

Mitochondrial Enhancers for ME/CFS and Fibromyalgia Pt II: L-carnitine and Acetylcarnitine

by Cort Johnson | May 10, 2021 | Alternative Health, Energy Enhancers, L-carnitine/Acetylcarnitine, Supplements | 38 comments



The Mitochondrial Enhancers for Chronic Fatigue Syndrome (ME/CFS), Fibromyalgia (FM), and long COVID Series

This is the second part in a series on mitochondrial enhancers for chronic fatigue syndrome (ME/CFS), fibromyalgia (FM) and long COVID series. The series uses the book “[Mitochondria and the Future of Medicine](#)”, by [Lee Know](#), a former naturopathic doctor in Canada, as a starting point, and includes insights from ME/CFS/FM practitioners.

- [Pt I: D-Ribose, CoQ10 and PQQ](#)
- [Pt II: L-carnitine and Acetylcarnitine](#)
- [Pt. III: Magnesium](#)
- [Pt IV: N-acetyl cysteine \(NAC\)](#)
- [Pt V: Oxaloacetate](#)
- [Pt. VI: Niacin, Niacinamide and Nicotinic Riboside](#)

Now the series turns to two interesting supplements that play vital roles in energy production: L-carnitine and acetylcarnitine.

L-carnitine and Acetylcarnitine

Several [different forms of carnitine](#) exist. While one form – L-carnitine L-tartrate – might be helpful in reducing muscle soreness and enhancing recovery after exercise, this review mostly focusses on L-carnitine and acetylcarnitine (also known as acetyl-L-carnitine).

L-carnitine

[L-carnitine](#) and acetylcarnitine (ALCAR) are similar but different. While [Self-hacked](#) reports that both can help with fatigue, L-carnitine is the bigger energy enhancer. It helps the [body convert fat into](#)

energy by transporting fatty acids to the mitochondria, and has strong antioxidant properties as well.

According to Know, low L-carnitine levels inevitably result in reduced fatty acid metabolism. That's important because our mitochondria love fatty acids: 60-70 percent of the energy produced by our mitochondria comes from metabolizing fatty acids. L-carnitine, also, interestingly enough, helps to mop up lactate – a byproduct of anaerobic metabolism – which may be causing a lot of trouble in ME/CFS/FM.

Weight-lifters and other athletes latched onto L-carnitine early and the study results have been good. A 9-week placebo-controlled, **double-blinded 2019** study of weight lifters found increases in peak power, antioxidant levels and reduced lactate levels. A quickie study found it **improved antioxidant levels** 1 hour after exercise – an interesting finding, as Nancy Klimas has reported that exercise triggers an unusually large burst of free radicals in ME/CFS. (Plus, **oxidative stress** appears to be high even at rest in ME/CFS). Another study found that supplementing **L-carnitine with choline** reduced oxidative stress after walking in women.

Fielding believes **L-carnitine may be increasing blood flows** and oxygen supply to the muscles – two other subjects of interest in ME/CFS.. One study, interestingly, given **the interest in ammonia in ME/CFS**, found **L-carnitine may** be able to reduce ammonia production during exercise.

Acetylcarnitine

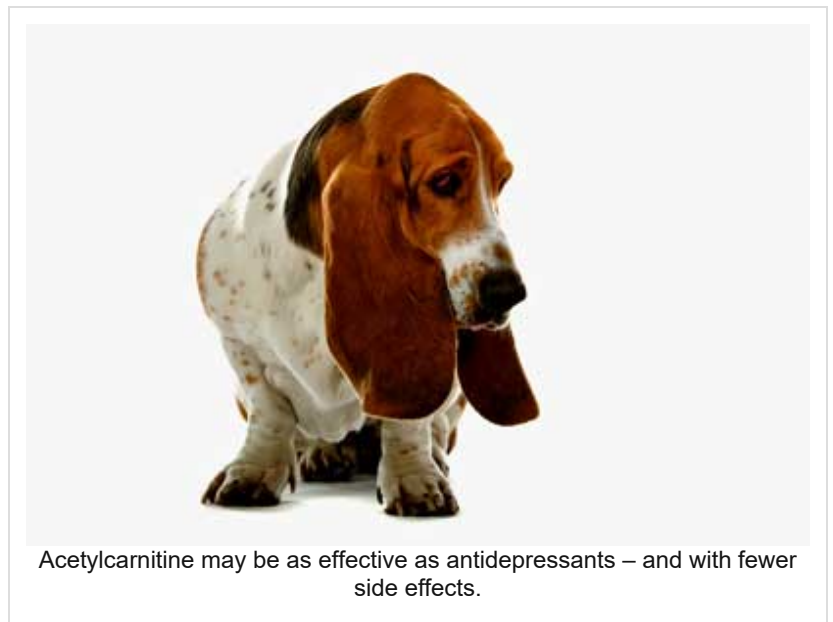
Acetylcarnitine (or acetyl-L-carnitine, ALCAR, LAC, LCAR or a number of other acronyms and names), on the other hand, boosts acetylcholine and is able to get through **the blood-brain barrier**. It appears to be more effective at improving mental clarity, reducing mental fatigue, improving mood and protecting the neurons in the brain.

An Antidote for Depression?

Acetylcarnitine is also being enthusiastically studied in depression. A 2018 two-center study (as well as other studies) have found **decreased acetylcarnitine (LAC)** levels in the brains of people with depression. The more severe the depression, the greater the LAC reductions. Greater LAC reductions were also found in women who had experienced childhood trauma.

The authors reported that LAC supplementation “*induces rapid and lasting antidepressant-like effects via epigenetic mechanisms*” which dampen down the release of the excitatory neurotransmitter glutamate.

One of the few meta-analyses I've read that uncategorically reported a positive outcome stated that **acetylcarnitine was as effective as antidepressants** and had fewer adverse effects:



“Acetyl-L-supplementation significantly decreases depressive symptoms compared with placebo/no intervention, while offering a comparable effect with that of established antidepressant agents with fewer adverse effects.”

Help for Neurological Disorders

Both L-carnitine and acetylcarnitine are also being studied in neurological disorders. A [literature review](#) reported that both substances are being studied for Alzheimer’s disease, depression, neuropathic pain, bipolar disorder, Parkinson’s disease and epilepsy in the elderly.

Besides the impact these substances may have on metabolism and energy production, the authors mentioned their ability to eliminate ammonia – which is, again, of interest in ME/CFS.

They stated that “*ammonia and energy depletion seem to underlie most of the neurotoxic events*” and concluded that acetylcarnitine “*emerges as a simple, economical and safe adjuvant option in order to impair the progression of most neurological disorders.*”

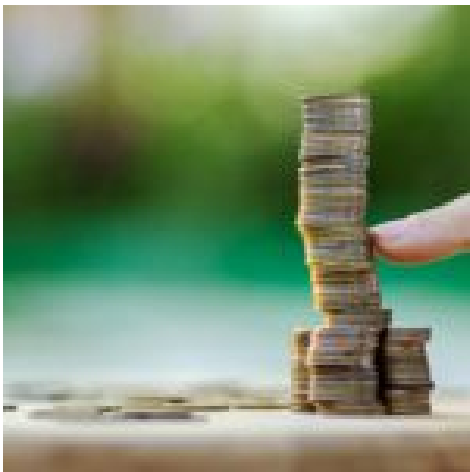
[RxList reports that acetyl-L-carnitine](#) is being used in a staggeringly wide variety of conditions ranging from Alzheimer’s to Lyme disease, to alcohol withdrawal, to multiple sclerosis and others. The website states that the evidence indicates that acetylcarnitine is possibly effective for improving memory problems, tiredness, testosterone deficiency, poor blood flows to the brain, reducing nerve pain, etc.

L-Carnitine Tartrate

To make matters a little more confusing, there’s also L-carnitine tartrate (LCLT), which [a 2013 blog](#) called a “new more promising form of carnitine”.

LCLT appears to be a somewhat pumped up form of L-carnitine. It’s reported to enhance fat metabolism, increase testosterone uptake into the muscles, reduce oxidative stress and improve lipid metabolism and energy production. It’s also most commonly used for its potent fat burning effects; i.e. apparently to leave one looking sleeker.

One site recommended taking LCLT with carbohydrates because of its possibly favorable impact on insulin.



Health Rising's End of the Year Fundraising Drive

If getting the latest news on cutting-edge research and treatments in ME/CFS, fibromyalgia, long COVID, and related diseases supports you, please support Health Rising in it's end of the year fundraising drive. We are entirely community supported.

Paypal, checks, Amazon gift cards, and bitcoin work for us.

Use the widget on the right hand side to donate via Paypal [or click here](#). To find out more, [click here](#). Thanks!

ME/CFS and Fibromyalgia Studies

Several, but not all, studies have found evidence of acetylcarnitine deficiency in ME/CFS. Four studies reported reduced plasma l-carnitine (free carnitine), total carnitine and/or acetylcarnitine levels in patients with ME/CFS. For instance, a small study found reduced **acetylcarnitine** in the brain in ME/CFS and a Chinese **metabolomic study** found that exercise decreased levels of L-carnitine in ME/CFS.

Several metabolomic studies suggest that **disturbances in fatty acid metabolism** may be present in ME/CFS. One found evidence of altered plasma levels of **carnitine and other metabolites**.

Some other studies, however, have failed to find reductions in either L-carnitine or acetylcarnitine.

The Australian Study

The premium ME/CFS carnitine study took place in Australia in 2010. Because carnitine exists in various forms in the body, the researchers speculated that assessing total carnitine levels might be obscuring deficiencies in individual carnitines. Their mass spectrometry study, "**Long-chain acylcarnitine deficiency in patients with chronic fatigue syndrome. Potential involvement of altered carnitine palmitoyltransferase-I activity**", looked at **twenty carnitines**.

The study found no difference in total carnitine levels but significant reductions in 8 individual carnitines. The authors particularly pointed to reductions in two carnitines: oleyl-l-carnitine (C18:1) and linoleyl-l-carnitine (C18:2), which were highly correlated with fatigue levels in ME/CFS.

They proposed that a reduction in the enzyme (CPT-1) responsible for the production of acetylcarnitine was likely responsible for the declines.

Piggybacking on a Maes study, the authors speculated that the ratio of **free** fatty acid to acylcarnitine (for certain acyl groups) was probably **2- to 3-times higher** in people with ME/CFS. Those "free" fatty acids aren't doing much good if they're not being burned up as fuel.

The authors proposed supplementing omega-3 fatty acids in combination with l-carnitine in order to boost the activity of the key enzyme (CPT-I) in this process. That was an interesting suggestion given that **low omega-3** levels have been found several times in ME/CFS, including one study in which over **90% of ME/CFS patients** were found to have low levels.

Treatment Trials

We're missing the large placebo-controlled, double-blinded studies that would give us results we could count on, but a couple of studies do suggest that acetylcarnitine supplementation could be helpful.

Two grams/day acetyl-l-carnitine improved mental fatigue and concentration in an open label ME/CFS study. **L-carnitine** improved most of the clinical parameters assessed in a 1997 ME/CFS study. One interesting study found ME/CFS patients who responded to azithromycin favorably tended to have **low levels of acetylcarnitine**. (Those who did not respond well to azithromycin did not.)

Fibromyalgia and Chronic Pain

A metareview of 18 metabolomics studies suggested that altered **acetylcarnitine metabolites** may play a role in chronic pain

A 102-person, **double-blinded**, 2007 Italian fibromyalgia study found that **2 capsules/day of 500 mg of acetyl-L-carnitine (LAC)** plus one intramuscular (i.m.) injection of 500 mg LAC for the first 2 weeks, plus 3 500 mg capsules daily for the next 8 weeks resulted in significant improvements in visual analogue pain scores for **both the treated and the placebo** group. (Placebo does work!) Only the acetyl-L-carnitine group, though, showed significant improvements in functional (SF-36) scores.

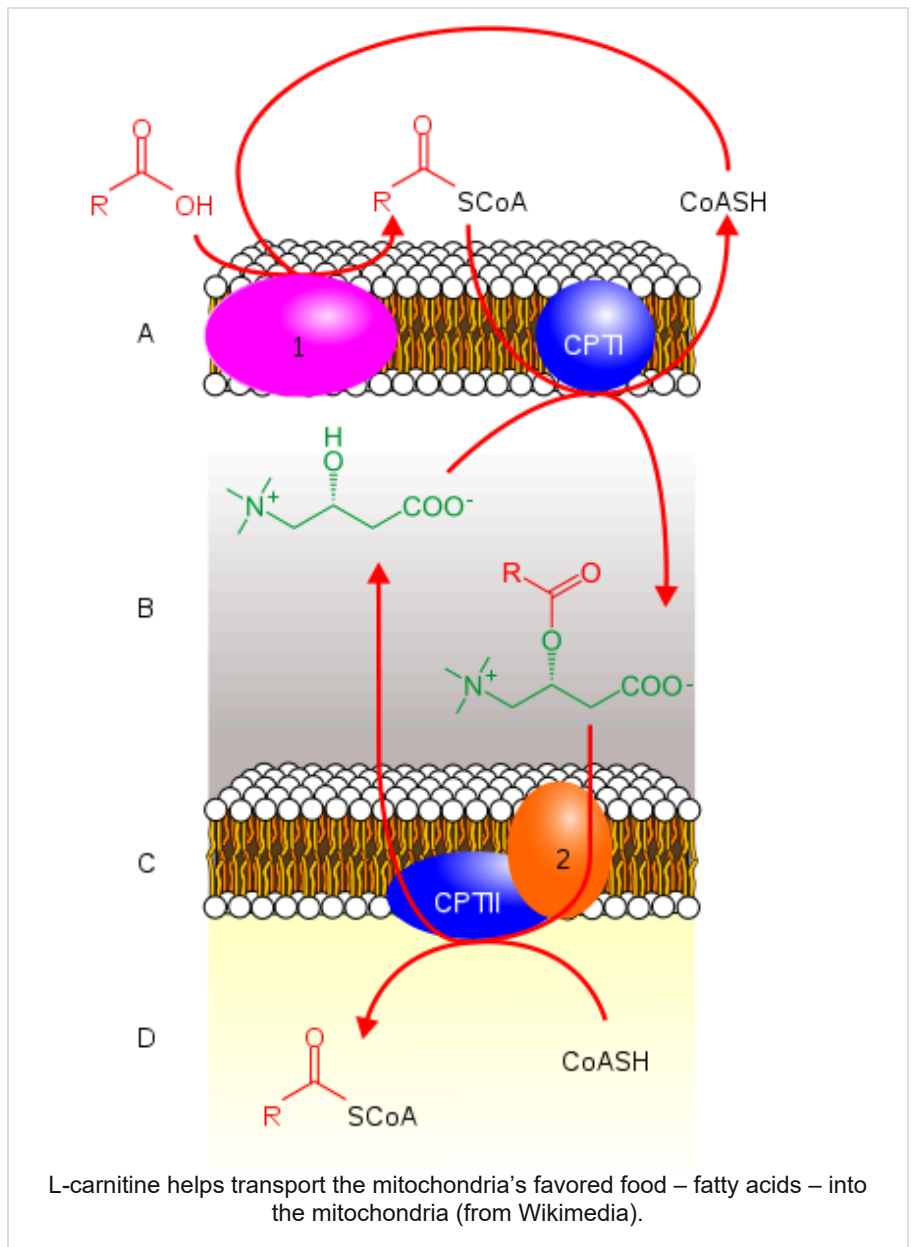
A 2015 randomized, controlled trial which compared duloxetine to **1500 mg/day acetyl-L-carnitine** (500 mg 3x's/day) for 12 weeks found that both treatments resulted in reduced pain, reduced depressive symptoms and improved quality of life.

Other Studies

An interesting **2008 trial** provided acetylcarnitine to almost 100 fatigued people over the age of 70 who met at least six of the minor Fukuda criteria for ME/CFS. Significant reductions in mental and physical fatigue were found. Plus, muscle pain and fatigue after exercise were reduced, and sleep was improved.

Acetylcarnitine supplementation reduced both mental and physical fatigue, and improved health-related quality of life in people undergoing treatment for hepatitis C (the treatment for hepatitis C produces symptoms that are similar to ME/CFS.)

A **large cancer study** did not find, however, that 2g of L-carnitine a day improved fatigue in cancer



The Gist

- L-carnitine and acetylcarnitine are two forms of carnitine that play vital roles in the energy production process.
- By enhancing the transport of the mitochondria's main source of energy – fatty acids – L-carnitine is the big energy booster and is (with L-carnitine-tartrate) the form of carnitine often used to boost

patients and a meta-review did not support the use of carnitine for **fatigue in cancer**.

Doctors' Reports

Sarah Myhill reports that her patients are almost always low in acetylcarnitine and regularly prescribes 2 grams of L-carnitine/day. **Dr. Teitelbaum** recommends 1-2000 mgs acetylcarnitine a day for 3-4 months and then dropping down to 500-1000 mgs/day. He reports that taking more than that may be less effective.

Side Effects

L-carnitine and acetylcarnitine are mostly described as side-effect free. At high doses, though, they may cause insomnia and gastrointestinal irritation.

One possible issue of concern people with ME/CFS/FM is the possibility that carnitine may **inhibit thyroid production**. High doses of carnitine (2-4 grams/day), in fact, have been used to reduce the **high thyroid production** found in hyperthyroidism. **One website** recommended avoiding any form of carnitine if you are on levothyroxine.

Other believe the issue is be more complex than that. Because **thyroid plays an important role in L-carnitine's** ability to transfer fatty acids into the mitochondria, low thyroid levels can negatively impact carnitine effectiveness and energy levels. Some sites actually recommend carnitine for people with low thyroid (hypothyroid), and a 2016 placebo-controlled trial found **L-carnitine improved physical** and mental fatigue in hypothyroid patients. Another website actually lists L-carnitine as an **essential supplement** for hypothyroidism. Neither Teitelbaum nor Myhill mentioned thyroid as a possible issue at the doses they recommend.

Because **L-carnitine's is metabolized to TMA-N-oxide** (TMAO) – a marker that's been associated many times with an **increased risk of cardiovascular disease** – concerns have been raised about it's effects on atherosclerosis and kidney disease.

This, too, is a complex issue as L-carnitine's ability to enhance fatty-acid metabolism and reduce

athletic performance. Athletic studies have generally found that L-carnitine can improve performance and may be able to reduce lactate levels.

- Acetylcarnitine, on the other hand, is more often used to improve cognition, alertness, mental fatigue and mood. It's being assessed in a surprisingly wide variety of neurological and mood disorders, and has been touted as a mostly side-effect free antidepressant.
- Some chronic fatigue syndrome and fibromyalgia studies have found reduced carnitine levels while others have not. The most sophisticated L-carnitine study found normal levels of total carnitine but reduced levels of individual carnitines, which correlated well with increased fatigue levels. Dr. Myhill reports that she invariably finds low carnitine levels in her ME/CFS patients.
- The L-carnitine/acetylcarnitine clinical trials in ME/CFS/FM are mostly rather primitive but have generally produced good results.
- Both Dr. Myhill and Dr. Teitelbaum suggest using 1-2 grams/day broken up into several doses.
- High doses (2-4 grams/day) may suppress thyroid functioning. Since low thyroid functioning also impairs carnitine functioning, some practitioners use

oxidative stress and inflammation has also lead it to be used **to support heart health**. While **twenty-four** weeks of L-carnitine supplementation did dramatically raise TMAO levels, it did not affect any of the markers (C-reactive protein, interleukin-6, tumour necrosis factor- α , L-selectin, P-selectin, vascular cell adhesion molecule-1, intercellular adhesion molecule-1 or lipid profile markers) **associated with atherosclerosis**. Other studies found that as L-carnitine supplementation raised TMAO levels it also decreased markers of **blood vessel injury** and oxidative stress, and **improved lipid profiles**, and did not increase signs of **vascular inflammation**. A **recent review** (funded by an L-carnitine manufacturer) proposed that TMAO is the result of an already present injury and is not causative.

Still many studies have linked high TMAO levels to cardiovascular issues. Like so many issues in medicine, the TMAO issue is not as clear as one would want.

If you decide to try L-carnitine, the advice to go low and go slow obviously applies. Consulting with your doctor is clearly a good idea.

Possible Synergies

Proposed synergies with other supplements include omega-3 fatty acids, choline and alpha-lipoic acid. **Alpha-lipoic acid** (ALA) is an antioxidant and neuroprotector. Animal studies suggest that acetyl-L-carnitine and ALA might work synergistically to improve cognition and **mood** but clinical trials have **not tested this idea** yet.

Dr. Teitelbaum reports that “taking 500 to 1,000 milligrams of L-lysine, which is cheaper, can decrease the amount of acetyl-L-carnitine you need to take by helping your body to make its own carnitine”. Vitamin C (200+ mgs/day) plus B-complex vitamins should also be taken.

Conclusion

L-carnitine and acetylcarnitine present interesting possibilities. Both play key roles in energy production and/or fatigue and both have been studied in ME/CFS and fibromyalgia. The role L-carnitine and acetylcarnitine deficiencies play in either disease, however, is not clear as some studies have found low levels while others have not.

carnitine in hypothyroid patients to improve energy levels. One study found that lower doses of carnitine improved the fatigue of their hypothyroid patients.

- The fact that L-carnitine is metabolized to TMAO – a factor associated with cardiovascular disease – raises other concerns. This is another complex issue as it's not clear that TMAO is causing cardiovascular diseases and studies suggest that L-carnitine can improve cardiovascular fitness and does not promote factors known to cause atherosclerosis.
- Supplementing carnitine with omega-3 fatty acids, choline, alpha lipoic acid, Vitamin C and B vitamins may be helpful.
- While studies suggest that something has gone wrong with the mitochondria in these diseases, we don't know exactly – making it impossible to devise a targeted treatment plan. Still, both L-carnitine and acetylcholine, probably in conjunction with other mitochondrial enhancers, present an intriguing possibility.

The Australian ME/CFS study was particularly intriguing as it found normal total carnitine levels but reduced levels of specific carnitines which appeared to impact fatigue levels. While most of the clinical trials have been rudimentary, the results, in general, have been favorable.

While both may be able to help with fatigue, L-carnitine has a leg up regarding energy production, while acetylcarnitine is being used more to improve cognition, mental clarity, improve mood and as a neuroprotector. Acetylcarnitine, in particular, is being studied in many diseases.

Two ME/CFS doctors recommended from 1-2000 mgs in divided doses a day. While one study found that using L-carnitine in hypothyroid patients improved their fatigue, several websites warn that using carnitine in high doses (2-4 grams/day) may be able to reduce thyroid production. Because L-carnitine is metabolized to TMAO – a marker associated with cardiovascular disease – concerns have been raised about that. Several studies, on the other hand, have found L-carnitine not to affect factors associated with atherosclerosis and to reduce markers of oxidative stress and blood vessel injury.

More study is clearly needed. Plenty of studies suggest that something has happened to the mitochondria, but exactly what we don't know. That means we're shooting blind to some extent trying to use mitochondrial enhancers to affect the complex mitochondrial energy production.

Still, it's intriguing to think what each might do as a part of a mitochondrial enhancing package. On that note, using these supplements in conjunction with omega-3 fatty acids, choline, lysine, Vitamin C and B, and/or alpha lipoic acid (ALA) may be helpful.

The Mitochondrial Enhancers for Chronic Fatigue Syndrome (ME/CFS), Fibromyalgia and long COVID Series

- **Pt I: D-Ribose, CoQ10 and PQQ**
- **Pt II: L-carnitine and Acetylcarnitine**
- **Pt. III: Magnesium**
- **Pt IV: N-acetyl cysteine (NAC)**
- **Pt V: Oxaloacetate**
- **Pt. VI: Niacin, Niacinamide and Nicotinic Riboside**

