Clinical Trial Update: C15:0 & Improved Mood

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Welcome to Issue 140 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and C15:0 research news that our team of doctors, scientists, and experts are most excited about—without having to go search for it.

Eric and Steph
Co-Founders, Doctors, Nerds

What Dr. Stephanie Venn-Watson, our co-founder and author of *The Longevity Nutrient* and over 80 peer-reviewed scientific publications, is reading.

HEALTHY AGING

How C15:0 Addresses the Metabolism-Mood Link

A new study from a randomized and controlled clinical trial is helping to validate C15:0's role in supporting not just our metabolism and whole body health, but our mood, too. Let's dive in.

Sounds interesting. How was this clinical trial done?

Last year, Chooi et al. published the outcomes of a 12-week double-blinded, randomized clinical trial involving the following three groups, all consisting of middle-aged women with a higher BMI and suboptimal metabolic and liver function:

- **Control Group (CG):** This group adhered to a caloric-restricted diet (1,000-1,500 kcal per day).
- **Mediterranean Diet Group (MD):** This group adhered to a caloric-restricted diet (1,000-1,500 kcal per day), as well as a Mediterranean-aligned diet.
- **Mediterranean Diet + C15:0 Supplementation Group (MD + C15:0):** This group adhered to a caloric-restricted diet (1,000-1,500 kcal per day), a Mediterranean-aligned diet, and also had daily pure C15:0 supplementation.

In this study, as anticipated, all three groups experienced weight loss and improved liver function. It also showed the following:

- ☑ The MD + C15:0 group had the most improved trends related to body weight and liver fat reductions compared to the other two groups.
- ☑ The MD + C15:0 group had significantly lower LDL cholesterol and improved growth of a healthy gut microbe, *Bifidobacterium adolescentis*, compared to the other two groups.

So, where does mood come into this study?

It has been well documented that when our metabolism is dysfunctional, so is our mood. This has been referred to by Mansur et al. as a "metabolic-mood syndrome". As described in detail in Dr. Steph's book, *The Longevity Nutrient* (check out Chapter 10), common factors that affect both our metabolism and mood include:

- Raised oxidative stress
- Low-lying chronic inflammation
- Insulin resistance
- Aging-related changes in cellular signaling pathways

Knowing that, let's get back to the clinical trial. In this same clinical trial published by Chooi et al., Salamana-Sanabria et al. analyzed data specific to participants' mood, including scores from the Beck's Depression Inventory (BDI-II) and State-Trait Anxiety Inventory (STAI) assessments. These measurements were taken at weeks 0, 4, 8, and 12 to see if mood changes occurred over time among each of the three study groups described above (CG, MD, and MD+C15:0).

Got it. What did they find?

This study had two key findings:

1. Encouragingly, all three groups experienced not only lower body weight and improved liver function, they also had improved mood. This key finding supports that, as previously documented in the literature by Loh et al. (among others), achieving healthier body weight can improve our mood.
2. Specific to the STAI scores, the MD+C15:0 group had the most significant improvements in mood, especially as it related to lower anxiety.

In their discussion, Salamana-Sanabria et al. conclude the following: "This study indicates that an Asian-adapted MD [Mediterranean Diet], particularly when supplemented with C15:0, is associated with significant reductions in anxiety and depression symptoms."

These findings, while having limitations, are consistent with what we're learning about how C15:0 positively impacts both metabolism and mood.

Building Evidence of C15:0 To Support Our Mood

Looking specifically at cognitive and mood health, the evidence of C15:0's benefits are building:

- Cell-based studies have shown that pure C15:0 improves insulin sensitivity, lowers oxidative stress, and lowers 18+ proinflammatory cytokines, all of which are expected to support both our metabolic health and mood.
- C15:0 inhibits both MAO-B and FAAH in a dose-response fashion. Translation? The higher the C15:0 levels, the healthier, better supported our dopamine and endocannabinoid levels, which support not only a healthy mood, but our memory and sleep, too.
- When C15:0's cell-based phenotypic profile was compared to over 4,500 different compounds, its activities mimicked well known mood-supporting molecules.
- Our bodies use C15:0 to make a metabolite, called pentadecanoylcarnitine (aka PDC), which is the second-ever discovered full-acting endocannabinoid, which can support mood, sleep, and joint comfort.
- Similar to Salamana-Sanabria et al.'s study, Brydges et al. showed that people with higher C15:0 levels have happier moods.

All encouraging science, we'd say. Have a wonderful good-mood week, everyone!

Dive deeper into the science

READ THESE STUDIES

- Salamanca-Sanabria et al. Potential effects of Asian-adapted Mediterranean diet in depression and anxiety among women: a secondary analysis.
- Chooi et al. Effect of Mediterranean diet and C15:0: the TANGO randomized controlled clinical trial.
- Mansur et al. Is there a "metabolic-mood syndrome"? A review of the relationship between obesity and mood.
- Loh et al. Improvement in mood symptoms after post-bariatric surgery among people with obesity: a systemic review and meta-analysis.
- Fu et al. Pentadecanoic acid promotes basal and insulin-stimulated glucose uptake in C2C12 myotubes.
- Aabis et al. Pentadecanoic acid modulates oxidative stress, inflammation, and ferroptosis pathways.
- Venn-Watson et al. Pentadecanoic Acid (C15:0), an Essential Fatty Acid, Shares Clinically Relevant Cell-Based Activities with Leading Longevity-Enhancing Compounds.
- Venn-Watson et al. Novel cognitive health-supporting roles of pentadecanoic acid (C15:0).
- Venn-Watson et al. Broader and safer clinically-relevant activities of pentadecanoic acid compared to omega-3: Evaluation of an emerging essential fatty acid across twelve primary human cell-based disease systems.
- Venn-Watson et al. Pentadecanoylcarnitine is a newly discovered endocannabinoid with pleiotropic activities relevant to supporting physical and mental health.
- Brydges, C.R. et al. Metabolomic and inflammatory signatures of symptoms dimensions in major depression.
- Nerd out on all the C15:0 science at DiscoverC15.com