

# 12

**Surprising Reasons**

**Ketones Deserve**

**Diet Consideration**

**in**

**Mild Cognitive Impairment**

**By Mary T. Newport, MD**

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## **1. THE BRAIN NEEDS FUEL TO MAKE ENERGY**

The brain is an incredibly complex and active organ that is involved in our every thought and move. Its weight is only 2% to 3% of our total body weight but it uses 20% to 25% of the calories we consume. The brain needs fuel to make an energy molecule called ATP (adenosine monophosphate), which virtually every cell in our brains and body needs to carry out its functions, such as communication between brain cells and flexing a muscle.<sup>1</sup>

## **2. THERE IS A “BRAIN-ENERGY GAP” IN NORMAL AGING**

Studies using PET scans in healthy young and older adults has identified in the older brain a gap of about five percent between how much energy the brain needs and how much it receives. The researchers who discovered this, Stephen Cunnane, PhD, and associates at Sherbrooke University in Canada, call this the “brain-energy gap.”<sup>1</sup> This gap may explain the “senior moments” and slowing down of thought processes that many people experience with aging.

### **3. THE “BRAIN-ENERGY GAP” IS LARGER IN PEOPLE WITH MCI**

The brain-energy gap widens to 10% or more in some people who have mild cognitive impairment (MCI) and 20% or more in those with Alzheimer’s disease. There are many different causes of MCI but people with MCI who have abnormal glucose uptake in areas of the brain are more likely to develop dementia eventually.<sup>1</sup> An FDG-PET (a special brain-imaging scan) to measure glucose uptake in the organ can be a useful tool to determine whether MCI is likely to progress to Alzheimer’s or another type of dementia, especially when combined with blood and spinal fluid biomarkers.<sup>2</sup>

### **4. THE MCI-DIABETES-DEMENTIA CONNECTION**

Alzheimer’s disease is sometimes called diabetes of the brain, or diabetes type 3, because there are similarities to diabetes type 2.<sup>3</sup> Insulin is required to allow glucose to enter the brain cells (as well as nearly all other cells in the body). In both Alzheimer’s and diabetes type 2, the affected cells do not respond normally to insulin, a condition called insulin-resistance. This also occurs in some people with MCI and various types of dementia.

Individuals with prediabetes and diabetes have a much higher risk of developing dementia and pass through a stage at some point that is comparable to

MCI. People with diabetes or prediabetes who develop MCI are much more likely to progress to dementia and tend to progress more rapidly than those without the two conditions.<sup>4</sup>

Chronically high blood sugar levels can result in inflammation throughout the body. Inflammation in the brain is common in people with MCI and is always present in the brains of subjects with Alzheimer's disease as well as in many other neurological diseases. Studies show that reducing sugar and increasing healthy fats in the diet improves blood markers of insulin-resistance in diabetics<sup>5</sup> and increases memory testing scores in studies of people with MCI.

## **5. KETONES ARE AN ALTERNATIVE FUEL FOR THE BRAIN**

The typical diet these days is relatively high in carbohydrates, and glucose, perhaps the best known one, is the predominant fuel for the brain and other organs. The world experiences periods of feast and famine. In times when food is plentiful, humans store fat to use as fuel when food is scarce. In the late 1960s, a group headed by Cahill, Owen, and colleagues studied starvation and reported that, when glucose stored in the body is used up after 36 to 48 hours, humans begin to break down fat into smaller fatty acids to use as fuel. Were it not for our fat stores, during starvation muscle would break down rapidly to convert to needed glucose. Fatty

acids can be used by our heart, muscles, and other organs but do not cross well into the brain, so it needs another source of fuel. Some of those fatty acids are converted in the liver to ketones, which are small molecules that easily cross into the brain. Brain cells can immediately switch from using glucose to ketones. During prolonged starvation, up to two-thirds of the fuel needed by the brain is provided by ketones.<sup>6</sup>

## **6. THE PUSH AND PULL OF BRAIN FUELS**

Glucose, for use as fuel, is pulled into the brain based on how active the organ is at a given time and how much energy it needs to operate. On the other hand, when ketone levels are increased in the bloodstream, ketones are pushed into the brain. Higher blood levels of ketones push larger amounts of ketones into the brain. Cunnane calls this the “push and pull of brain fuels.”<sup>7</sup> When ketones and glucose are both available to brain cells, ketones are the preferred fuel.

## **7. KETONES ARE VITAL TO THE NEWBORN AND ADULT BRAIN**

The newborn who is strictly breastfed goes into “ketosis” beginning at several hours of age. The human newborn is fat compared to the offspring of other mammals and fat provides fatty acids and ketones to help tide the baby over until the mother’s milk comes in. Ketones provide about three-quarters of the fuel to the

large newborn brain. In the growing infant, ketones also serve as building blocks for the important lipids that make up about 60% of the brain.<sup>8</sup>

Mother's milk is high in fat (about 45-50% of total calories)<sup>9</sup> and some of those fats are medium-chain triglycerides (MCTs) that are converted in the liver to ketones.<sup>10</sup> MCTs are found in the milk fat of other mammals, but the richest natural sources are coconut oil, followed closely by palm kernel oil. Everyday vegetable oils, like soy, corn, and olive oils, do not contain MCTs.<sup>9</sup> Infant formula manufacturers strive to mimic human breast milk, and, for this reason, coconut oil and/or palm kernel oil have been added to most infant formulas since the 1980s. MCT oil is also added to premature infant formulas.

In adults of all ages who eat a typical high-carbohydrate diet, ketones supply about 5% of the fuel to the brain.<sup>1</sup> This percent increases for people who eat a high-fat, low-carbohydrate ketogenic diet.

Cunnane, Castellano, and colleagues have learned through PET scan studies that people with MCI and with Alzheimer's disease do not take up glucose in certain areas of the brain but do take up ketones in those places. This profound discovery supports the idea that ketones could be used to bypass the problem of insulin-resistance in the brain and provide symptomatic relief for people with MCI, Alzheimer's, and some other neurological conditions.<sup>11</sup>

## **8. KETONES CAN FILL IN THE “BRAIN-ENERGY GAP” IN MCI**

Since about 2004, many small- to medium-size clinical trials of MCT oil and studies of the ketogenic diet have shown positive results in people with MCI. For example, in a study by Fortier, Cunnane, and colleagues, ketone and glucose PET scans confirmed that MCT oil can fill in the brain-energy gap, and cognitive testing improved in people with MCI who were taking two tablespoons per day of MCT oil over a six-month period.<sup>12</sup> Craft, Neth, and colleagues, of Wake Forest University in North Carolina, reported similar results in a pilot study of people with Alzheimer’s who were eating a Mediterranean-style ketogenic diet.<sup>13</sup> Based on these and other studies, there is reason to believe that taking MCT oil or eating a ketogenic diet could also help prevent cognitive decline related to aging or delay the onset of dementia.

## **9. THE “KETOGENIC DIET” IS NOT JUST ONE DIET**

The label “ketogenic diet” actually embraces a spectrum of diets that can result in mild elevations of ketones that are considered “mild nutritional ketosis,” or levels five to 10 times higher to produce “deep ketosis.” Protein is kept at moderate levels since excessive protein can be converted to glucose. How much you reduce carbohydrates (sugary drinks, sweets, and starchy foods) and increase

fats will determine how high the levels of ketones will rise. The strictest form of the ketogenic diet resulting in the highest levels of blood ketones contains 85% to 90% of its calories as fat. It has been used for about 100 years to successfully treat (i.e., reduce seizures) many children and adults with epilepsy who do not respond to medications. These days, the strictest form of the diet is also under study for use in conjunction with standard treatments for cancer. This is feasible because most cancer cells love glucose but cannot use ketones; therefore, a ketogenic diet can potentially starve or shrink the cancer cells.<sup>14</sup>

Taking one or two tablespoons of MCT oil several times per day with your usual meals can help maintain mild nutritional ketosis. This is also true for a reasonable diet that contains 50 grams or less of carbohydrates per day, with more healthy fat to compensate for the difference in calories. Combining a low-carbohydrate diet and MCT oil makes staying in ketosis much easier.

You can simply reduce your carbohydrates and increase fats in your regular diet. However, changing to a Mediterranean-style diet has many additional health benefits. This type of diet typically includes daily consumption of vegetables, fruits, whole grains, and healthy fats, such as olive oil, nuts and seeds, weekly intake of fatty fish, poultry, beans and eggs, moderate portions of dairy products, and limited intake of red meat. Eating small portions of grains and eating low sugar fruits like berries will help lower the amount of carbohydrates in the diet. Other

types of diets are adaptable to the ketogenic diet, such as Paleo, vegetarian, and even vegan diets as long as there is careful research to ensure adequate amounts of the right types of proteins in the diet.

## **10. COCONUT OIL HAS SEVERAL SURPRISING PROPERTIES THAT COULD HELP WITH MCI AND ALZHEIMER'S**

MCT oil is usually extracted from coconut oil or palm kernel oil, the richest natural sources. Virgin coconut oil is widely available online and in grocery and health food stores. There are two small studies and many anecdotal reports of cognitive improvement while taking coconut oil, but more studies need to be done to strengthen the evidence.

While it takes more coconut oil than MCT oil to increase ketone levels, coconut oil is about half lauric acid, which is the main MCT in human milk and is known to provide protection from infection for the newborn. Lauric acid kills many types of common bacteria, viruses, and fungi, some of which have been implicated in studies as possible causes or contributors to Alzheimer's disease. Also, a study in Japan demonstrated that lauric acid potently and directly increases ketone levels in astrocytes in lab cultures. Astrocytes are brain cells that nourish nearby neurons. If this action can be confirmed in humans or lab animals, it could explain why some people improve with coconut oil.<sup>15</sup>

There is a misconception that coconut oil increases heart risk by increasing LDL cholesterol. This might be true for overly processed and hydrogenated coconut oil. However, virgin coconut oil tends to increase so-called “good” HDL cholesterol and improve the ratio of total to HDL cholesterol, which is a better indicator of cardiac risk.<sup>16</sup>

Like extra virgin olive oil, virgin coconut oil also contains anti-inflammatory polyphenols that could help reduce brain inflammation. While standard MCT contains minimal lauric acid, some newer MCT products, called “liquid coconut cooking” oils, contain close to one-third lauric acid.

## **11. OTHER KETOGENIC STRATEGIES COULD ALSO HELP MCI**

Exercise, such as walking at a moderate pace for 30 minutes, can increase blood ketone levels for up to 8 hours so long as a high-carbohydrate meal is not eaten before the exercise. This could partly explain the cognitive benefits of exercise.<sup>17</sup>

Fasting can also increase ketone levels. While there are many ways to fast, the overnight fast lasting 12 hours or longer is a simple way to accomplish this and can help you start your day in mild ketosis. After 10 to 14 hours of fasting, we

have used up the glucose stored in our liver and begin to break down fat and produce ketones. The longer you fast, the higher the ketone level becomes.<sup>17</sup>

Since early 2016, exogenous ketone supplements have become available to the public, mainly as ketone salts and ketone esters. These supplements provide the identical ketone, betahydroxybutyrate, that is made in the body from fat and from MCT oil. The ketone ester is currently marketed to athletes since the US Food and Drug Administration (FDA) recognizes these supplements as safe for athletic performance. People with neurological or other medical conditions, the elderly, and children should seek approval and monitoring by their medical provider, since these ketone tactics tend to lower blood sugar and increase levels of sodium and other electrolytes in the body. Doses recommended for athletes are much higher than doses that might be used to treat medical conditions. These supplements are undergoing clinical trials at present.

## **12. NUTRITIONAL KETOSIS IS NOT DIABETIC KETOACIDOSIS**

For many years, medical textbooks have taught that ketones are dangerous byproducts of diabetic ketoacidosis. However, we now know that ketones are a vital brain fuel and driver of other metabolic pathways. Diabetic ketoacidosis is an abnormal process that occurs in which a diabetic, usually type 1, has no insulin available and blood glucose levels are extremely high. The cells are not receiving

fuel and fat begins to break down rapidly, resulting in extremely high levels of ketones in the bloodstream. These levels are many times higher than those achieved with coconut oil, MCT oil, and ketogenic diets. There are some other conditions in which ketone levels can become very elevated, even on a standard diet, but these are rare.

## **SUMMARY**

Because one frequent feature of MCI is a deficiency of glucose, or an inability to use it, in parts of the brain, ketones may serve as an alternative brain fuel. Strategies to increase ketones, such as eating a reasonable ketogenic diet, MCT oil, and coconut oil, taking ketone supplements, exercising regularly, and fasting could fill in the brain-energy gap that occurs with aging and even more markedly with MCI.

## Steve Newport and Alzheimer's: The Aid of Ketones

By Mary T. Newport, MD

My husband, Steve Newport, was a physically active man who was an avid reader and worked as an accountant and manager for my medical practice. At age 51, he began to have problems with memory and organizing his time. These grew worse over time and, at age 54, he was diagnosed with early-onset Alzheimer's disease. This was a devastating blow to our family. By 2006, he could no longer use a computer or do any accounting work, and he stopped driving.

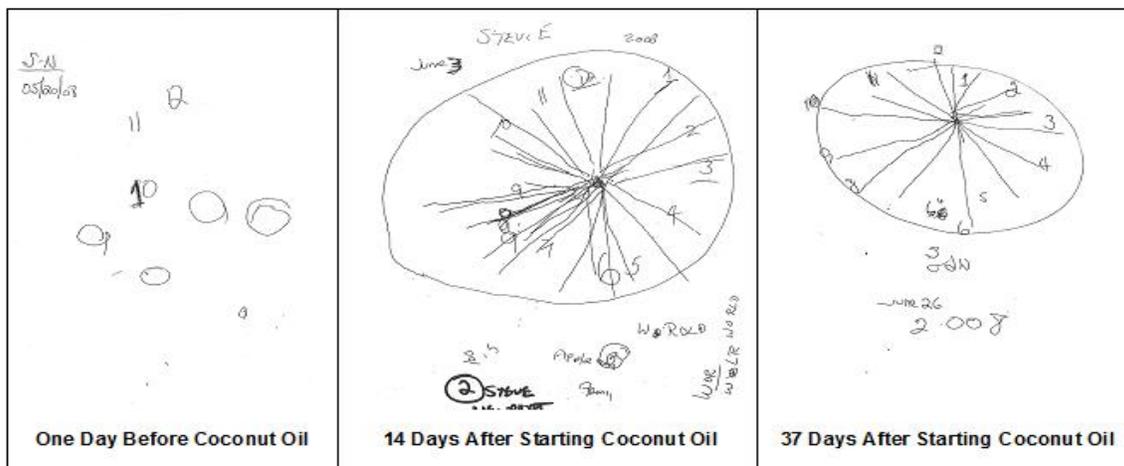
By May 2008, Steve was in a late stage of Alzheimer's and was scheduled to be screened for participation in two clinical trials of potential drugs. Then, I came across a press release about a medical food that was said to improve memory and cognition in nearly half of the people with Alzheimer's who received it in clinical trials.

I learned this food's key ingredient was medium-chain triglyceride (MCT) oil, which comes from coconut or palm kernel oil. I calculated how much coconut oil to give him to equal the medical food dose. He was screened for the first clinical trial before taking the oil and his memory score was too low for acceptance. The following day, he screened for the second clinical trial four hours after taking coconut oil and gained enough cognition points to qualify for the trial. His clock drawing test improved dramatically in just two weeks (see Figure). He continued to improve steadily in memory, ability to function, ability to read, ability to converse, and in physical symptoms over the next 10 months as the amount of coconut oil was increased and MCT oil was added to his diet.

In 2010, he was the first person to receive a ketone ester from the National Institutes of Health in a pilot study for Alzheimer's. He improved and stabilized for another 20 months. Altogether, he enjoyed nearly four extra years of good quality life before he had a major setback.

Steve lost his battle to Alzheimer's and Lewy body dementia on January 2, 2016. I can only imagine how much more time we might have had together if we had learned about the possibility of ketones aiding when he first began to have memory issues.

Figure 1. Steve's Clock-Drawing Cognition Test.



## REFERENCES

1. Cunnane SC, Trushina E, Morland C, et al. Brain energy rescue: an emerging therapeutic concept for neurodegenerative disorders of ageing [published online ahead of print July 24, 2020]. *Nat Rev Drug Discov*. doi: [10.1038/s41573-020-0072-x](https://doi.org/10.1038/s41573-020-0072-x).
2. Caminiti SP, Ballarini T, Sala A, et al. FDG-PET and CSF biomarker accuracy in prediction of conversion to different dementias in a large multicentre MCI cohort. *Neuroimage Clin*. 2018;18:167-177. doi: [10.1016/j.nicl.2018.01.019](https://doi.org/10.1016/j.nicl.2018.01.019).
3. de la Monte SM, Wands JR. Alzheimer's disease is type 3 diabetes – evidence reviewed. *J Diabetes Sci Technol*. 2008;2(6):1101-1113. doi: [10.1177/193229680800200619](https://doi.org/10.1177/193229680800200619).
4. Xu W, Caracciolo B, Wang H-X, et al. Accelerated progression from mild cognitive impairment to dementia in people with diabetes. *Diabetes*. 2010;59(11):2928-2935. doi: [10.2337/db10-0539](https://doi.org/10.2337/db10-0539).
5. Feinman RD, Pogozelski WK, Astrup A, et al. Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base. *Nutrition*. 2015;31(1):1-13. doi: [10.1016/j.nut.2014.06.011](https://doi.org/10.1016/j.nut.2014.06.011).
6. Owen OE, Morgan AP, Kemp HG, et al. Brain metabolism during fasting. *J Clin Invest*. 1967;46(10):1589-1595. doi: [10.1172/JCI105650](https://doi.org/10.1172/JCI105650).

7. Cunnane SC, Courschesne-Loyer A, Vandenberghe C, et al. Can ketones help rescue brain fuel supply in later life? Implications for cognitive health during aging and the treatment of Alzheimer's disease. *Front Mol Neurosci*. 2016;9:53. doi: [10.3389/fnmol.2016.00053](https://doi.org/10.3389/fnmol.2016.00053).
8. Cunnane SC, Menard CR, Likhodil SS, et al. Carbon recycling into de novo lipogenesis is a major pathway in neonatal metabolism of linoleate and  $\alpha$ -linolenate. *Prostaglandins Leuko Essent Fatty Acids*. 1999;60(5-6):387-392. doi: [10.1016/s0952-3278\(99\)80018-0](https://doi.org/10.1016/s0952-3278(99)80018-0).
9. USDA Food Database. USDA website. <https://fdc.nal.usda.gov>.
10. Bergen SS, Hashim SA, TB Van Itallie TB. Hyperketonemia induced in man by medium-chain triglyceride. *Diabetes*. 1966;15(10):723-725. doi: [10.2337/diab.15.10.723](https://doi.org/10.2337/diab.15.10.723).
11. Castellano C-A, Nugent S, Paquet N, et al. Lower brain  $^{18}\text{F}$ -fluorodeoxyglucose uptake but normal  $^{11}\text{C}$ -acetoacetate metabolism in mild Alzheimer's disease dementia. *J Alzheimers Dis*. 2015;43(4):1343-1353. doi: [10.3233/JAD-141074](https://doi.org/10.3233/JAD-141074).
12. Fortier M, Cunnane SC, et al. A ketogenic drink improves brain energy and some measures of cognition in MCI. *Alzheimers Dement*. 2019;15(5):625-634. doi: [10.1016/j.jalz.2018.12.017](https://doi.org/10.1016/j.jalz.2018.12.017).

13. Neth BJ, Mintz A, Whitlow C, et al. Modified ketogenic diet is associated with improved cerebrospinal fluid biomarker profile, cerebral perfusion, and cerebral ketone body uptake in older adults at risk for Alzheimer's disease: a pilot study. *Neurobiol Aging*. 2020;86:54-63.  
doi: [10.1016/j.neurobiolaging.2019.09.015](https://doi.org/10.1016/j.neurobiolaging.2019.09.015).
14. Newport MT, ed. *The Complete Book of Ketones: A Practical Guide for Ketogenic Diets and Ketone Supplements*. Nashville, TN: Turner Publishing Company; 2019.
15. Nonaka Y, et al. Lauric acid stimulates ketone body production in the KT-5 astrolyte cell line. *J Oleo Sci*. 2016;65(8):693-699.  
doi: [10.5650/jos.ess16069](https://doi.org/10.5650/jos.ess16069).
16. Chatterjee P, Fernando M, Fernando B, et al. Potential of coconut oil and medium chain triglycerides in the prevention and treatment of Alzheimer's disease. *Mech Ageing Dev*. 2020;186:111209.  
doi: [10.1016/j.mad.2020.111209](https://doi.org/10.1016/j.mad.2020.111209).
17. Mattson MP, Moehl K, Ghena N, et al. Intermittent metabolic switching, neuroplasticity and brain health. *Nat Rev Neurosci*. 2018;19(2):63-80.  
doi: [10.1038/nrn.2017.156](https://doi.org/10.1038/nrn.2017.156).

## About the Author

Dr. Mary Newport, the Chief Ketone Consultant at MCI911.com, is a world leader in spotlighting the positive influence dietary ketones can have on mild cognitive impairment and Alzheimer's disease.

She came to this expertise through an unusual path containing personal grief and discovery.

A board-certified pediatrician and neonatologist, she was founding medical director of two newborn intensive care units, and she practiced pediatrics in Florida for 30 years. Her husband, Steve, was manager of the practice.

In 2008, Steve began developing early -onset Alzheimer's disease and Lewy body disease. Finding no generally-accepted drugs or other remedies, Mary became aware of the possible helpful effects of ketones, which can provide energy "food" to the brain.

Through her personal research and experimentation with various foods and medium chain triglyceride oils, and by conferring with other scientists, Mary devised a ketone-heavy diet, including coconut oil, which produced striking demonstrable improvements in Steve's cognition. Sadly, because of other factors, Steve passed away in 2016.

Dr. Newport now carries on his legacy as an author and international speaker on ketones as an alternative fuel for the brain. Her latest book, of many, is [The Complete Book of Ketones: A Practical Guide to Ketogenic Diets and Ketone Supplements](#).

She also has appeared in numerous video programs, including TED talks. A typical one may be seen at

YouTube: <https://www.youtube.com/watch?v=Dvh3JhsrQ0w&t=187s>.