



# Magnesium Bisglycinate: The Science Behind Its Calming—and Sometimes Stimulating—Effects

Magnesium bisglycinate is a popular supplement praised for its ability to ease anxiety, improve sleep, and relax muscles. For most people, it's a game-changer. But for a small group, it has the opposite effect—leaving them feeling wired, restless, or even anxious. Why does this happen? The answer lies in a fascinating molecular tug-of-war between magnesium and glycine, two key players in your brain's chemistry. Let's dive into the science behind this “double agent” supplement and uncover why it works great for most—and backfires for others.

## How Magnesium Calms Your Brain

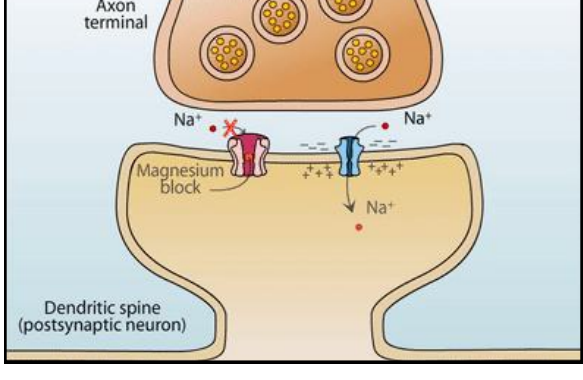
Magnesium is a multitasking mineral that's essential in your nervous system. Its calming effects come from two actions in your brain:

### Boosting GABA Activity

GABA (gamma-aminobutyric acid) is your brain's primary inhibitory neurotransmitter. Think of it as a “mute button” for overactive neurons that drive anxiety and your sleep cycle. Magnesium enhances GABA's effects by binding to GABA-A receptors, specifically at a site called the benzodiazepine-binding region. This binding changes the receptor's shape, making it more sensitive to GABA. In other words, magnesium turns up the volume on GABA's soothing whispers, helping you feel calm and relaxed.

### Blocking NMDA Receptors

NMDA receptors are glutamate-activated ion channels that play a key role in learning, memory, and pain signaling. When overactive, they can cause excitotoxicity—a kind of “brain burnout” that leads to stress and hyperactivity. Magnesium acts as a natural “circuit breaker” by sitting inside the NMDA receptor's channel, blocking it like a physical plug. This prevents calcium from flooding into neurons and keeps the brain from becoming overstimulated.



Note the magnesium clogging the red channel (NMDA). By doing this, glutamate can't go through the receptor, activate it, and allow that excitotoxicity to occur. Instead, by there being a decrease in glutamate, over-stimulation is prevented. This can contribute to relaxation when taking magnesium bisglycinate.



## Glycine's Dual Personality: Calm vs. Chaos

Glycine is the amino acid paired with magnesium in this supplement. Much like Jekyll and Hyde, it's a bit of a double agent, and has two distinct roles in your nervous system depending on where it's working:

### The Brake Pedal: Inhibitory Role in the Spinal Cord

In your spinal cord and brain stem, glycine acts as an inhibitory neurotransmitter. It binds to glycine receptors, which are chloride (Cl<sup>-</sup>) channels. When glycine activates these receptors, chloride ions flood into the neuron, making it more negatively charged (hyperpolarized) and harder to activate. This calming effect helps control reflexes and prevents overreactions—like pulling your hand away from a hot stove without flailing your entire body.

### The Ignition Key: Excitatory Role in the Brain

In your brain, glycine plays a completely different role. It acts as a co-agonist at NMDA receptors, meaning it's required for these receptors to function. NMDA receptors need two keys to unlock:

- **Glutamate:** Binds to the receptor's main site.
- **Glycine:** Binds to a separate “co-agonist” site (something called the GluN1 subunit). Without glycine, the NMDA receptor cannot open, even if glutamate is present. This makes glycine essential for processes like learning and memory.

## The Paradox: Why Glycine Can Overpower Magnesium

For most, magnesium's calming effects dominate. But in some cases, glycine's excitatory role can override magnesium's block and lead to over-stimulation that prevents relaxation and sleep. Here's how:

### Genetic Factors

**NMDA Receptor Mutations:** Variants in genes like GRIN2A can make NMDA receptors hypersensitive to glycine. Even small amounts of glycine might “force” the receptor open, despite magnesium's block ([Strehlow et al., 2019](#)).

**Glycine Transport Issues:** Mutations in SLC6A9, a gene that regulates glycine levels in the brain, can cause glycine to build up around NMDA receptors, overwhelming magnesium's calming effect. ([Kurolap et al., 2016](#))

### Epigenetic and Environmental Triggers

- **Chronic Stress:** Increases glutamate release and NMDA receptor density, making the brain more excitable. ([Popoli et al., 2011](#))
- **Inflammation:** Triggers oxidative stress, which may weaken magnesium's ability to block NMDA receptors ([Haroon, Miller, & Sanacora, 2016](#)).

In sensitive individuals, glycine essentially “picks the lock” on NMDA receptors, allowing glutamate to rush in and overstimulate the brain. This can lead to restlessness, insomnia, or even anxiety—despite magnesium's best efforts to keep things calm.



## The ADHD and Autism Connection: A Molecular Mismatch?

The relationship between magnesium bisglycinate and neurodevelopmental conditions like ADHD and Autism Spectrum Disorder is still being explored. Here's what we know so far:

### ADHD

Some studies suggest that ADHD brains have NMDA receptor hypofunction (underactivity), which might contribute to poor focus and impulsivity ([Kus et al., 2023](#)). In theory, glycine's ability to boost NMDA activity could help by improving signal clarity. However, no clinical trials have confirmed this yet.

### Autism Spectrum Disorder (ASD)

Some ASD subtypes involve NMDA receptor hyperfunction (overactivity), which can cause sensory overload and hypersensitivity ([Nisar et al., 2022](#)). For these individuals, glycine's excitatory role might worsen symptoms by further revving up NMDA receptors. Again, this is speculative—there's no direct evidence linking magnesium bisglycinate to autism symptom flares.

## What to Do If You or Your Child are Sensitive to Magnesium Bisglycinate

*If you've tried magnesium bisglycinate and found it overstimulating, don't worry—there are plenty of alternatives:*

### 1. Switch Forms

- Try magnesium citrate or magnesium threonate, which don't contain glycine.
- Magnesium threonate is particularly effective for brain health, as it crosses the blood-brain barrier efficiently.

### 2. Adjust Timing

- Take magnesium bisglycinate in the morning to avoid nighttime overstimulation.

### 3. Test Your Genes

- Services like Nutrigenomix can check for genetic variants in GRIN2A or SLC6A9 that might make you more sensitive to glycine.

Visit our [website](#) to learn more!