

# Riboflavin for Migraine Prevention

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✓ Fact Checked

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## STORY AT-A-GLANCE

- › While the exact mechanisms behind migraines remain unclear, a number of different hypotheses have been raised. It appears to be a disorder of your central nervous system. Mitochondrial dysfunction also appears to be part of the puzzle
- › The influence of neurotransmitters may also play a role, as may nutritional deficiencies. Studies have identified several nutritional deficiencies that significantly raise your risk of migraines, including riboflavin (vitamin B2) deficiency
- › Riboflavin has been shown to ameliorate hallmarks of migraine, including oxidative stress, mitochondrial dysfunction, neuroinflammation, homocysteine neurotoxicity and glutamate excitotoxicity
- › Foods rich in riboflavin include spinach, beet greens, crimini and portabella mushrooms, pastured eggs, asparagus, almonds, organic turkey, grass fed beef liver and beef tenderloin
- › In one study, 400 milligrams of riboflavin per day reduced migraine frequency by 50%, from four days a month to two days a month, after three months of use

Migraine affects an estimated 1 billion people worldwide, and is the third most common disease globally.<sup>1</sup> In the U.S., self-reported migraine and severe headache affects 1 in 6<sup>2</sup> Women are up to three times more likely to suffer with migraines than men, likely due to hormone fluctuations.<sup>3</sup>

Despite its high prevalence, decades of research have failed to pin down the exact mechanisms behind the attacks – most of which tend to recur once or twice a month.<sup>4</sup> The pain, which often occurs on one side of the head only, can be moderate to severe in intensity.

Along with throbbing, piercing or "burning" pain, other common symptoms include nausea, visual disturbances, dizziness, numbness in your extremities or face, and extreme sensitivity to light, sound, smell and touch.<sup>5</sup> Attacks typically last from four hours to three days,<sup>6</sup> often requiring bed rest in complete darkness and silence.

## Reigning Migraine Hypotheses

While the exact mechanisms remain unclear, a number of different hypotheses have been raised. Over the last decade or two, researchers have started leaning toward migraine being a disorder of your central nervous system, most likely originating in your brain stem.<sup>7,8,9,10</sup> While most brain regions do not register or transmit pain signals, the trigeminal nerve network does.

Pain is relayed through the trigeminal network to an area in your brain stem called the trigeminal nucleus. From there, it is conveyed to the sensory cortex in your brain that is involved in awareness of pain and other senses. As explained by [Migrainedisorders.com](http://Migrainedisorders.com):<sup>11</sup>

*"[P]eople with migraine illness have a nervous system that is not working normally. It overreacts ... when stimulated, there is an unusual wave of brain activity that leads to a headache.*

*Almost all migraine sufferers have a problem with a specific part of the nervous system, called the trigeminal nerve. The trigeminal nerve is a network of wiring that attaches to special sensors.*

*When stimulated, they send electrical signals to the brainstem with connections to nerves of the cortex and its covering, the dura. Normally this system allows us know what is going on in the world. When the system does not work properly,*

*electrical signals set off a slowly moving wave of electrochemical activity across the surface of the brain.*

*People with migraine start to experience odd sensations, such as white sparks in an eye (a misfiring of the ocular nerve) followed by an intense pain in some part of the head and concluding with a long period of nausea (activation of the gastrointestinal system) and exhaustion (general inflammation and swelling of the cortex)."*

The initial activation of your trigeminal nerve is thought to be triggered by a variety of internal and external stimuli, ranging from stress, hormone fluctuations and irregular sleep to a variety of foods, flashing lights, noise and weather changes.<sup>12</sup>

Still, migraines can sometimes occur even in the absence of an apparent trigger, suggesting we still don't have a complete picture of the phenomenon. Mitochondrial dysfunction also appears to be part of the puzzle. As noted in one 2013 paper:<sup>13</sup>

*"Abnormal [mitochondrial] function translates into high intracellular penetration of Ca(2+), excessive production of free radicals, and deficient oxidative phosphorylation, which ultimately causes energy failure in neurons and astrocytes, thus triggering migraine mechanisms."*

The influence of neurotransmitters such as calcitonin gene-related peptide (CGRP)<sup>14,15</sup> may also play a role, as may nutritional deficiencies. At the very least, studies have identified nutritional deficiencies that significantly raise your risk of migraines. Among them is riboflavin (vitamin B2).

## **Riboflavin Deficiency Linked to Migraine**

A paper,<sup>16</sup> published in *Frontiers in Neurology* in 2017 looked at riboflavin's influence on migraine and Parkinson's disease, highlighting its neuroprotective potential.

According to this paper, "riboflavin ameliorates oxidative stress, mitochondrial dysfunction, neuroinflammation and glutamate excitotoxicity; all of which take part in

the pathogenesis of PD, migraine headache and other neurological disorders."

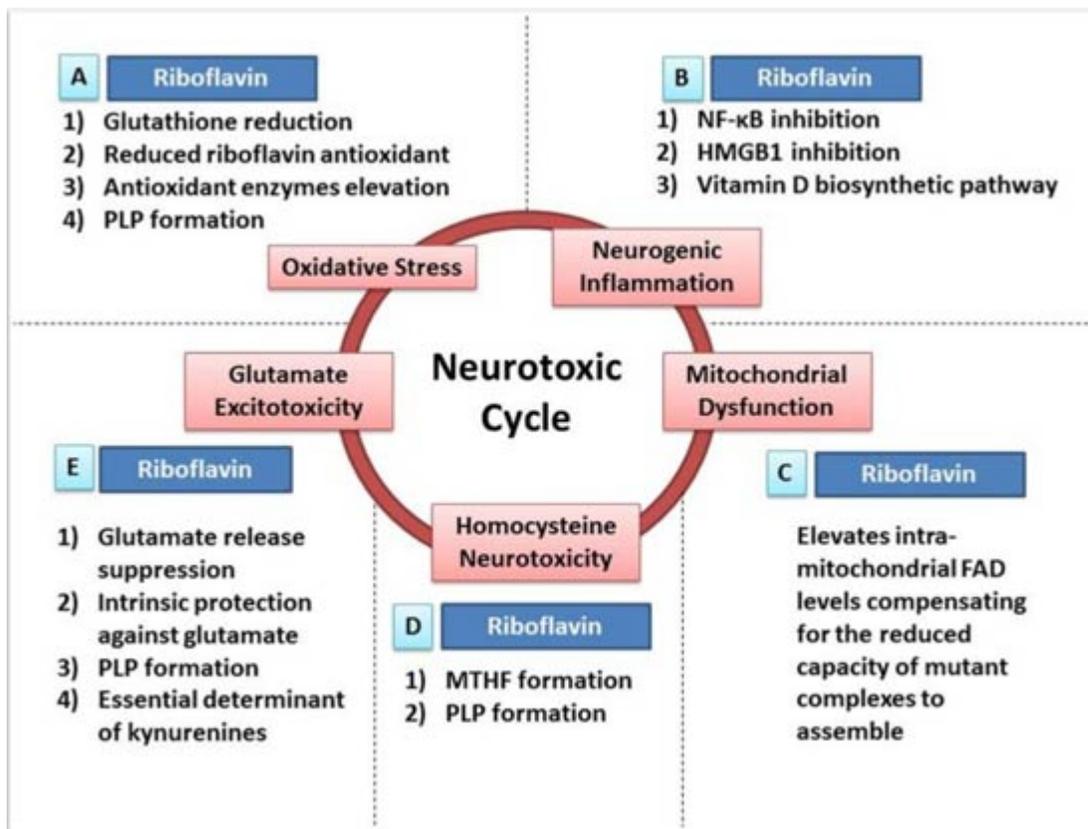
Here, the authors link migraine pain to neurovascular dysfunction, inflammation and "dysfunction in cranial vascular contractility," and cite research showing people who have migraine with aura have lower levels of antioxidants and higher levels of oxidative stress than migraine-free controls.

They've also been shown to have higher levels of mitochondrial dysfunction, and at least two polymorphisms in mitochondrial DNA have been shown to heighten migraine susceptibility. The authors also note that:<sup>17</sup>

*"[C]ommon triggers of migraine have the ability to generate oxidative stress; mechanisms include mitochondrial dysfunction, calcium excitotoxicity, activation of microglia, activation of NADPH oxidase, and as a byproduct of MAO (monoamine oxidase), cytochrome P450, or NO synthase. Collectively, it is indicated that oxidative stress is an important hallmark of migraine disease."*

Riboflavin may help by ameliorating many of the hallmarks of migraine, including oxidative stress, mitochondrial dysfunction, neuroinflammation, homocysteine neurotoxicity and glutamate excitotoxicity, as shown below.<sup>18</sup>

The paper goes into some detail, explaining the biochemical influence of riboflavin on all of these, so for a more comprehensive understanding, I'd suggest reading through the original paper.



Source: [Frontiers in Neurology 2017; 8: 333, Figure 1](#)

## Are You Getting Enough Riboflavin?

In conclusion, the authors of this *Frontiers in Neurology* paper note that:<sup>19</sup>

*"Riboflavin has demonstrated its ability to tackle significant pathogenesis-related mechanisms in neurological disorders, exemplified by the ones attributed to the pathogenesis of ... migraine ... In addition, riboflavin is required for pyridoxine activation.*

*Riboflavin and PLP, the active form of pyridoxine, play essential roles in homocysteine metabolism, and tryptophan-kynurenine pathway. Indeed, any accumulation of homocysteine or kynurenines due to vitamin insufficiency can lead to significant neurological consequences.*

*Taking into consideration the limited riboflavin absorption and utilization in 10–15% of global population, long term riboflavin insufficiency could participate in the development of multiple neurological disorders, emphasizing the*

*importance of long-term riboflavin-sufficient diet especially in vulnerable populations."*

Since riboflavin is a water-soluble B vitamin, you need to get a consistent supply from your diet. Foods rich in riboflavin include:<sup>20</sup>

<b>Spinach</b>	<b>Beet greens</b>
Tempeh	Crimini and portabella mushrooms
Pastured eggs	<b>Asparagus</b>
<b>Almonds</b>	Organic turkey
Grass fed beef liver	Grass fed beef tenderloin

## Identifying Riboflavin Deficiency, and Dosing Suggestions

While riboflavin deficiency is thought to be rare in the U.S., older adults, women on birth control pills, alcoholics, pregnant and lactating women, vegans and those with liver disorders are at increased risk for deficiency.<sup>21</sup> Common signs and symptoms of deficiency include:<sup>22</sup>

Fatigue	Swollen throat	Blurred vision
Depression	Itchy or cracking skin	Dermatitis around the mouth
Liver degeneration	Hair loss	Reproductive problems

Urine analysis can identify a riboflavin deficiency. As a general rule, deficiency is said to be present if your urinary riboflavin is below 40 micrograms per day.<sup>23</sup> The

recommended daily intake is 1.3 milligrams for adult men, 1.1 mg for adult women, 1.3 mg for male adolescents (14 to 18 years of age) and 1.0 mg for female adolescents.<sup>24</sup>

If you struggle with migraines, however, you may need far higher doses. As noted in a study published in the European Journal of Neurology in 2004, researchers found 400 mg of riboflavin per day reduced migraine frequency by 50%, from four days a month to two days a month, after three months of use. The duration and intensity remained largely unaffected, however.<sup>25</sup>

## Other Vitamin Deficiencies Implicated in Migraines

Aside from riboflavin, other nutrients deficiencies that have been implicated in migraines include:

- **Vitamins B6, B12 and folic acid** — One 2009 study<sup>26</sup> evaluated the effect of 2 mg of folic acid, 25 mg vitamin B6 and 400 mcg of vitamin B12 in 52 patients diagnosed with migraine with aura. Compared to the placebo group, those receiving these supplements experienced a 50% reduction in the prevalence of migraine disability (from 60% to 30%) over a six-month period.
- **Magnesium** — Magnesium has also been shown to play an important role in the prevention and treatment of migraines, and migraine sufferers are more likely to suffer from magnesium deficiency than non-migraineurs.<sup>27</sup>

Since magnesium administration is both easy and safe, researchers have noted that empiric treatment with a magnesium supplement is justified for all migraine sufferers.<sup>28</sup> As a prophylactic, be prepared to boost your magnesium intake for at least three months to experience results, ideally in combination with CoQ10.

In many cases, receiving a high dose of magnesium can also abort an attack in progress. The most effective way to administer magnesium for migraine would be to get an intravenous (IV) infusion. I used to regularly administer magnesium IVs for those with acute migraines and it seemed to work for most patients to abort the headache.

Barring that option, magnesium threonate may be your best option for an oral supplement. It has superior absorbability compared to other forms of magnesium, and since its ability to cross the blood-brain barrier makes it more likely to have a beneficial effect on your brain.

Foods rich in magnesium<sup>29</sup> include: almonds and cashews, boiled spinach, peanut butter, avocado, potato, brown rice, banana, wild Alaskan salmon and yogurt made from organic grass fed milk with no added sugars, just to name a few.

- **Coenzyme Q10 (CoQ10)** – A migraine study<sup>30,31,32</sup> presented at the annual American Headache Society meeting in 2016, which involved 7,420 children, teens and young adults, found 51% had low levels of CoQ10, 31% had low vitamin D status and 16% had low levels of riboflavin.

Those suffering from chronic migraines were overall more likely to have CoQ10 and riboflavin deficiency compared to those with episodic migraines. While the final study results do not appear to have been published yet, other research have found similar links.

For example, a 2015 study<sup>33</sup> in The Journal of Headache and Pain found supplementation with a proprietary combination of magnesium, riboflavin and CoQ10 for three months lowered migraine frequency from 6.2 days at baseline to 4.4 days at three months. Pain intensity was also significantly reduced. Foods rich in CoQ10<sup>34</sup> include: grass fed beef, herring, organic pastured chicken, sesame seeds, broccoli and cauliflower.

- **Vitamin D** – While many studies appear to refute a link between low vitamin D and migraine, there have been some showing vitamin D may play a role. For example, migraine research using vitamin D supplementation has demonstrated a reduction in C-reactive protein (a marker for inflammation) and a statistically significant reduction in migraine frequency.<sup>35</sup>

Another study<sup>36</sup> by Finnish researchers, while not focused on migraines specifically, found men with the lowest vitamin D levels had 113% higher odds for frequent

headaches than those with the highest levels. Overall, the lower the men's blood level of vitamin D, the more frequent their headaches.

A 2013 study<sup>37</sup> looking at the relationship between vitamin D levels and migraine found a weak but positive relationship in terms of frequency, but not in terms of severity. The best way to optimize your vitamin D level is through regular sun exposure. If taking an oral supplement, be sure to use vitamin D3 (not D2), along with magnesium, vitamin K2 and calcium.

## Migraine Prevention 101

When it comes to migraines, your best bet is to take preventive action, as treating migraines acutely is very difficult. Migraine medications often do not work, and can have serious side effects.<sup>38</sup>

Your first step would be to identify and avoid potential triggers. While there are many (and what triggers a migraine for one might not trigger it in another), the list below includes some of the most common culprits. Keeping a journal where you record and track suspected triggers can help you determine any correlations.

**Food and drink** — Especially wheat and gluten, dairy, cane sugar, yeast, corn, citrus, eggs, artificial preservatives or chemical additives, cured or processed meats, alcohol (especially red wine and beer), aspartame, caffeine and MSG.<sup>39</sup>

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**Allergies** — Including food allergies,<sup>40</sup> food sensitivities and chemical sensitivities. Research<sup>41</sup> published in the journal *Lancet* back in 1979 showed migraineurs with food antigen immunoreactivity experienced profound relief when put on an elimination diet.

Another randomized, double-blind crossover study<sup>42</sup> published in 2010 found that a six-week-long diet restriction produced a statistically significant reduction in migraines in those diagnosed with migraine without aura.

If you suspect you might have a food allergy, I suggest doing a diet elimination challenge to see if your symptoms improve. Keep in mind that depending on your typical migraine frequency, you may need to avoid the suspected food for a few weeks in order to evaluate whether it had an effect or not.

To confirm the results, reintroduce the food or drink on an empty stomach. If the suspected food is the culprit, you will generally be able to feel the symptoms return within an hour, although migraines can sometimes have a longer lag time than, say, bloating or drowsiness.

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**Hormones** – Some women experience migraines before or during their periods, during pregnancy or during menopause. Others may get migraines from hormonal medications like birth control pills or hormone replacement therapy.

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**Light, noise and smells** – Bright lights, fluorescent lights, loud noises and strong smells (even pleasant ones) can trigger and/or exacerbate a migraine. A study<sup>43,44</sup> from Harvard Medical School found even blind migraine sufferers who still had melanopsin receptors were sensitive to light.

Blue light in particular can be problematic. Many digital devices and LED light sources emit mostly blue light. Research has found that this light increases migraine pain and activates your trigeminal nerve, associated with the pain of migraines.<sup>45</sup> Meanwhile, green light may help ease migraine pain and photosensitivity.<sup>46,47</sup>

At this time there are no lightbulbs or sunglasses that increase your exposure to pure wavelength green light that are cost effective. However, there are orange or red-tinted glasses that will block blue light, which may be helpful. You may also consider eliminating your exposure to your digital devices while you're in the middle of a migraine.

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**Changes in sleep cycle** – This includes both missing sleep and oversleeping.

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**Stress** – Any kind of stress or emotional trauma can trigger a migraine, even after the stress has passed.

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**Dehydration and/or hunger** – Skipping meals or fasting are also common triggers.

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**Physical overexertion** – Extremely intense exercise, and even sex, has been known to bring on migraines.

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**Weather changes, and/or changes in altitude**

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