NEURODEVELOPMENTAL & MENTAL HEALTH

# Biochemical Patterns in Autism, ADHD, Anxiety, and Related Conditions

## Using Laboratory Markers to Guide Targeted Nutrition

Why autism, ADHD, and anxiety share a common biochemical signature—and how targeted laboratory testing turns that signature into personalized nutrition.

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Decades of clinical research and practice have revealed a crucial connection: neurodevelopmental disorders such as autism spectrum disorder (ASD) and ADHD, as well as other neurological conditions including anxiety, have similar underlying factors. Autism, ADHD, and anxiety are heterogeneous conditions, meaning that they do not have one cause or presentation and instead have a variety of underlying contributing factors, symptoms, and responses. Zinc deficiency, copper excess, vitamin B6 insufficiency, oxidative stress, methylation imbalances, mitochondrial dysfunction, and pyrrole disorder show up across diagnoses, in different combinations and magnitude, shaping each person's unique neurological picture.

This means that individuals with these conditions need a personalized nutrition approach that addresses the specific factors and needs of the individual, and laboratory testing is essential to identifying the specific biochemical patterns driving an individual's symptoms.

## 01 Shared Biochemical Patterns in Neurodevelopmental Conditions

While each individual is different, neurodevelopmental and neurological disorders such as autism, ADHD, anxiety, and other conditions share many of the same underlying biochemical factors. Four core processes recur across diagnoses:

### I Oxidative Stress / Redox Balance

The homeostatic balance of oxidation and antioxidant status.

### II Methylation / One-Carbon Metabolism

Neurotransmitter synthesis, detoxification, gene regulation.

### III Energy Production / Mitochondrial Function

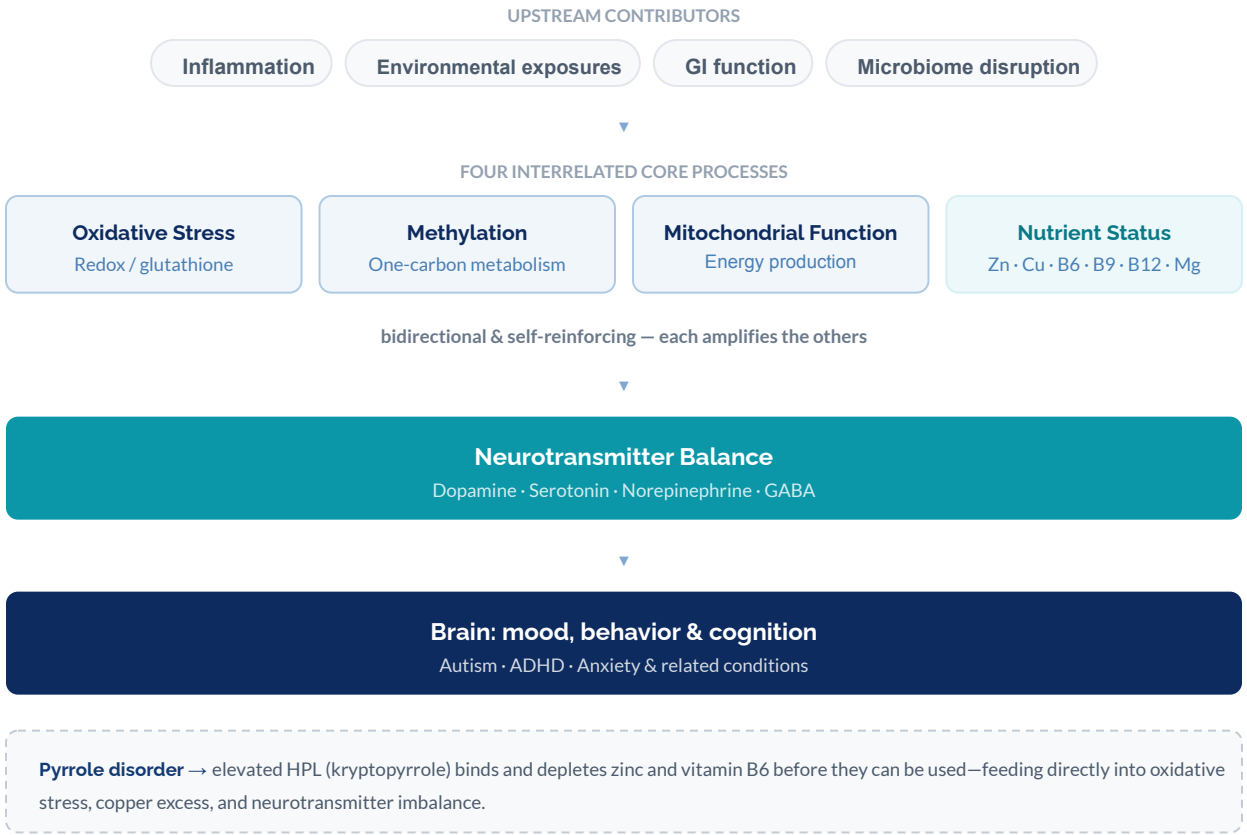
Cellular energy for the brain's high metabolic demands.

### IV Nutrient Status

The measurable cofactors that fuel biochemical processes.

These core biochemical processes may be influenced by upstream contributors such as inflammation, environmental exposures, gastrointestinal function, and microbiome disruption. These biochemical factors directly influence the brain, contributing to neurological conditions. Additionally, they are overlapping processes that affect each other, compounding the situation.

FIGURE 1 **The interconnected biochemistry of neurodevelopmental conditions**



## 02 Oxidative Stress / Redox Balance

Oxidative stress is one of the most consistent findings in autism as well as in ADHD, anxiety, depression, and most chronic health conditions. Redox balance is the homeostatic process of oxidation and antioxidant status. When this process goes out of balance it leads to oxidative stress contributing to inflammation, mitochondrial stress, and neurotransmitter imbalance. Glutathione is our body's master antioxidant and the redox ratio of reduced to oxidized glutathione indicates the state of oxidative stress. Glutathione is produced in the transsulfuration pathway, which is downstream from methylation.

Research shows that children with autism have increased oxidative stress with a significantly lower ratio of reduced glutathione to oxidized glutathione than children without autism.[1] A meta-analysis of six studies found a significant association between ADHD and oxidative stress. [2] Research on anxiety, depression, bipolar, and schizophrenia implicates oxidative stress in these mental health disorders including free-radical damage, antioxidant insufficiency, inflammation, and neurotoxicity. [3] A study using methylcobalamin injections (vitamin B12) and folinic acid (a bioactive form of folate) supplementation in children with autism found that oxidized glutathione decreased, and glutathione redox ratio increased, indicating improved redox balance with decreased oxidative stress and enhanced antioxidant capacity. [4] Another study in ASD found that methylcobalamin and folinic acid supplementation improved glutathione redox ratio and behavior, with greater glutathione redox status correlating with greater improvement in expressive communication, daily living skills, and social skills. [5]

> **Oxidative stress is one of the most consistent findings in autism—and across ADHD, anxiety, and depression.**

## 03 Methylation / One-Carbon Metabolism

One-carbon metabolism (including methylation) is central to neurotransmitter synthesis, glutathione production, methylation-dependent detoxification, and DNA methylation—processes that are commonly impacted in autism, as well as ADHD and anxiety. It plays a key role in the production and regulation of neurotransmitters such as dopamine, serotonin, and norepinephrine, which influence mood, behavior, and cognitive function.

Methylation is the transfer of a methyl donor to DNA or other substances to activate an enzyme, regulate gene expression, influence neurotransmitter synthesis, or modulate a wide range of biological processes including detoxification and immune function. The broader set of processes called one-carbon metabolism includes the folate cycle, methionine cycle, methylation, and transsulfuration. The transsulfuration pathway originates from homocysteine (in the methionine cycle), leading to cysteine and then to glutathione production. Nutrients involved in these pathways include vitamins such as folate, B12, and B6, additionally riboflavin, niacin, and choline, as well as minerals including zinc and magnesium.

S-adenosylmethionine (SAM) serves as the methyl donor for catechol-O-methyltransferase (COMT), the enzyme responsible for breaking down dopamine, epinephrine, and norepinephrine. The folate cycle and B12 are essential for BH4 (tetrahydrobiopterin) synthesis, a crucial cofactor for the production of serotonin and dopamine. These neurotransmitters are clinically significant in ADHD, autism, and anxiety, as they play key roles in attention, mood, behavior, and stress response.

A published study on children with autism found significantly decreased levels of plasma methionine and a decreased SAM/SAH [S-adenosylmethionine (SAM) / S-adenosylhomocysteine (SAH)] ratio, a measure of methylation capacity. [6] Research shows concurrent deficiencies in B6, B9, and B12 in ASD can disrupt one-carbon metabolism, leading to impaired methylation, elevated homocysteine, reduced glutathione, and a buildup of 5-MTHF consistent with a functional folate deficiency. [7]

Histamine is partly metabolized by histamine N-methyltransferase (HNMT), which uses SAM as the methyl donor. As such, histamine is used as a proxy for methylation status: high histamine suggesting reduced methylation capacity, and low histamine associated with increased methylation activity. For this reason, whole blood histamine is a marker often used by practitioners as a measure of methylation capacity, along with SAM/SAH ratio.

## 04 Energy Production / Mitochondrial Function

Our mitochondria are the energy producers in every cell. Because every cell relies on mitochondrial energy, mitochondrial dysfunction can affect many systems, including the gut, brain, and immune system. Our brain has high energy demands, so when our mitochondria are not functioning well, this can affect our cognitive function and mood. Mitochondrial function is closely interconnected with methylation and transsulfuration pathways, which help support energy production and antioxidant capacity. The metabolic state of the mitochondria influences the amount of oxidative stress produced, while conversely oxidative stress can impair mitochondrial function, causing a self-reinforcing cycle. These interactions highlight how these systems are interrelated and can compound biochemical imbalances.

Mitochondrial dysfunction is common in ASD. While some studies find the prevalence of mitochondrial dysfunction in ASD to be approximately 30–50%, [8] one study suggested that it may be present in up to 80% of children with ASD. [9]

Supplying the nutrients needed for mitochondrial function and these interconnected biochemical systems can be beneficial—including B vitamins, magnesium, iron, CoQ10, carnitine, and antioxidants—for energy production and to protect against oxidative stress. While mitochondrial function is not always measured directly, it can be assessed indirectly through organic acids, lactate, carnitine, CoQ10, and related oxidative stress, methylation, and nutrient markers.

## 05 Nutrient-Dependent Enzymatic Activity

Nutrients are the cofactors that fuel the biochemical pathways and systems described above—those that affect the brain including mood, behavior, cognition, and neurotransmitter balance. Fortunately, these nutrients are measurable and modifiable, offering practitioners a direct point of intervention in the underlying biochemistry driving these symptoms and conditions. These nutrients are more likely to be deficient in those with ASD, ADHD, anxiety, and other neurological conditions. Understanding laboratory markers helps practitioners select the best tests to make more informed clinical decisions.

> **These nutrients are measurable and modifiable—a direct point of intervention in the biochemistry driving symptoms.**

### Folate, Vitamin B12, and Vitamin B6

Folate, vitamin B12, and vitamin B6 are essential cofactors in one-carbon metabolism, supporting methylation and transsulfuration pathways that influence neurotransmitter production, detoxification, and antioxidant capacity. While folate and vitamin B12 support neurotransmitter balance indirectly through methylation, vitamin B6 plays a direct role in neurotransmitter synthesis, serving as a cofactor in the production of serotonin, dopamine, and GABA.

Studies have reported deficiencies of folate, vitamin B12, and vitamin B6 in autism[10] and ADHD; [11] these deficiencies and their effects on methylation / one-carbon metabolism have been suggested as potential contributors to the etiology of ASD and ADHD. Supplementation of these nutrients has been reported by families and individuals with ASD to provide an overall benefit. [12] Additionally, in a cross-sectional study of adults, higher intake of folate, B12 and B6 and other methyl donors was associated with reduced odds of anxiety, depression, and psychological stress. [13]

### Zinc / Copper

Zinc (Zn) modulates glutamate receptors and GABA signaling, so a deficiency disrupts the excitatory/inhibitory balance that is already compromised in autism, ADHD, and anxiety. Zinc is also required for superoxide dismutase (SOD), a crucial antioxidant enzyme; therefore, a deficiency of zinc can contribute to oxidative stress. Zinc and copper (Cu) compete for absorption, so a deficiency of zinc can cause an excess of copper. Additionally, copper is required for an enzyme (dopamine-beta-hydroxylase; DBH) that converts dopamine to norepinephrine. Copper excess can therefore cause elevated norepinephrine, contributing to anxiety, hyperactivity, and emotional dysregulation.

Zinc-copper imbalance—commonly characterized by low zinc, elevated copper, and reduced Zn/Cu ratio—is frequently observed in autism and may contribute to neurological dysfunction through effects on oxidative stress, neurotransmitter balance, and detoxification capacity. These imbalances can impair key systems including antioxidant defenses, metallothionein function (which supports zinc/copper regulation, antioxidant defense, and heavy metal detoxification), and GABA/glutamate signaling, potentially influencing symptom severity and overall neurological function in children with autism. [14] Another study on children with ASD found a decreased Zn/Cu ratio, along with an inverse correlation of decreased Zn/Cu ratio to increased severity of autism measured through the Childhood Autism Rating Scale (CARS).[15]

Elevated hydroxyhemopyrrolin-2-one (HPL), commonly referred to as kryptopyrrole, binds and depletes zinc as well as vitamin B6 before they can be utilized. Since zinc deficiency contributes to glutamate and GABA imbalance, oxidative stress, and copper excess, and B6 deficiency impairs neurotransmitter production, pyrrole disorder can play a significant role in symptoms of ADHD, anxiety, and autism. [16]

### Magnesium

Magnesium is a mineral that supports multiple interconnected biochemical systems. It plays a direct role in mitochondrial function and energy production, helps regulate redox balance, and supports enzymatic processes that influence methylation. Magnesium modulates neurotransmitter activity—balancing excitatory glutamate and inhibitory (calming) GABA—and is also involved in stress response and hundreds of enzymatic reactions throughout the body.

A meta-analysis of seven studies found individuals with ADHD had lower levels of magnesium (in serum) than healthy controls, [17] and a study of children with autism found lower levels of magnesium (in serum and whole blood) compared to controls. [18] A systematic review found magnesium supplementation may reduce anxiety and stress, with mixed findings across studies.[19] Caregivers of children with autism reported magnesium supplementation to be beneficial, particularly for improving anxiety and constipation. [12]

## 06 Clinical Application: Using Labs to Guide Targeted Nutrition

Laboratory testing provides practitioners a way to move beyond generalized suggestions to precision nutrition recommendations. Rather than generic protocols based on conditions, these markers help reveal underlying imbalances in oxidative stress / redox status, methylation, mitochondrial function, and nutrient-dependent processes—allowing for more targeted, personalized nutrition strategies.

## Oxidative stress

The following glutathione markers assess oxidative stress, antioxidant capacity, and redox balance, with GSH:GSSG serving as the most clinically relevant for practitioners.

**Glutathione, reduced (GSH)**

**Glutathione, oxidized (GSSG)**

**Total glutathione**

**Glutathione redox ratio (GSH:GSSG)** — the most clinically relevant measure of oxidative stress

## Methylation

These markers help assess methylation capacity and guide targeted nutrient recommendations including folate, B12, B6, and other cofactors:

**Whole blood histamine** — elevation is associated with undermethylation, while low histamine may suggest overmethylation

**Vitamin B12 (serum)** — reflects circulating levels of B12 but may not capture functional deficiency

**Methylmalonic acid (MMA)** — elevated MMA may identify a functional B12 deficiency at the cellular level

**Folate (serum)** — reflects short-term dietary folate status

**Folate, RBC (red blood cell folate)** — reflects tissue / long-term folate storage

**Homocysteine** — reflects impaired remethylation or transsulfuration, indicating insufficient folate or B12 (remethylation) or B6 (transsulfuration)

**SAM, SAH, SAM/SAH ratio** — a direct measure of methylation capacity

## Mineral balance (zinc and copper)

These markers help practitioners assess mineral status and identify imbalances that may influence neurotransmitter function and overall neurological health.

**Zinc, plasma** — most reliable measure of zinc status

**Copper, serum** — elevated levels may reflect copper overload, best interpreted alongside ceruloplasmin

**Ceruloplasmin** — the body's primary copper transport protein; measured alongside serum copper, it helps distinguish bound from free copper, as free (unbound) copper is more biologically active and potentially disruptive

**Zinc/Copper ratio (Zn/Cu)** — often more clinically informative than either marker in isolation

## Kryptopyrrole

The following urinary marker provides insight into patterns associated with zinc and vitamin B6 status:

**Kryptopyrrole — hydroxyhemopyrrolin-2-one (HPL)** — elevated levels indicate excessive HPL, depleting zinc and B6

## Additional lab markers

The following markers may help assess underlying nutritional and biochemical factors that influence neurotransmitter function, neurological wellness, and mood:

**Amino acids (plasma amino acid profile)** — identifies deficiencies in neurotransmitter precursors such as tryptophan for serotonin

**Iron status (ferritin, with or without full iron panel)** — low ferritin affects dopamine synthesis and cognitive function

**Magnesium (serum or RBC)** — RBC magnesium reflects long-term storage

**Omega-3 fatty acids, organic acids, and gut/microbiome testing** — may provide additional clinical insight into factors influencing brain health and nutrient availability

## 07 Conclusion

These systems are overlapping and often bidirectional: mitochondrial dysfunction can cause oxidative stress, and oxidative stress can exacerbate mitochondrial dysfunction. This makes these conditions complex to navigate; however, quantitative data from laboratory testing equips practitioners with the necessary information to address these underlying factors with targeted, personalized nutrition strategies—often leading to improvements in symptoms for those with autism, ADHD, anxiety, and other neurological conditions. These personalized approaches may include diets that incorporate anti-inflammatory foods, methyl-donor-rich foods, low-copper diets when needed, gut-supportive approaches such as gluten-free and dairy-free diets or other therapeutic diets, as well as targeted precision nutritional supplementation.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