



Understanding Anxiety in Autism

If you have an autistic child, (aka highly sensitive, too fast for this reality and awake) chances are you've noticed your child often displays physical and behavioral signs of anxiety such as restlessness, recurring headaches, withdrawing from family or refusing to go to school.

Unfortunately, anxiety is a common occurrence in autism – according to a research paper published in *Neuropsychiatry*, “up to 80% of children with ASDs experience clinically significant anxiety, with high comorbidity rates for social phobia, generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD) and separation anxiety disorder (SAD) (30, 35, 37 and 38%, respectively).” [1]

Children with autism are often very stressed by their environment; this can be one cause of increased anxiety. They may have sensory processing disorder – crowded spaces, loud noises, and bright lights of a shopping center or public event can constitute an assault to their system and cause their body to go into fight or flight mode. Doing normal everyday things can cause anxiety for them. And this decreases their ability to manage stress and thus leads to increased anxiety.

Social interactions are often an issue for children with autism – this can explain why these children commonly have difficulty establishing and maintaining relationships. Add anxiety to the equation and the child will have increased ASD symptom severity as well as greater impairments in sociability. What this means is that those children with autism who also have anxiety are likely to struggle even more with their social environment and interactions.

To help you better understand why anxiety is such an issue for individuals with autism, this article will cover the biochemistry of anxiety in autism and what you can do.

Biochemical aspects of anxiety

Many believe that anxiety is not something you can control. This couldn't be further from the truth. Maybe people may be aware that mindfulness and stress reduction strategies can help anxiety, but understanding the biochemical roots of anxiety will help you get to the underlying foundation of the problem and support your child from the inside out.

1. Chronic inflammation

Did you know that chronic inflammation is an underlying factor in anxiety conditions? In other words, anything that can trigger inflammation (read chemicals, allergens and pro-inflammatory foods) can also exacerbate or cause anxiety. You see, during an inflammatory response, the body produces chemicals known as cytokines – since the early 1980s, researchers have discovered that these cytokines cause a wide variety of neurological symptoms including anxiety [2, 3].

2. Decreased methylation function

Children with autism are known to be at greater risk of decreased methylation function. Methylation is a vital biochemical process involved in various essential reactions in the body. For instance, methylation plays a key role in the brain's activities and the production of neurotransmitters such as serotonin and dopamine which are involved in mood regulation and can help alleviate depression and anxiety. Put simply, decreased methylation function could lead to an inadequate production of serotonin and dopamine which could cause a wide range of cognitive behavioral issues such as anxiety.

3. Altered dopamine signaling

As mentioned earlier, dopamine is a neurotransmitter which is involved in social interaction and reward behaviors. Usually, the dopamine transporter is able to sweep up excess dopamine from the synapse (the gap or junction across which nerve cells can send impulses to other nerve cells usually by a neurotransmitter). However, researchers recently discovered that genetic variations linked to ASD disrupt the function of this transporter – this can contribute to anxiety in autism [4].

4. Increased intestinal permeability

When the intestinal lining is damaged, the tight junctions between the intestinal wall and the bloodstream can no longer prevent incompletely digested proteins, bacteria or bacterial fragments from leaking out into the bloodstream. This condition is known as increased intestinal permeability or 'leaky gut'. When these substances reach the bloodstream, they trigger the immune system and can send it into overdrive. This results in systemic inflammation.

Wondering what the gut has to do with anxiety? A lot actually: the brain and the gut communicate closely with one another via the gut-brain axis. What this means is that if the gut is unhealthy or 'leaking', it will promote the formation of inflammatory cytokines which are able to reach the brain by crossing the blood brain barrier. Once in the brain, these cytokines will wreak havoc and can cause a panoply of symptoms such as anxiety, irritability, depression and headaches [5, 6, 7].

But what does this have to do with autism? Well, research indicates that individuals with autism are more likely to suffer from increased intestinal permeability compared to healthy subjects (36.7% vs. 4.8%) [8]. Besides

increasing inflammation, a leaky gut will also provide optimal conditions for pathogens to thrive in the gut. Not only do these nasty bugs negatively affect mood and increase anxiety, but they also compete with beneficial bacteria (which help reduce anxiety).

That's not all; increased intestinal permeability is often accompanied by poor digestive function. This results in suboptimal absorption of amino acids and nutrients crucial for good mental health and preventing anxiety.

5. High levels of HPHPA

HPHPA stands for 3-(3-hydroxyphenyl)-3-hydroxypropionic acid (aren't you glad it has an abbreviation?). This toxin, produced by the pathogenic *Clostridia* bacteria in the gut, could be a causal factor in autism. For ABC News Dr. James Greenblatt explains that "HPHPA causes deactivation of an enzyme [Dopamine Beta-Hydroxylase] so that dopamine cannot be converted to the neurotransmitter norepinephrine." When this enzyme is inhibited, it can cause a considerable increase in dopamine levels in the brain leading to oxidative stress and a depletion of glutathione, a potent antioxidant responsible for detoxification and elimination of environmental toxins [9]. This can worsen anxiety in children with autism. In fact, Dr. S. Jill James, PhD, famous for her research on ASD explains that the active form of glutathione is reduced 80% in children with autism.

6. High levels of glutamate

Glutamate, a major excitatory neurotransmitter in the brain, has been found to be high in autism [10]. Moreover, children with autism are also deficient in glutamic acid decarboxylase, an enzyme involved in converting glutamate to GABA (γ -Aminobutyric acid). GABA, often considered as glutamate's calming cousin, is an amino acid that produces calming effects by inhibiting nerve transmission in the brain [10, 11]. Although larger studies are needed, this deficiency in glutamic acid decarboxylase could be explained by the presence of antibodies against glutamic acid decarboxylase 65 (GAD65) which has been detected in the serum of children with autism [12]. Based on my research, the increased levels of glutamate in autism is currently poorly understood – further studies are needed to determine whether this is due to metabolic issues, glutamate receptor and/or transporter problems, vitamin B6 involvement or the overall diet.

7. Presence of cerebral folate receptor autoantibodies

Folate is an essential nutrient involved in methylation which, as mentioned earlier, is involved in the production of neurotransmitters. However, children with autism often lack folate specifically in the central nervous system (CNS) despite having normal levels of folate metabolites in the blood – this disorder is known as cerebral folate deficiency or CFD [13]. To understand CFD, it is necessary to know that for 5-MTHF (the active form of folate) to enter the CNS, it needs to be transported across the blood-brain barrier by a carrier known as folate receptor protein alpha or folate receptor 1 (FRA or FR1). Once 5-MTHF has entered the CNS, it can be transported into the neurons by the reduced folate carrier (RFC) or it can diffuse across the blood-brain barrier without a carrier if blood concentrations of folate are high enough.

By now you must be wondering why I am talking about folate receptors. Well, it turns out that autoantibodies to these receptors are common in ASD. These autoantibodies attach to the FRA, making it unable to bind to folate. It is believed that children with autism who have CFD were exposed to folate receptor alpha antibodies during pregnancy, and research shows that this can cause behavioral deficits including anxiety [14].

8. Pyroluria

Pyroluria, or pyrrole disorder, is a condition induced by stress. Individuals with this condition produce too much of kryptopyrrole, a by-product of hemoglobin synthesis. This kryptopyrrole binds to and depletes the body of vitamin B6 and zinc, two nutrients involved in the production of neurotransmitters and mood regulation. As such, deficiencies of these nutrients can eventually result in increased anxiety, cognitive issues, trouble sleeping, difficulties to concentrate and even nervous twitching. As you may have guessed, pyroluria is common in autism: it is estimated that 46 to 48% of children with autism also suffer from pyroluria [15].

9. Food Reactions As a nutritionist who has worked with children with autism for 15 years, I have seen food cause symptoms of anxiety. The food triggers vary from person to person based on their BioIndividual Nutrition needs and underlying factors. However, common offenders that

cause anxiety include gluten, casein (the protein in dairy products), soy and eggs. When foods are not tolerated, they can release endorphins or create inflammation that can trigger anxiety.

We have discussed how glutamate is excitatory and can stimulate the nervous system. In other words, foods containing glutamate, such as soy products, corn starch, corn syrup and products containing carrageenan can cause anxiety.

Foods containing a large amount of histamine and those that can trigger a release of histamine can also cause inflammation and anxiety. Histamine-rich foods include aged or fermented foods, cured meats, canned or smoked seafood, yogurt, citrus fruits, most berries, spinach, tomatoes and tomato-containing products, spices and artificial food colors and preservatives.

In addition to glutamate and histamine, salicylates can also cause anxiety. Examples of salicylate-rich foods include grapes, berries, apples, green bell peppers, canned mushrooms, red chili, chicory, apricots, herbs and spices. Almonds and peanuts are also rich in salicylates.

Finally, oxalates can also not only trigger inflammation but also are known to cause anxiety.

Diet and Nutrition Considerations

Diets that support good digestion such as gluten and grain-free diets can be very helpful to improve digestive capacity and reduce anxiety. Dietary strategies may include: a gluten-free and casein-free diet, a grain-free diet such as the Paleo diet, Specific Carbohydrate Diet or GAPS diet, low glutamate diet, low histamine diet, low salicylate diet, or a low oxalate diet. Below are some additional suggestions that can help reduce anxiety in children with autism:

- Keep blood sugar levels balanced – this can be achieved by including healthy fats (like grass-fed butter, grass-fed clarified butter, virgin coconut oil, or extra virgin olive oil) and healthy proteins (such as pasture-raised poultry, wild fish, organic eggs or grass-fed meats) in all your meals. Also

make sure to consume nutrient rich foods such as deep colored veggies.

- Steer clear of inflammatory foods such as wheat (and anything containing wheat), industrial seed oils (like canola, sunflower, safflower, or cottonseed oil) and soy products.
- Avoid artificial additives such as food dyes, artificial sweeteners, BHA/BHT, propyl gallate, potassium bromate, artificial nitrates and sulfites, propylene glycol, disodium inosinate and guanylate and MSG – these toxic ingredients can cause anxiety.
- Consider the need for a BioIndividual Nutrition approach where the diet is customized to the unique needs of the individual.
- Include probiotic rich foods to supply good bacteria. But be careful if you notice a negative reaction – these foods are high in glutamates and amines and can cause anxiety in some people.

Understanding someone's underlying biochemistry and SNPs (single nucleotide polymorphisms) can help determine proper supplementation needs. For example: folate and B12 are important for methylation; B6, zinc, magnesium to support transsulfuration and pyroluria, and magnesium for its calming effects.

I also strongly advise that you work with your doctor on any medical issues that may be underlying the anxiety, such as an autoimmune condition, or a clostridia infection or PANDAs, two infectious conditions that can cause agitation and anxiety.

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