

The Role of GABA in Health and Well-Being

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December 10, 2023

STORY AT-A-GLANCE

- › Most modern people live in constant fight-or-flight mode and find it hard to relax. GABA helps put you into parasympathetic mode, thereby promoting relaxation and stress reduction, indirectly
- › Glutamate is the primary excitatory neurotransmitter and GABA the main inhibitory neurotransmitter. These two are always working in conjunction with each other to maintain a balance. Glutamate converts into GABA in your brain. If you have trouble converting glutamate into GABA, you'll have excitatory-like symptoms, as the glutamate over-accumulates
- › Underlying factors that can prevent the efficient conversion of glutamate to GABA include a lack of cofactors (B6 and magnesium), and a lack of the enzyme glutamate decarboxylase, which is what converts the glutamate to GABA. Two common problems that inhibit the function of this enzyme are infections and chronic stress
- › Mentally, GABA deficiency is associated with anxiety, fear, depression, short temper, phobias, impulsiveness, disorganization, addictions, schizophrenia and OCD. IBS, diarrhea, hypertension, tinnitus, chronic pain, migraines, allergies, frequent urination, flushing, sweating, salt cravings and muscle tension are physical symptoms of GABA deficiency
- › Supplements that help raise GABA include N-nicotinoyl GABA or nanoliposomal varieties of GABA, kava, valerian root and cannabinoids such as CBD and CBG. Other ways to increase GABA include exercise, and things like meditation, mindfulness training, breathing exercises and yoga, which raise GABA by putting you in a parasympathetic state

In this interview, Dr. Scott Sherr, director of integrative hyperbaric medicine and health optimization at [Hyperbaric Medical Solutions](#), reviews the action of gamma aminobutyric acid (GABA) and the role it plays in your physical and mental health.

"I worked with people all over the world, and I worked with clinics all over the world, using hyperbaric therapy as the fulcrum or main focus point of what I do," Sherr explains.

"I then gravitated towards a colleague of mine who was working in a foundational approach to medicine called health optimization medicine and practice, which is an educational platform.

It's a nonprofit that's training doctors and practitioners, including myself, on how to optimize health. And from there I've kind of delved into multiple things, including neurotransmitter balancers like GABA."

Most modern people live in constant fight-or-flight mode and find it hard to relax. GABA helps put you into parasympathetic mode, which is why it helps promote relaxation and stress reduction. Indirectly, GABA can also aid detoxification because detoxification happens during parasympathetic mode.

Serotonin Is Not a 'Happy Hormone'

Most have heard of serotonin, dopamine, glutamate and norepinephrine, but they don't realize that GABA is a major player involved in 20% of your brain's neurotransmission.

Glutamate is the primary excitatory neurotransmitter and GABA the main inhibitory neurotransmitter. These two are always working in conjunction with each other to maintain a balance.

Serotonin is typically referred to as "the happiness hormone," and deficiency is thought to be the source of depression. That's why depression is routinely treated with selective serotonin reuptake inhibitors (SSRIs) that raise serotonin levels in your brain.

The problem is, serotonin is NOT responsible for depression, and raising your serotonin is the last thing you want to do. Elevated **serotonin** destroys empathy, love and wisdom, and impairs thyroid function, reduces metabolism, and contributes to reductive stress and insomnia.

Increasing GABA, on the other hand, can indeed be part of the solution for depression. Many who struggle with depression are GABA deficient, and augmenting the GABA system can in these instances make a big difference.

"GABA deficiencies are associated with so many things," Sherr says. "It's associated with anxiety, with fear, with depression, with a short temper, phobias, impulsiveness, disorganization, addictions. It's even associated with schizophrenia and OCD [obsessive-compulsive disorder]."

You can also have things like IBS and diarrhea, hypertension, tinnitus, chronic pain, migraines, allergies, frequent urination, flushing, sweating, salt cravings, muscle tension. These are all things that could be signs of GABA deficiency.

Many have been prescribed an SSRI for some of these symptoms, but it may not have been related to a serotonin deficiency. Actually, we know that depression is not related to serotonin deficiency. That's been well-studied over the last several years now."

Why GABA Is so Important for Mental Health

As explained by Sherr, GABA decreases the firing of neurons. When GABA binds to its receptor, it prevents that neuron from firing. So, it's what we would call a postsynaptic neuron. The presynaptic neuron fires and the postsynaptic neuron doesn't fire because GABA prevents it from doing so.

GABA also functions as an interneuron. An interneuron is a neuron located between other neurons, and it regulates the firing between the other neurons. Sherr explains:

"[Interneurons] are extremely important for learning, processing, memory and skill acquisition, because it's not about how much you can intake in your brain; it's how much you can stop that information from coming in so that your brain can actually process it, so you can learn and understand and have new memories and skill acquisition ...

So, if we can enhance and balance the GABA system, we can see a significant shift in the health of our patients and clients. I've been seeing this in real time, looking at the whole arc of GABA production, everything from the amino acid glutamine, which gets converted into glutamate in the brain.

Glutamate is your excitatory neurotransmitter. And then glutamate gets converted into GABA. GABA is made, for the most part, in the brain from glutamate. And you need the cofactors, vitamin B6 and magnesium to do it."

The conversion of glutamate to GABA only goes in one direction, so GABA doesn't convert back into glutamate. According to Sherr, if you have trouble converting glutamate into GABA, you'll have excitatory-like symptoms, as the glutamate overaccumulates.

Factors That Inhibit Glutamate's Conversion to GABA

Underlying factors that can prevent the efficient conversion of glutamate to GABA include:

- **A lack of cofactors** – B6 and magnesium.
- **A lack of the enzyme glutamate decarboxylase**, which is what converts the glutamate to GABA. Two common problems that inhibit the function of this enzyme are:
 - **Infection**, either acute or chronic.

- **Chronic stress causing cortisol and glucocorticoid elevations** – When your stress hormones are elevated, you're going to decrease the production of GABA.

The chronic stress angle is one of the reasons I quit low carb and intermittent fasting, as one of the side effects of those strategies is an increase in stress hormones, primarily epinephrine and cortisol. That said, Sherr points out that the ketogenic diet does increase GABA production. It's an effect related to the production of ketone bodies. So, there is some balance there.

The stress of fasting, however, could easily deplete your GABA reserves, depending on what those stores are to begin with. Eating too little can also affect your gut lining and cause problems via that route. I firmly believe that optimizing mitochondrial function with appropriate carb intake is the best way to increase GABA. Ideally you will also need about 0.7 grams of protein per pound of body weight. Sherr explains:

"[People who eat very little] might not be getting enough protein in the day, for example. As a result of that, they're not getting enough glutamine. Glutamine is an amino acid that's extremely important for the health of the gut lining.

If you have any leaky gut, for example, or stress in the gut with infection, or if you have a leaky brain, which is very common if you have a leaky gut, you're probably going to need significantly greater amounts of glutamine to convert to glutamate, because you're using all the glutamine for your colonic cells. It's the main fuel of your cells in the gut themselves. So, you have to be looking at the whole picture when you're thinking about this.

The other thing is that GABA supplements don't typically work because the molecule itself, GABA, is too big to get across the blood-brain barrier. However, if you have a leaky brain, they may work. So if you're taking GABA and it's working, it may be because you have a leaky brain, which sounds scary, but that just means that you have a leaky gut as well.

So, be aware that if you're trying to enhance the GABA system, you're going to be thinking about all the aspects of the biology – leaky gut, leaky brain,

glutamine production, glutamate conversion, cofactors.

And then if you're looking to enhance the GABA system, you have to be thinking about other things rather than just GABA itself. And there are many other ways to do that. There are herbals, there are even ways of attaching GABA to other things to help it get through the blood-brain barrier."

Does Oral GABA Work?

Now, there's ongoing debate as to whether oral supplementation with GABA works on brain-related issues as it's still unclear whether, and how well, GABA can cross the blood-brain-barrier (BBB). Studies looking into this matter have come to wildly differing conclusions.

For decades, the drug industry and mainstream medicine have spent a ton of money on questionable studies to "prove" GABA supplementation has no effects on the brain. This is understandable once you realize that many of the most popular anti-anxiety meds, such as benzodiazepines, are GABA agonists.

If you can just take a GABA supplement to treat your anxiety, depression and sleeplessness, the drug industry would suffer major losses. Interestingly, companies are now working on [alcohol replacement products based on GABA](#), so, the industry faces a tricky problem. If oral GABA can't cross the BBB, just how could a GABA-based synthetic alcohol produce alcohol-like effects in the brain? Sherr comments:

"Alcohol has a high affinity for the GABA receptor. This is where benzodiazepines, barbiturates and Quaaludes will also bind. Those are called allosteric binding sites of the GABA receptor. So, GABA binds to the receptor, and it's got all these other binding sites on the receptor where other things can bind.

So, alcohol and benzos and barbiturates bind very tightly to the GABA receptor, and when they do that, it enhances GABA production and GABA function. So you have more of the inhibition. So yes, this is how alcohol works.

Unfortunately, things like alcohol, benzos and barbiturates are highly addictive because they bind so tightly to the GABA receptor at their sites, and then they cause a conformational shift in the receptor themselves. So, if you go cold turkey off of those things, it could cause withdrawal and even death.

But there are other natural equivalents that are much safer. Things like kava, for example, have been known for thousands of years to affect the GABA receptor without causing any potential addiction, withdrawal or tolerance. Honokiol from magnolia bark is another one that binds to a receptor site outside of the GABA receptor itself but actually does the same thing.

It helps with enhancing GABA production. Valerian root is another one that increases GABA production in the brain, but it doesn't bind to the GABA receptor itself. It binds to these allosteric sites.

There's something called N-nicotinoyl GABA, which is vitamin B3 attached to a GABA molecule. Because it's attached to B3, it very easily gets through the blood brain barrier and then hydrolyzes vitamin B3 and GABA in the brain.

As a result of that, you have increased vitamin B3 in GABA directly. So that becomes a GABA agonist, also called an orthosteric ligand at the GABA receptor. So, you have other ways to modulate the receptor, even if you can't get GABA in directly.

Now, I have heard that nanoliposomal varieties will potentially work because they're attached in a fat molecule itself. And if you take very, very high doses of GABA directly, that may have an effect as well. But, at least clinically, if patients have a pretty good gut overall, they don't have any effect of the GABA supplements themselves.

Then, I give them vitamin B3 attached to GABA. If we give them these allosteric molecules like the ones I've just described, then they start having significant improvement. Then their anxiety and stress get better and they sleep better as well."

Cannabinoids such as CBD and CBG will also enhance the GABA system, as will THC, although it can produce a paradoxical response. "The reason some people who take THC will get a lot of anxiety is that it's doing something to the GABA receptor where you [end up having] less GABA to play around with. As a result of that, you get more excitatory anxiety and things like that," Sherr explains.

Other ways to increase GABA include exercise, which helps reset the balance between glutamate and GABA, and things like meditation, mindfulness training, breathing exercises and yoga. All these strategies put your body in a parasympathetic state, which increases GABA production.

The Importance of Carbon Dioxide

One of the reasons breath work is so helpful for resetting your sympathetic and parasympathetic balance has to do with carbon dioxide (CO₂), commonly misunderstood as nothing more than a harmful waste product of respiration. As it turns out, CO₂ has many important roles, including improving oxygenation and tolerance to stress. Sherr explains:

"I've been an oxygen guy for a decade, doing hyperbaric oxygen therapy and understanding how oxygen works. It wasn't until maybe two years ago, when I met a couple of colleagues in the breath space and the CO₂ retention space, that I truly started to understand that if I wanted oxygen to work better, I needed to understand how CO₂ was working.

Because, if you're hyperventilating, for example, you don't unbind oxygen from your red blood cells and you can't get it to your peripheral tissue because of how you shift your oxygen dissociation curve. The oxygen dissociation curve shifts depending on multiple different things.

Oxygen availability is one of them, CO₂ is another. The pH in the body will shift. I used to think about it as, 'Oh, we just make carbon dioxide and breathe it out.'

But CO2 has lots of other major effects, especially in the brain. It causes vasodilation, for example.

If you have too little CO2, you're going to constrict blood vessels, and if you're constricting blood vessels, you're going to have a challenge with getting oxygen to the tissues that need it.

So, the breath work that works on CO2 tolerance is really important, because that's going to shift your oxygen dissociation curve. As a result of that, you're going to have a better parasympathetic and sympathetic balance because you're going to be more tolerant to stress overall if you have more CO2 tolerance overall.

So, I think a part of what's going on with breath work and balancing out your sympathetic and parasympathetic nervous system is CO2 tolerance. By extension, I think GABA is playing a role as we have more parasympathetic balance around as well."

Most people think you need to breathe more — heavier and more quickly — to get more oxygen, but it's the exact opposite. Rapid deep breathing lowers your oxygen. Slow, shallow breathing allows CO2 to rise, which in turn allows more oxygen to be distributed. Nasal breathing is also important for improving your oxygen carrying capacity.

More Information

If you're intrigued by Sherr's approaches and want to learn more, be sure to check out his website, drscottsherr.com. To learn more about health optimization medicine, which focuses on optimizing cellular health, gut health and the effects of neurotransmitters like GABA, check out homehope.org. You can also connect with Sherr on [Instagram](#).