes. One hardly stops to consider the number or direction of its stripes, immediately assigning the name 'zebra' at first glance by its stereotypical hide. It turns out that the pattern is unique to each animal, like its own identifying fingerprint. When I learned about this fact, it inspired me to coin the acronym THE ZEEBRA to describe my integrative, individualized approach to treating the mind, body, and spirit of patients struggling with mental illness:

T is for Take care of yourself (Healthy Diet and Lifestyle)

H is for Hormones and Herbs

E is for Exclude (Allergens and Food Sensitivities)

Z is for Zinc and Other Minerals

E is for Essential Fatty Acids and Cholesterol

E is for Exercise and Energy

B is for B-vitamins

R is for Restore (Intestinal Microbiome)

A is for Amino Acids and Protein.

THE ZEEBRA model encompasses a set of the most frequently encountered problems I have seen in my clinical practice as well as those topics supported by significant research evidence. With growing scientific and medical knowledge and advanced tools at our fingertips, this approach provides specific treatment targets that can be measured, compared, and monitored. Individual patients may have one or multiple components out of balance, but reversing nutrient deficiencies and restoring neurotransmitter balance can resolve multiple symptoms and improve the efficacy of other treatment modalities.¹ In this way, the methodology of THE ZEEBRA approach provides an entirely new and objective way of treating patients with the goal of long-term recovery.

The nutrients we obtain from food go far beyond fueling our daily movements and activities. Vitamins, minerals, amino acids, and essential fatty acids are critical building blocks for the hormones and neurotransmitters that direct the function of our brains and drive mood and emotion. Impediments to the digestion, absorption, transportation, and utilization of nutrients from food

all have implications for mental health. Innate errors of metabolism, allergies and food sensitivities, and poor lifestyle habits all contribute to an individual's biochemistry. The steps of THE ZEEBRA model applied to each patient reflect a comprehensive biological snapshot of what needs to be reinforced, balanced, or compensated for due to genetic polymorphisms.¹ This article focuses on the "R" in THE ZEEBRA, describing an integrative approach to restoring harmony to the brain by way of the gut. This model offers help to clinicians on their journey to *redefine* the outdated model of contemporary psychiatry.

The Gut-Brain Connection

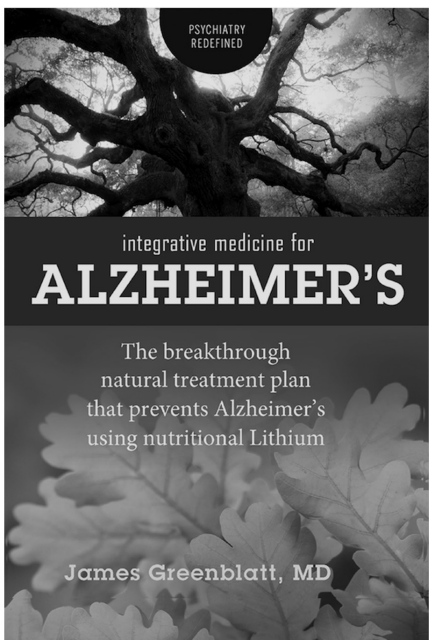
Regardless of whether we know or understand the science, we are all familiar with the connection between the gut and the brain. Everyone has experienced the powerful influences that hunger or an upset stomach can have on mood and focus. Our intestines are home to trillions of bacteria, forming a diverse and fluctuating community

of beneficial and potentially harmful species that we call the microbiome. Despite a common wariness of bacteria, the presence and composition of the microbiome is essential in both the brain and body. As research on our gut bacteria continues to accumulate, there seems to be endless links between the nature and activity of these hardworking microbes and human health. While a majority effort has focused on the effects of the microbiome on gastrointestinal function and immunity, emerging evidence suggests many aspects of our psychology are also driven by these mysterious cohabitants.²

The gut-brain axis is a compact term that represents a dynamic, bidirectional superhighway of information communicated between the intestines and the nervous system. Messages travel to the brain directly via the vagus nerve, and more indirectly by immune cells, hormones, and neurotransmitters. Neurotransmitters serve as the boldest chemical messengers of information



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➤ that regulate emotion and behavior. Specific concentrations and ratios of neurotransmitters are required for optimal mental function; and imbalances between stimulatory and inhibitory signals exert powerful effects on mood, attention, and impulse control. Stable mental well-being is highly dependent on the balance of hundreds of neurotransmitters and the signals they provide to neurons in the brain.³

Throwing Off the Balance

A balance of bacterial populations in the gut is key to unhindered communication along the gut-brain axis. Intestinal dysbiosis occurs when the microbiome population contains a greater proportion of hostile bacteria that can wreak widespread damage and manifest as part of many chronic diseases outside the gastrointestinal system, including allergies, diabetes, and cardiovascular disease.⁴ The *Clostridia* genus encompasses approximately 100 species of bacteria of both beneficial and potentially harmful strains, including *C. difficile*, the notorious originator of *C. diff* infections commonly acquired at hospitals. *Clostridia* are well-publicized for becoming antibiotic-resistant due to overuse of high-dose and long-term antibiotics. Overpopulations of *Clostridia* bacteria are often found in young children incessantly treated with antibiotics for ear infections and other childhood illnesses.²

Metabolic byproducts of the microbiome can also pass from the intestine into the bloodstream and deliver messages to the brain. Like their microbial source, these chemical signals can be both positive and negative. Beneficial bacteria linked to antidepressant and anxiolytic effects, often called psychobiotics, produce neurotransmitters such as serotonin and *gamma*-amino butyric acid (GABA) that stabilize mood and promote calm.⁵ Unfriendly bacteria, including some strains of *Clostridia*, generate substances that can alter normal neurotransmitter signals and disrupt

mood and focus. Though symptoms of autism, attention deficit hyperactivity disorder (ADHD), major depression, and schizophrenia appear widely distinct and variable, discovery of a novel biomarker may explain a shared antagonist in psychiatric patients characterized by aggressive and compulsive behaviors. *C. difficile*, along with seven other *Clostridia* species, promote the synthesis of 3-(3-hydroxyphenyl)-3-hydroxypropionic acid (HPHPA) in combination with human metabolism of the amino acid phenylalanine. Clinically used as a biomarker of dysbiosis, HPHPA may also represent an important diagnostic indicator to guide the treatment of many mental health conditions.^{2,6}

Associations between urinary levels of HPHPA and mental illness were first reported by Armstrong, et al., in 1957, who provided chemical evidence of the role of dietary factors in the etiology of many psychiatric disorders.⁷ More recently, Dr. William Shaw brought HPHPA back into the spotlight after investigating its role in two young boys with autism and discovering its underlying mechanisms.^{2,8} The potent influence of HPHPA has been demonstrated through the reversal of symptoms with targeted antibiotics in patients with various mental health conditions. Detected through an assay of organic acids in urine, the highest recorded HPHPA level was measured in a young female patient with first-episode schizophrenia.⁹ Eradication of harmful *Clostridia* in this patient eliminated her auditory hallucinations. In addition to Shaw's initial cases with autism, other autistic children with gastrointestinal distress and irritable, aggressive behavior have shown remarkable improvement with treatment for *Clostridia*.⁶

HPHPA's primary mode of action involves upsetting the balance of neurotransmitters in the brain by directly targeting a critical enzyme in the metabolic breakdown of dopamine. Dopamine beta-hydroxylase (DBH) facilitates the conversion of dopamine

to norepinephrine, regulating the concentrations of dopamine that are created from its precursor phenylalanine. As the population of intestinal *Clostridia* grows, more HPHPA travels the gut-brain axis to inhibit DBH, increasing brain concentrations of dopamine and reducing norepinephrine. A neurotransmitter imbalance favoring dopamine creates a hyper-stimulating, oxidative milieu that is toxic to neurons. In addition to damaging brain receptors with potential effects on motor control, excess dopamine drives abnormal risk-taking and reward-seeking behaviors. Substance abuse disorders, obsessive-compulsive disorder, ADHD, and psychosis have all been associated with elevated dopamine levels. Even at milder degrees, dopamine excess contributes to irritability, agitation, and anxiety. DBH inhibition by HPHPA also interferes with normal synthesis of norepinephrine, significantly impacting decision-making, attention, and memory.^{2,3}

Happy Gut: Happy Brain

Beyond improving mental health, resolving *Clostridia* overgrowth is essential to restoring gastrointestinal health. Dysbiosis leads to severe damage of intestinal tissue leading to poor dietary absorption and digestion, reduced immunity, and greater risk of allergy. Furthermore, suppression of favorable bacteria contributes to intestinal dysfunction by inhibiting their synthesis of beneficial byproducts. The presence of elevated HPHPA does not rule out additional perpetrators of intestinal dysfunction; food allergies are frequent contributors in virtually every psychiatric condition, requiring minimal to drastic dietary changes.³

My thirty years of clinical experience suggests a significant number of children and adults with ADHD, anxiety, autism, and schizophrenia, particularly those with gastrointestinal symptoms will test high for urinary HPHPA. A number of clinical reports and published data corroborate the importance of assessing elevated HPHPA across the spectrum of psychiatric illness, warranting its routine inclusion in lab assays for patients

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displaying these risk factors. When urinary HPHPA concentrations exceed 180 mmol/ml of creatine, my first line strategy is always a multi-strain, high-dose probiotic in doses of at least 200 billion CFUs per day; often 600 CFUs per day is required.³

In many cases, reintroducing commensal bacteria with a multi-strain, high-dose probiotic over a period of two to three months is enough to overcome the bacterial imbalance and realign the gut-brain axis. Individuals who do not respond to probiotics in the expected time may require a *Clostridia*-specific antibiotic to create an optimal environment for probiotics to take effect. In most patients requiring adjunct antibiotics, vancomycin in a 30-day pulsing protocol (1 day on; 2 days off) is sufficient to eliminate *Clostridia* and jumpstart recovery with probiotic treatment. In addition to restoring homeostasis of the microbiome, resolving *Clostridia* overgrowth often increases the efficacy of other necessary supplementations or medications.³

The Power of the Organic Acids Test and Probiotics

A 25-year-old adult male with a history of atopy, including multiple food allergies and a diagnosis of celiac disease, dry eye, and asthma arrived at my office after a referral for generalized anxiety and major depression. This patient had been in therapy and psychiatric treatment for over a decade and responded poorly to multiple prescription medications. His struggles

with mental health began in high school and college, which seemed to align with severe gastrointestinal symptoms and disordered eating behaviors and, which the patient said, correlated with a highly stressful, demanding period of time. In recent years, the patient's symptoms had escalated to more significant issues with anger, rage attacks, panic, and self-harm. An organic acids test confirmed elevated HPHPA as the primary culprit. A prescription for a multi-strain, high-dose probiotic liberated this patient from years of suffering and removed barriers to success in his young life. This case emphasizes the array of debilitating physical and mental effects that HPHPA can inflict.

I regularly find elevated HPHPA in children with ADHD and autism, and frequently begin immediately with the organic acids test, especially in patients disposed to aggression, angry outbursts, and impulsivity. One patient, a four-year-old boy, was brought into my office by his mother with stereotypical ADHD symptoms that were characterized by many incidences of anger and violence towards others and pets. He often experienced "sensory overload" that triggered tantrums and impulsive, abnormal behaviors, followed by feelings of remorse. Not surprisingly, these episodes resulted in significant problems at home and school. Stimulant medications were ineffective and brought adverse side effects. His urinary HPHPA level, along with several other indicators from the organic acids test, was markedly elevated. A prescription

of a multi-strain, high-dose probiotic and restriction of dairy from his diet resolved much of his symptoms and aggression and supported the return to a normal developmental track.

These are two cases that show the profound effect of elevated HPHPA on psychiatric symptoms and the astonishing transformation that can occur in response to simple and straightforward treatments. The HPHPA levels in the organic acids test represents one of the most highly valuable diagnostic tools available to mental health practitioners. Its utility for confirming intestinal dysbiosis has implications for many psychiatric conditions.^{2,6} Restoring balance to the microbiome can lay the foundation for psychological healing. Psychiatry can no longer be called the measureless medicine. As psychiatrists and mental health clinicians, we understand how to utilize concepts of functional medicine and orthomolecular medicine. We can provide objective personalized treatment to alleviate the pain and anguish of mental illness. I believe testing for HPHPA has the potential to alleviate an inconspicuous source of mental health symptoms and support patients on a road to recovery.

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Dr. James M. Greenblatt, MD, is chief medical officer and vice president of medical services at Walden. He provides medical management, leadership and oversight of Walden's eating disorder and psychiatric programs in Massachusetts and Connecticut. Dr. Greenblatt is board-certified in child and adult psychiatry.

He received his medical degree and completed his adult psychiatry residency at George Washington University in Washington, DC. He completed a fellowship in child and adolescent psychiatry at Johns Hopkins Medical School. In addition, Dr. Greenblatt is a clinical faculty member in the psychiatry department at Tufts Medical School as well as the Geisel School of Medicine at Dartmouth College in New Hampshire.

He lectures extensively throughout the United States and Canada on integrative therapies for mental health. Dr. Greenblatt is the author of six books including one textbook and books on depression, eating disorders and ADHD. His latest book is on Integrative Therapies for Alzheimer's disease, exploring the research on nutritional lithium. Dr. Greenblatt is the founder of **Psychiatry Redefined**, a healthcare education training program for integrative psychiatry.

He can be reached at: Walden Behavioral Care, 9 Hope Avenue, Suite 500, Waltham, Massachusetts, 02453; 781-647-2901. For more information on Dr. Greenblatt please visit www.jamesgreenblattmd.com.