

# Choline - Can it Relieve Pain?

## HIGHLIGHTS

- › Boosting choline, a precursor for acetylcholine, may be an important part of pain relief, but an estimated 90% of the U.S. population is deficient
- › Researchers from the University of Chicago revealed that targeting an acetylcholine receptor led to pain-relieving effects in mice, even in animals that were tolerant to opioids
- › The pathway did not activate the brain's reward system, so there's little chance of addiction, and there was no tolerance built up or withdrawal symptoms when the treatment stopped
- › Choline plays a significant role in human health, from neurotransmitter synthesis to cell structures, and may be involved in the development of nonalcoholic fatty liver disease (NAFLD), atherosclerosis and neurological disorders
- › Krill oil and eggs, particularly the yolks, are excellent choline sources

The neurotransmitter acetylcholine may be an untapped pathway for pain relief that doesn't involve dangerous drugs like opioids. Researchers from the University of Chicago revealed that targeting an acetylcholine receptor led to pain-relieving effects in mice, even in animals that were tolerant to opioids.

The pain relief was powerful enough to rival that from opioids, but without the negative effects. The pathway did not activate the brain's reward system, so there's little chance of addiction, and there was no tolerance built up or withdrawal symptoms when the

treatment stopped. Boosting choline, a precursor for acetylcholine, may therefore be an important part of pain relief, but many in the U.S. are deficient.

## **How Acetylcholine May Relieve Pain**

Acetylcholine is an excitatory neurotransmitter that excites nerve cells, triggering it to send a message. A 2011 study revealed that acetylcholine decreased activity of pain-excited neurons and increased the activity of pain-inhibited neurons in the cornu ammonis region of the hippocampus.

The University of Chicago study specifically involved an area of the brain called the ventrolateral periaqueductal gray (vlPAG), a “critical nexus” for systems involved in pain control.

In 2017, the study’s senior author, Daniel McGehee, Ph.D., and colleagues found that targeting alpha-7 ( $\alpha 7$ ), an acetylcholine receptor in the vlPAG, relieved pain. While this receptor typically increases nervous system activity, when it was stimulated in the study it led to a quiet state that resulted in pain relief for several hours. McGehee said in a University of Chicago news release:

*“That was a huge and extremely unexpected outcome. Persistent inhibition was not on our radar at all. It was always a conundrum to me, but we saw that there is recruitment of another signaling pathway that is altering potassium channel function and causing these cells to shut down.”*

Fortunately, the acetylcholine receptor involves a different pathway from opioids. So when the team boosted acetylcholine in opioid-tolerant mice, the same pain-relieving effects were seen. Study author Shivang Sullere, Ph.D. explains:

*“Not only do these cells relieve pain, they also accurately mirror the pain state of the organism. Through imaging methods, we can reproducibly monitor these neurons and acetylcholine in the vlPAG. This provides us a valuable biomarker for the pain state of an organism.”*

*This unexplored role of acetylcholine also points towards its potential involvement in the central sensitization processes that contribute to the development of chronic pain conditions. Modifying acetylcholine signaling provides an opportunity to relieve pain and prevent the establishment of the chronic pain state.”*

## **Why Do You Need Choline?**

Choline was identified in 1862 and officially recognized as an essential nutrient by the Institute of Medicine in 1998. It plays a significant role in human health, from neurotransmitter synthesis to cell structures, and has a large impact on the development of nonalcoholic fatty liver disease (NAFLD), atherosclerosis and neurological disorders.

During development, choline supports healthy development of the brain and may help reduce the risk of neural tube defects. In older adults, it's also important. In one study, 77% of men and 80% of postmenopausal women who were deprived of dietary choline developed signs of subclinical organ dysfunction, including fatty liver and muscle damage. The dysfunction resolved when the participants consumed a high-choline diet.

While your body can produce some choline in the liver, it's not enough to meet human needs. There's also an interrelationship between folate and choline deficiencies, as both are methyl donors. When the diet is deficient in folate, choline becomes the primary methyl donor, creating greater insufficiency or deficiency of the nutrient.

As a precursor for acetylcholine, choline increases acetylcholine release, which plays a role in many body functions, including muscle control, memory and circadian rhythm. Other important functions of choline in the body include:

- Synthesis of phospholipids needed for cell membranes, including phosphatidylcholine and sphingomyelin
- Modulating gene expression

- Cell membrane signaling
- Fat transport and metabolism – Choline is needed to carry cholesterol from your liver, and a choline deficiency could result in excess fat and cholesterol buildup
- Early brain development

Choline may also help prevent cardiovascular disease by converting homocysteine to methionine. Homocysteine is an amino acid that may increase your risk for heart disease and stroke if it accumulates in the blood. Choline is also important for healthy mitochondrial function<sup>18</sup> as well as mental health. Choline deficiency may lead to abnormal fat deposits in your liver, causing NAFLD.

Further, low choline intake is associated with increased anxiety, while high dietary choline is linked to better cognitive performance. Meanwhile, choline deficiency is linked with DNA damage and apoptosis, and breast cancer risk may be reduced by 24% among women who eat a high-choline diet.<sup>21</sup> Low levels of acetylcholine are also linked to Alzheimer's disease. According to the National Institutes of Health:

*“Cholinergic neurons use the neurotransmitter acetylcholine, and Alzheimer's disease is often treated by increasing acetylcholine levels or preventing its breakdown.”*

## **There's a Good Chance You're Choline-Deficient**

An estimated 90% of the U.S. population is deficient in choline, and, according to a study published in the journal *Nutrients*, only 8% of U.S. adults (including only 8.5% of pregnant women) are getting enough on a daily basis. The amount of choline you need depends on your age, sex and whether or not you're pregnant or nursing. Generally, the recommended intake is 425 milligrams (mg) a day for women and 550 mg/day for men.

Pregnant and nursing women require more choline – from 450 mg to 550 mg a day – and some people have genetic polymorphisms that increase the need for choline.

Certain ethnic and racial groups are more likely to be affected. In addition to pregnant and lactating women, groups at especially high risk for choline deficiency include:

- **Endurance athletes** – Endurance exercises, like marathons and triathlons, can deplete choline levels. Studies show that supplementing with choline before these types of stressful exercises can help keep levels of choline in the blood from getting too low.
- **People who drink a lot of alcohol** – Excess alcohol consumption can increase your need for more choline while simultaneously increasing your risk of deficiency.
- **Postmenopausal women** – Postmenopausal women have lower estrogen concentrations, which can increase the risk of organ dysfunction in response to a low-choline diet.
- **Vegetarians and vegans** – Animal foods like beef liver, eggs and krill oil are the highest sources of dietary choline. Because vegetarians and vegans have dietary restrictions that eliminate some or all of these choline-rich foods, it can be more difficult to get an adequate amount of the nutrient through diet alone.

## The Best Sources of Choline

Eggs, particularly the yolks, are an excellent choline source. Among egg consumers, more than 57.3% met the adequate intake levels for choline, compared to just 2.4% of people who consumed no eggs. In fact, the researchers concluded that it's “extremely difficult” to get enough choline unless you eat eggs or take a dietary supplement. Other dietary sources of choline include:

Grass fed beef liver	Cauliflower	Atlantic cod
Alaskan salmon	Kidney beans	Quinoa
Brussels sprouts	Broccoli	Shiitake mushroom

Krill oil, however, may be an ideal choline source. It contains 69 choline-containing phospholipids to synthesize phosphatidylcholine, a critical component of human cell membranes. This is key to its benefits as a source of choline, because it's estimated that 60% of choline in organic salts is otherwise lost when gut bacteria convert it to the metabolite trimethylamine (TMA).

Enzymes may then turn TMA into trimethylamine-N-oxide (TMAO), a potential biomarker for insulin resistance and heart problems. But krill oil contains fatty acids in the form of phosphatidylcholine (PC) – unlike fish oil, which contains them in triglyceride form.

As noted by the researchers, “Choline in the form of PC is considerably less converted to TMA as demonstrated in a single-dose study with krill oil, potentially resulting in more efficient delivery of choline.” It's been shown for instance, that 28 days of krill oil supplementation increased choline levels in healthy young adults.

Further, in a study comparing phosphatidylcholine, present in krill oil, and choline bitartrate salt, it was found that the krill oil led to higher levels of the important metabolites betaine and dimethylglycine (DMG) along with lower levels of TMAO, which can lead to health issues, compared to the other choline source. Researchers explained:

*“Krill oil is increasingly recognized as a useful source of phosphatidylcholine, in addition to its acknowledged role in providing the omega-3 fatty acids EPA and DHA. In a former study, phosphatidylcholine was shown to raise plasma choline levels more efficiently compared to ingestion of free choline as choline chloride.”*

## **More Help for the Pain Epidemic**

About 21% of U.S. adults are suffering from chronic pain, with new cases occurring more often than new cases of other common conditions like diabetes, depression and high blood pressure. If you're among them, seek out natural options first before resorting to drugs.

The solution you need depends on the underlying cause of your chronic pain. Back pain, for instance, typically responds well to exercises, chiropractic adjustments, acupuncture and massage. Often, addressing the emotional component of your pain using tools like the Emotional Freedom Techniques is also helpful.

In addition to adding more choline-rich foods to your diet, other foods can also support pain control by lowering the inflammatory response and improving your gut health. Ginger is often used as a pain reliever for low back pain, osteoarthritis, migraines and delayed onset muscle soreness.

Increasing your intake of animal-based omega-3 fats may also reduce pain, including that associated with rheumatoid arthritis and inflammatory bowel disease.

Ultraprocessed foods, on the other hand, are inflammatory and may contribute to chronic pain conditions. In animal studies, they've been found to increase the excitability of muscle nerves, increasing the likelihood of muscle pain

Other natural pain relief options include hypnotherapy, music therapy and use of hot or cold packs. Even taking a swim in cold water offers effective relief from chronic pain in some cases. You'll want to get regular high-quality sleep as well, as lack of sleep and poor sleep quality are closely linked to chronic pain.

Often, it's possible to relieve pain effectively using a combination of these and other lifestyle strategies. But if not, seek the help of a holistic health care provider who can help guide you on a path toward healing. Opioids should be a last resort and are not always necessary to treat even moderate to severe pain. Ibuprofen and acetaminophen (which do have their own set of risks) may work just as well.

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